A prospective study of secondary degeneration following subcortical infarction using diffusion tensor imaging

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Abstract

Background: Secondary degeneration of the pyramidal tract distal to the primary lesion after a stroke has been detected by some studies using diffusion tensor imaging (DTI), but its potential clinical significance and the degeneration of the fiber tract proximal to the primary lesion have received little attention.

Methods: Twelve patients underwent DTI at 1st, 4th and 12th week following a subcortical infarct involving the posterior limb of the internal capsule and 12 age- and gender-matched controls underwent DTI one time. The DTI parameters including mean diffusivity (MD) and fractional anisotropy (FA) and the clinical scores before DTI examination, including National Institutes of Health Stroke Scale (NIHSS), Fugl-Meyer (FM) scale and Barthel index (BI) of the patients were assessed. The relations between the percent changes of DTI parameters and clinical scores were analysed.

Results: From 1st to 12th week after stroke onset, FA values decreased ($P < 0.01$, respectively) in the fibre tract at above and below the internal capsule, and the NIHSS decreased ($P < 0.01$) but FM scale and BI increased ($P < 0.01$, respectively) progressively. The percent reductions of FA value in the fibre tract above and below the internal capsule were correlated to the percent changes of NIHSS and FM scale negatively ($P < 0.05$, respectively).

Conclusions: Secondary degeneration on the fibre tract proximal and distal to a primary lesion can be detected by DTI obviously and quantitatively and deteriorates with the time course progressively, which may hamper the functional recovery after a subcortical cerebral infarct.

Key words: Secondary degeneration; Subcortical Infarction; Diffusion Tensor Imaging, Fractional anisotropy
INTRODUCTION
Animal experiments and post-mortem examinations have demonstrated that a focal cerebral infarct can cause secondary degeneration in fibre pathways remote from the primary lesion. Delayed disintegration of such a fibre tract is considered to be Wallerian degeneration (WD), defined as anterograde degeneration of a nerve tract distal to an injury. Conventional MRI can detect the ipsilateral cerebral peduncle atrophy during the chronic stage of a focal cortical infarct, but cannot reveal the delayed degeneration in the pyramidal tract on other regions obviously and quantitatively. Diffusion Tensor Imaging (DTI), which uses diffusion-sensitive gradients applied in at least 6 non-collinear directions, can determine the diffusivity of every voxel and fully depict tissue diffusion characteristics. DTI has been used to detect and quantify the secondary degeneration in fibre tract in vivo.

Thomalla G and his colleagues reported that secondary degeneration revealed by DTI occurs in the pyramidal tract distal to the primary lesion from the acute (5 days from onset) to the chronic stage (288 days) in two patients with ischemic stroke. In some cross-sectional studies, it is found that fractional anisotropy (FA value) is generally reduced along the pyramidal tract on the infarct side distal to the primary lesion. After middle cerebral artery territory infarction, lower FA value in the cerebral peduncle is associated with a greater neurological deficit acutely and with worse outcomes 3 months later. However, to date, no prospective, controlled, contrast-enhanced studies have monitored the secondary degeneration, and its potential clinical significance of the degeneration distal to the primary lesion has not been confirmed. In addition, only a case report reveals that a pontine infarct can cause retrograde degeneration in the fibre pathway proximal to the primary lesion. However, there is little research on the retrograde degeneration of the fibre tract after subcortical infarction, and its impact on patients' outcome is not well understood.

In this study, DTI was used to prospectively quantify and monitor changes in diffusivity in the fibre pathway both proximal and distal to a recent subcortical infarct in 12 patients. The relations between the percent changes of DTI parameters and clinical scores were analysed.

MATERIAL AND METHODS
Subjects
We selected 12 consecutive patients within 7 days after stroke onset who had unilateral subcortical cerebral infarct involving the posterior limb of the internal capsule. Patients were excluded if they had other signal abnormalities on T1- and T2-weighted images and fluid-attenuated inversion recovery (FLAIR) images of MR. No patients had a history of brain or spinal cord diseases. Following a predefined protocol, all patients had DTI in the first week (W1, 5 ± 2 days), at the end of the fourth week (W4, 28 ± 2 days) and at the end of the twelfth week (W12, 88 ± 2 days).

Patient demographic characteristics and vascular risk factors were collected. All patients had a detailed neurological examination 2 hours before MR examination, including an evaluation of neurological deficits using the National Institutes of Health Stroke Scale.
(NIHSS), motor deficits using the Fugl-Meyer (FM) scale, and a life independence assessment using the Barthel index (BI). The volume of the initial lesion was estimated on MR FLAIR images at the end of the third month (Volume = \( \pi \times \frac{6}{6} \times \text{length} \times \text{width} \times \text{the number of slice involved} \)). Twelve age- and gender-matched healthy volunteers had a DTI using the same MRI protocol.

The research protocol was approved by the local ethical committee for clinical research and all procedures involving the participant were conducted according to institutional guidelines in compliance with the regulations. Both oral and written informed consents were obtained from all participants.

**Magnetic resonance imaging**

MRI was performed using a 1.5 Tesla MRI system (Signa General Electric Medical Systems, USA) equipped with gradient hardware allowing up to 23 mT/m gradients. The baseline scan was in the antero-posterior plane, using a standard head coil. Prior to scanning, head movement was limited by vacuum fixation cushions. Axial T1-weighted FLAIR, fast spin-echo T2-weighted imaging (FSE T2); traditional FLAIR, and DTI were used. Consecutive slices were acquired in an identical location for all sequences, with a 5 mm slice thickness. Typical acquisition parameters were: T1- FLAIR (TR 2250 ms / TE 7.7 ms), FSE T2 (TR 3800 / TE120 ms); traditional FLAIR (TR 9000 / TE 120 / TI 2200 ms). For DTI, an echo-planar imaging (EPI) sequence was used (TR10000 / TE115 ms, NEX = 2, matrix 128 \times 128, field of view 24 \times 24 cm). Diffusion-weighted images were obtained with \( b = 1000 \text{ s/mm}^2 \) and diffusion-sensitive gradients were applied along 13 gradient directions. In addition, a reference image without diffusion weighting (\( b = 0 \text{ s/mm}^2 \)) was acquired. Acquisitions were repeated 20 times, and the results were averaged. The maximum strength of the diffusion gradients was 23 MT/m.

**Image post-processing**

In order to correct for distortions related to eddy currents associated with the large diffusion-sensitive gradients, we applied an unwrapping algorithm to the diffusion-weighted data set before the tensor estimation was performed. With this correction, the diffusion tensor parameters were calculated on a pixel-by-pixel basis. With the software of Fuctool 2.3.1 (Signa General Electric Medical Systems, USA), regions of interest (ROIs) were manually defined as an ellipse with an area of 36 mm\(^2\), first on T2-weighted images, then on the corresponding DTI images. ROIs were symmetrically placed on axial slices in the left and right centrum semiovale (at the mid-point of the anterior two-thirds part on the second slice over of the bottom of lateral ventricle); in the coronal radiata (at the mid-point of the anterior two-thirds part on the second slice below of the bottom of lateral ventricle); the middle part of posterior limb of internal capsule along its longitudinal direction; the anterior part of the cerebral peduncle; and the pons and medulla respectively. All ROI positions were determined according to the scanning baseline and the anatomic structure. The ROIs in the fiber tract both above and below the internal capsule had no abnormal signal on T2-weighted and FLAIR images, so all of them were not involved with the ischemic damage. The mean diffusivity (derived from the Trace of the diffusion tensor (MD =Trace [D] / 3) and measured on ADC images) and the fractional anisotropy index (FA value) (measured on the anisotropy images) were.
analyzed.

**Statistical analysis**
Data were presented as median and quartile range. A Mann-Whitney test was firstly used for the comparison between the left and right sides in the medians of MD and FA values of any of the regions studied in controls. As the infarction appeared in either left or right side in patients, we used the medians of MD and FA value from both sides of the control subjects to compare with patients’ DTI quantitative data either from infarct side or contralateral side to avoid any possible bias. A Mann-Whitney test was used for each comparison. To reveal the time-progressive effect, a liner regression for each patient was firstly established to describe the tendency of clinical scores and DTI quantitative data obtained at W1, W4 and W12. Then the medians of within-subject regression coefficient of all patients were tested by Wilcoxon’s signed ranks test for whether the population within-subject regression coefficient equal to zero or not. Finally, Spearman correlation analysis was used to assess the association between the absolute value of percent change [(W12 – W1) / W1] × 100% of FA values and of clinical scores, and the correlation between the within-subject regression coefficient of FA value and clinical scores. Values of P < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS 13.0 (Abacus Concepts Inc., Chicago, IL, USA).

**RESULTS**

**Subject characteristics**
Six patients had only one vascular risk factor, and one patient had no known risk factors (Table 1). In all patients, on T2 weighted and FLAIR images, the primary subcortical lesion involved the posterior limb of the internal capsule, and the volume of the initial lesion was obtained. All patients and controls were right handed.
Table 1. Patient demographics and clinical data

<table>
<thead>
<tr>
<th></th>
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<th>Infarct on FLAIR images</th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Side</td>
<td>Volume of lesion (mm³)</td>
</tr>
<tr>
<td>1</td>
<td>46</td>
<td>M</td>
<td>R</td>
<td>25500</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>M</td>
<td>R</td>
<td>4500</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>F</td>
<td>L</td>
<td>4000</td>
</tr>
<tr>
<td>4</td>
<td>41</td>
<td>F</td>
<td>R</td>
<td>17000</td>
</tr>
<tr>
<td>5</td>
<td>46</td>
<td>M</td>
<td>L</td>
<td>3300</td>
</tr>
<tr>
<td>6</td>
<td>52</td>
<td>M</td>
<td>R</td>
<td>10500</td>
</tr>
<tr>
<td>7</td>
<td>52</td>
<td>M</td>
<td>R</td>
<td>11600</td>
</tr>
<tr>
<td>8</td>
<td>27</td>
<td>F</td>
<td>L</td>
<td>1900</td>
</tr>
<tr>
<td>9</td>
<td>45</td>
<td>M</td>
<td>L</td>
<td>21300</td>
</tr>
<tr>
<td>10</td>
<td>42</td>
<td>F</td>
<td>R</td>
<td>18300</td>
</tr>
<tr>
<td>11</td>
<td>68</td>
<td>M</td>
<td>L</td>
<td>14000</td>
</tr>
<tr>
<td>12</td>
<td>57</td>
<td>F</td>
<td>R</td>
<td>5300</td>
</tr>
</tbody>
</table>

The age of the patients and controls did not differ: patients, 48 ± 8.88 years (range: 27 – 68 years) vs. controls, 48 ± 8.89 years (range: 26 – 67 years). F, female; M, male; L, left; R, right; FLAIR, fluid attenuated inversion recovery. (Controls were recruited specifically to match age and gender of patients.)

DTI data

Twelve patients and controls completed all MRI examinations. Within the first week of onset, T2-weighted and FLAIR images showed hyperintensity consistent with cerebral infarction in every patients, but there was no hyperintensity elsewhere (Fig. 1 A-G)). On DTI images the infarct region in each patient was identified as an area of reduced FA and increased MD signal. On axial FA images (Fig. 2 A-F), the reduced signal was obvious in the primary lesion, as well as in the fibre tract proximal to the primary lesion on the infarct side (at the level of the corona radiata and centrum semiovale) and distal to the primary lesion (at the level of the cerebral peduncle, pons, and medulla on the infarct side). On coronal images(Fig. 2 G), reduced FA signal was observed in the infarct region, and spreading in opposite directions from the infarct, up along the proximal fibre pathway to the corona radiata and centrum semiovale, and down along the distal fibre tract to the cerebral peduncle, pons, and medulla. In controls and on matched regions
located on the contralateral side in patients, no obvious changes were found. On ADC images, no abnormal signal was observed outside of the primary lesion.

Compared to matched regions in controls, FA values in patients were significantly lower in the infarct and in the ipsilateral proximal and distal fibre pathway (Table 3). Wilcoxon signed-ranks test showed that the population medians of the within-subject regression coefficients of FA value in internal capsule [-0.011 (-0.013, -0.010), \( P < 0.001 \)], in the fibre tract above [-0.004 (-0.004, -0.004), \( P < 0.001 \)] and below [-0.004 (-0.004, -0.003), \( P < 0.001 \)] internal capsule were not equal to zero, which indicated the FA value from these regions decreased progressively with the time course.
Table 2 FA value (dimensionless units) in the infarct region and at different levels of fibre tract in patients and controls [Median, (QL-QU)].

<table>
<thead>
<tr>
<th>Region</th>
<th>FA value of patient group (n=12)</th>
<th>FA value of Control group (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
<td>W4</td>
</tr>
<tr>
<td></td>
<td>Infarct side</td>
<td>Unaffected side</td>
</tr>
<tr>
<td>Centrum semiovale</td>
<td>0.33 (0.32, 0.34)</td>
<td>0.33 (0.32, 0.33)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.34 (0.33, 0.34)</td>
<td>0.33 (0.32, 0.34)</td>
</tr>
<tr>
<td>Corona radiata</td>
<td>0.39 (0.38, 0.40)</td>
<td>0.37 (0.36, 0.38)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.39 (0.38, 0.42)</td>
<td>0.41 (0.39, 0.41)</td>
</tr>
<tr>
<td>Infarct side</td>
<td>0.36 (0.35, 0.37)</td>
<td>0.35 (0.34, 0.36)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.38 (0.36, 0.39)</td>
<td>0.38 (0.36, 0.39)</td>
</tr>
<tr>
<td>Infarct side</td>
<td>0.44 (0.43, 0.45)</td>
<td>0.42 (0.41, 0.43)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.47 (0.47, 0.48)</td>
<td>0.47 (0.46, 0.48)</td>
</tr>
<tr>
<td>Infarct side</td>
<td>0.40 (0.39, 0.41)</td>
<td>0.38 (0.38, 0.39)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.42 (0.42, 0.43)</td>
<td>0.42 (0.41, 0.43)</td>
</tr>
<tr>
<td>Infarct side</td>
<td>0.39 (0.38, 0.39)</td>
<td>0.38 (0.37, 0.38)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.40 (0.39, 0.43)</td>
<td>0.40 (0.39, 0.41)</td>
</tr>
<tr>
<td>Infarct side</td>
<td>0.41 (0.41, 0.42)</td>
<td>0.39 (0.39, 0.40)</td>
</tr>
<tr>
<td>Unaffected side</td>
<td>0.43 (0.42, 0.44)</td>
<td>0.42 (0.42, 0.44)</td>
</tr>
</tbody>
</table>

* Significant result of Mann-Whitney test: compared with controls, *P* < 0.01. FA, Fractional anisotropy; W1, within the first week; W4: the end of the fourth week; W12, the end of the twelfth week; above the internal capsule (including corona radiata and centrum semiovale); blow the internal capsule (including cerebral peduncle, pons and medulla).
In patients, over the time period from W1 to W12, the FA value of the fibre tract above the internal capsule (derived from the mean value of the corona radiata and centrum semiovale) was reduced 14% [0.36 (0.35, 0.37), W1 vs. 0.31 (0.30, 0.33), W12; \( P < 0.01 \)]. Similarly, in patients from W1 to W12, the FA value of the fibre tract below the internal capsule (derived from the mean value of the cerebral peduncle, pons, and medulla) was reduced 10% [0.41 (0.41, 0.42), W1 vs. 0.37 (0.36, 0.39), W12; \( P < 0.01 \)]. The FA value of every region located on the contralateral fibre tract of patient was not significantly different from controls at any time point.

Compared to controls, MD in the infarct was decreased in W1 [0.86 (0.85, 0.87) \( \text{mm}^2/\text{s} \), patients vs. 1.04 (1.02, 1.05) \( \text{mm}^2/\text{s} \), control; \( P < 0.01 \)], but it was increased at W4 [1.24 (1.20, 1.26) \( \text{mm}^2/\text{s} \), patients vs. 1.04 (1.02, 1.05) \( \text{mm}^2/\text{s} \), controls; \( P < 0.01 \)] and at W12 [1.82 (1.72, 1.91) \( \text{mm}^2/\text{s} \), patients vs. 1.04 (1.02, 1.05) \( \text{mm}^2/\text{s} \), controls; \( P < 0.01 \)]. However, from W1 to W12, there was no significant change in MD in any region beyond of the infarct area, either on the infarct side or the contralateral side, compared to matched regions in controls.

**Clinical scores**

All patients had some degree of motor deficits. The FM scale ranged from 4 to 79 [21.00 (11.50, 61.50)] in the first examination; 11 patients had hemiplegia; and one had a minor upper limb motor deficit and Broca’s aphasia. Four patients had one or two limbs sensory disturbances. All patients received similar therapy for stroke, and each vascular risk factor was treated appropriately. By the end of the third month, all patients recovered somewhat, in which 8 patients returned to work, 3 were partially dependent, and 1 was completely dependent. Table 2 shows the medians of clinical scores at the 3 time points. The Wilcoxon signed ranks test showed that the population medians of the within-subject regression coefficients of the clinical scores were not equal to zero. That means the NIHSS decreased but the FM scale and the BI increased progressively with time course.

**Table 3. Clinical scores of patients at different time points and within-subject regression coefficient [Median, (QL-QU ]**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>W1</th>
<th>W4</th>
<th>W12</th>
<th>regression coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIHSS</td>
<td>12</td>
<td>11.00 (5.75, 14.75)</td>
<td>7.00 (2.25, 9.00)</td>
<td>2.50 (0.00, 6.50)</td>
<td>- 0.64 (- 0. 79, - 0.31)*</td>
</tr>
<tr>
<td>FM Scale</td>
<td>12</td>
<td>21.00 (11.50, 61.50)</td>
<td>54.00 (36.25, 88.50)</td>
<td>77.00 (53.25, 97.75)</td>
<td>3.66 (2.61, 4.34)*</td>
</tr>
<tr>
<td>BI</td>
<td>12</td>
<td>40.00 (25.00, 82.50)</td>
<td>57.50 (46.25, 100.00)</td>
<td>95.00 (61.25, 100.00)</td>
<td>3.09 (1.61, 4.08)*</td>
</tr>
</tbody>
</table>

*NIHSS, NIH Stroke Scale; FM scale, Fugl-Meyer scale and BI,Barthel Index.*

Wilcoxon’s signed rank test, \( P < 0.01 \)
Correlations between DTI parameter and clinical scores
The percent changes of FA values from both fibre tract above and below the internal capsule were negatively correlated to the percent changes of NIHSS and FM scale, but not significantly correlated to BI. There was no significant correlation between the percent of changes of FA values in the internal capsule and the clinical scores (Table 4). There was only significant correlation between the within subject regression coefficient of FA value from the fibre tract below the internal capsule and NIHSS (Table 5).

Table 4 Spearman correlation between the percent changes of FA and clinical scores (n = 12)

<table>
<thead>
<tr>
<th>The region of percent reduction of FA</th>
<th>Percent reduction of NIHSS rs (P)</th>
<th>Percent reduction of FM scale rs (P)</th>
<th>Percent reduction of BI rs (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above the internal capsule</td>
<td>-0.47 (0.04)</td>
<td>-0.56 (0.02)</td>
<td>-0.39 (0.09)</td>
</tr>
<tr>
<td>Internal capsule</td>
<td>-0.41 (0.08)</td>
<td>-0.44 (0.06)</td>
<td>-0.11 (0.27)</td>
</tr>
<tr>
<td>Below the internal capsule</td>
<td>-0.51 (0.03)</td>
<td>-0.68 (0.01)</td>
<td>-0.22 (0.19)</td>
</tr>
</tbody>
</table>

The percent changes of FA value: ((W12FA value – W1FA value) / W1FA value × 100%), the percent changes of clinical scores: ((W12scores – W1scores) / W1scores × 100%). The significance was highlighted. FA, Fractional anisotropy; NIHSS, National Institutes of Health Stroke Scale; FM scale, Fugl-Meyer scale; BI, Barthel index.

Table 5 Spearman correlation between the within-subject regression coefficient of FA value and clinical scores (n = 12)

<table>
<thead>
<tr>
<th>Region of FA value</th>
<th>NIHSS rs (P)</th>
<th>FM scale rs (P)</th>
<th>BI rs (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above the internal capsule</td>
<td>0.25 (0.44)</td>
<td>-0.38 (0.22)</td>
<td>-0.07 (0.82)</td>
</tr>
<tr>
<td>Internal capsule</td>
<td>-0.08 (0.81)</td>
<td>-0.126 (0.70)</td>
<td>-0.07 (0.82)</td>
</tr>
<tr>
<td>Below the internal capsule</td>
<td>0.86 (0.000)</td>
<td>-0.56 (0.06)</td>
<td>-0.38 (0.23)</td>
</tr>
</tbody>
</table>

FA, Fractional anisotropy; NIHSS, National Institutes of Health Stroke Scale; FM scale, Fugl-Meyer scale; BI, Barthel index. The significance was highlighted.

DISCUSSION
In the present study, all of twelve patients with or without primary lesions in basal ganglia or thalamus had infarct lesion in internal capsule. FA value decreased progressively from W1 to W12 in the internal capsule where primary infract lesion
involved and on the fibre tract above and below the internal capsule in infarct side where primary infarct lesion uninvolved, MD decreased at W1 and then increased from W4 to W12 in the internal capsule, but preserved unchanged from W1 to W12 on the fibre tract above and below the internal capsule. The different pattern of diffusion changes in the different part of the fibre tract indicates that the damage in the fibre tract above and below the internal capsule differs from primary ischemic infarct in internal capsule. The damage in the fibre tract above and below the internal capsule may result from the secondary degeneration, since the pattern of diffusion changes beyond the internal capsule is similar to the WD in the peripheral nerve in experimental animal models.  

Some cross-sectional studies have shown that at early or chronic stage, the FA value reduction with MD unchanged on the infarct side in the fibre tract distal to the infarct foci. In a small group of patients with an MCA territory ischemic stroke at 2 to 16 days after onset, the FA value reduction with MD unchanged at the cerebral peduncle on the infarct side was observed. Werring DJ and colleagues reported, in patients 2-6 months after a stroke, a 15% decrease of FA value but MD unchanged in the fibre tract distal to primary lesion. Another study found a 32% decrease in FA value with MD unchanged in the fibre tract distal to the cerebral infarction in patients more than one year after stroke. Only a longitudinal DTI study involving two patients with striatocapsular infarction showed that FA value of cerebral peduncle decreased from 16% to 25% over more than 9 months in one case, and from 17% to 48% over 3 months in another case, with a slight rise in MD. In this study, we prospectively observed the secondary degeneration in the fiber tract distal to the primary infarction in 12 stroke patients from W1 to W12 and in controls, and confirmed that the FA value decreased progressively with MD unchanged during the observing time period. Our data illustrate the course of secondary structural degradation more clearly, which defines WD over time in the fiber tract distal to primary lesions.

In the present study, we also found that FA value decreased progressively with MD unchanged from W1 to W12 in the fibre tract proximal to the primary infarct. Several studies have demonstrated retrograde degeneration in the corticospinal tract after damage, and such a mechanism of “dying back” might contribute to it. An increase in MD without a change in FA value after middle cerebral artery territory infarct was observed with DTI in the ipsilateral thalamus 1 month after stroke onset. Because the thalamus was remote from the primary lesion and the change of MD in thalamus was later than in infarct foci, it was regarded as retrograde degeneration of the thalamo-cortical neurons secondary to fibre damage. A case of pontine infarction with retrograde degeneration of the pyramidal tract has been detected by T2-weighted MRI and confirmed by postmortem. It is possible that the retrograde degeneration may also occur in the coronal radiata and centrum semiovale and may be detected by DTI. In the present study, the progressive reduction of FA value in the fibre tract above the initial infarction reflects the gradual degeneration of the fibre tract proximal to the primary lesion. There are at least two fiber types in the fiber tract above the internal capsule. One is from neurons in the motor cortex, descending from the subcortex to the spinal cord and formulating the pyramidal tract. The other is derived from the relay nuclei in the thalamus that deliver somatosensory messages through the corona radiata and the centrum semiovale to
sensory areas located in the frontoparietal cortex, known as the thalamic radiation. Therefore, in the fiber tract above the internal capsule, secondary degeneration in the pyramidal tract is retrograde, while in the thalamic radiation is anterograde.

The relations between the reduction of FA value in the fiber tract beyond the primary lesions and patients’ outcome are not well understood. A longitudinal study found that progressive reductions in FA value in pyramidal tract distal to the primary lesion were associated with persistent moderate-to-severe hemiparesis. Another study reported that patients with a larger degree of FA reduction at the cerebral peduncle distal to the initial infarct had a greater motor deficit in the early stage and a worse motor outcome three months later. In the present study, we found that all of the stroke patients recovered gradually during the three months, and the percent decreases of FA value in fibre tract above and blow the internal capsule correlated negatively with the percent changes of NIHSS and FM scale. In addition, significant correlation between the within subject regression coefficient of FA value from fibre tract below the internal capsule and NIHSS was found. These results demonstrate that during the course of neurological recovery, the secondary degeneration in fibre tract both above and below the primary lesion persists and deteriorates, and a larger extent of secondary degeneration accompanies with a smaller extent of the recovery. It is obvious that the secondary degeneration in fibre tract distal and proximal to the infarction may hamper the neurological recovery.

In conclusion, our study shows that secondary degeneration occurs and deteriorates not only in fibre tract distal to but also proximal to a subcortical cerebral infarct at lest 12 weeks after stroke, and may hamper the neurological recovery. To understand the mechanism and extent for the impact of secondary degeneration on neurological recovery, future investigations with a larger sample size, more homogeneous of infarct in patient and longer observing period are needed.
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Figure legends

Fig. 1: An example of the MR images obtained from a patient with a left subcortical infarct on the first week after stroke onset. From axial T2 weighted images (panels A to F) and the coronal FLAIR image (panel G) the subcortical infarct involved the posterior limb of internal capsule is observed (white arrows). Beyond the primary lesion, there is no hyperintense signal.

Fig. 2: An example of the DTI images obtained from the same patient as in Fig 1. From the axial FA images (panels A to F), reduced FA signals are observed not only at the primary lesion (panel C, white arrow) but in the fiber tract above the primary lesion include centrum semiovale and coronal radiata (panels A to B, black arrows), and below the primary lesion include cerebral peduncle, pons and medulla ipsilaterally (panels D to F, black arrows). In panel G, a coronal view shows the reduced FA signals at the infarct region (white arrow) and in the fiber tract proximal and distal to the infarct lesion (black arrows).
References


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