Analysis of White Matter Fractal Features in Medulloblastoma Survivors

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Introduction:

Pediatric brain tumor survivors have problems of cognitive delays or deficits caused by cranial irradiation therapy (CRT). These intellectual deficits have been associated with normal appearing white matter (NAWM) volumes [1]. Furthermore, diffusion tensor imaging (DTI) studies showed that the loss of anisotropy in white matter was correlated with the patients' academic achievements [2]. These findings suggested that white matter (WM) damage could be a useful index of cumulative impact of central nervous system (CNS) insult from multiple sources. The WM damage has been evaluated by volumetric and DTI studies. However, morphological evaluation of WM damage has been largely restricted by visual estimation. In this study, we applied the fractal geometry in an attempt to quantify the WM integrity in medulloblastoma survivors.

Methods:

Study participants were recruited from an ongoing treatment protocol for primary medulloblastoma at our institution. All patients that enrolled in the treatment protocol and had proper MR examinations before or during radiation therapy (CRT time ± 3 months) and approximately two years after radiation therapy (24 ± 3 months) were included. Fifty eight patients were divided into two groups based on their NAWM volume changes, i.e. 39 patients with decreased NAWM volume as group A, and 19 patients with increased NAWM volume as group B.

The whole brain was not imaged and therefore could not be evaluated in this retrospective analysis. Instead, an index slice at the level of the basal ganglia, including both genu and splenium of the corpus callosum and generally showing the putamen and lateral ventricle was selected to represent the whole brain. This representative slice has been tested to be highly predictive of the full cerebrum in other patient populations [3]. Brain parenchyma on MR images were segmented into NAWM, GM, CSF and blood vessels by a fully automated hybrid neural network algorithm based on T1-, T2-, and proton density-weighted images [4]. The fractal dimensions (FDs) of WM boundaries were determined by a box-counting approach, which is based on the property of self-similarity of fractal objects. A set S is self-similar if S is composed of N distinct subsets, each of which is scaled by ratio r from the original, and is identical in all respects to rS, $1 = Nr^D$ *or* $D = -\log N / \log r$. The FDs of NAWM intensities were determined using a Fractional Brownian Motion (FBM) model approach. The self-similarity of Fractional Brownian motion is expressed as $E|\Delta B_H(\Delta \vec{x})| \propto \|\Delta \vec{x}\|^H$, in which $E|\ |$ is an expectation operator, $\Delta B_H(\Delta \vec{x})$ is the intensity variation at the spatial distance $\Delta \vec{x}$, and H is the Hurst coefficient, related to the FD (D) by $D = D_E + 1 - H$, where D_E is the Euclidean dimension of FBM, i.e. for a 2-dimensional images $D_E = 2$.

Results:

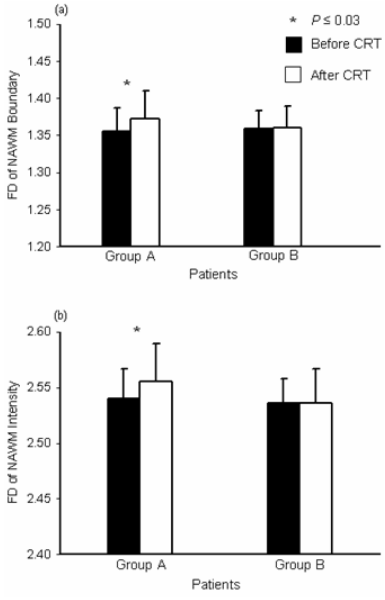

Fig. 1. Comparisons of fractal features in patients before/during CRT and after CRT, (a) FD of NAWM boundary and (b) FD of NAWM intensity.

Fig. 1 illustrates a comparison of fractal features in patients between before/during and after CRT. Both FDs of the NAWM boundary and its intensity were significantly increased in patients with decreased NAWM volumes, whereas fractal features were virtually the same in patients with increased NAWM volumes. Regression analyses results between NAWM volumes and fractal features were summarized in Table 1.

Table 1 Correlations between NAWM volumes and fractal features†

	Correlations (R^2) between NAWM volumes and FDs			
Patients	FD_{11}	FD_{12}	FD_{21}	FD_{22}
Group A	ns	0.464 ($P < 0.001$)	0.22 ($P \leq 0.003$)	0.462 ($P < 0.001$)
Group B	ns	ns	ns	0.262 ($P \leq 0.03$)

† $FD_{i,j}$, values of i represent FDs of NAWM boundary (i = 1) and FDs of NAWM intensity (i = 2), respectively; values of j represent FDs of patients before/during CRT (j = 1) and after CRT (j = 2), respectively. Not significance is expressed as ns.

Discussion:

Patients were divided into two groups according to NAWM volume changes; the reason for this different change was addressed in a previous study [5]. FD is an extreme compact measure of complexity for given objects. FDs of NAWM boundary summarized the irregularity of the shape of NAWM. The increasing FDs of NAWM boundary in patients with decreased NAWM volumes suggested the deficit of NAWM integrity in these patients. The strong correlations between NAWM volumes and FDs of NAWM boundary after CRT implied that the deficit of NAWM integrity could be one of reasons for decreased NAWM volumes. FDs of NAWM intensity measure the irregularity of NAWM intensity variations. The increasing FDs of NAWM intensity in patients with decreased NAWM volumes suggested the intensity variation is higher in these patients, which implied WM density changes. The correlations between NAWM volumes and intensity FDs were not as clear as those between NAWM volumes and boundary FDs. This may be caused by the fact that the FBM approach calculates FDs of NAWM intensity based on the whole image matrix including background pixels. However, the correlation is stronger in patients with decreased NAWM volumes after CRT than other patients, suggesting that changes in WM density could be another reason for loss of NAWM volumes.

Conclusion:

Algorithms for quantitative evaluation of WM morphology were developed and applied to investigate the NAWM integrity in medulloblastoma survivors. The results demonstrated significant deficits in NAWM integrity and changes in density in children treated for medulloblastoma. The method could be used to monitor neuro-toxicity morphologically in brain tumor survivors.

References:

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