Assessment of Tumor Cell Infiltration along White-Matter Fiber Tracts Using Diffusion Tensor Imaging

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Abstract

White-matter fiber tracts (WMFT) serve as a major pathway for malignant tumor cells to migrate. We have used diffusion tensor imaging (DTI) to investigate tumor cell infiltration along WMFT in malignant gliomas patients. Up to 74% reduction in relative diffusion anisotropy index was observed in the WMFT affected by the neoplasm. The decrease in diffusion anisotropy was also correlated with tumor recurrence in two patients. These findings indicate that DTI can be a valuable technique for assessing tumor cell invasion along WMFT and may predict tumor recurrence based upon diffusion anisotropy indices.

Introduction

Malignant glioma is one of the most deadly tumors that often strikes adults at their prime. Glioma growth is both expansive and infiltrative with ~45% of the cases extending beyond one lobe and ~25% cross over to the opposite hemisphere [1]. When tumor recurs, malignant cells often extend far beyond the primary tumor site. It has been reported that glioma infiltration is preferentially along white-matter fiber tracts [1]. With tumor invasion, the organized structure of the fiber tracts loses its integrity, allowing water molecules to diffuse more isotropically. Diffusion tensor imaging (DTI) is a robust tool to characterize diffusion anisotropy *in vivo* [2], making it potentially suitable for evaluating tumor cell spread. In this study, we have employed DTI to assess tumor cell infiltration along white-matter fiber tracts in malignant glioma patients.

Methods

A total of eight patients with primary brain tumors (glioblastoma multiforme) were enrolled in this study. All patients underwent MRI-DTI scan one day prior to surgical resection of the tumor. Tumor cell infiltration in the adjacent white-matter fiber tracts was evaluated by quantitatively measuring the relative diffusion anisotropy (RDA) index and comparing the results with that of the contra-lateral side without tumor. Following surgery, MRI-DTI scan was performed again using a similar protocol. The RDA index was evaluated for the white-matter fiber tracts in the vicinity of the surgical cavity and correlated to tumor recurrence as revealed by follow-up MRI scans and clinical findings.

All DTI images were acquired on a 1.5T GE Signa Lx-NV/i scanner (Milwaukee, WI) equipped with a high performance gradient system (amplitude = 40mT/m, slew rate = 150T/m/s). A set of N diffusion-weighted images ($I_1, I_2, \ldots I_N$), each having a distinct diffusion-gradient orientation, was acquired using a DTI pulse sequence modified from a commercial diffusion-weighted echo planar imaging (EPI) pulse sequence. The acquisition parameters were: TR=4s, TE=77ms, matrix=128^2, b=750s/mm^2, N=27, NEX=2, FOV=24cm, slice thickness=5mm, and gap=4mm. An additional image (I_0) with a zero diffusion gradient was also acquired using the same DTI sequence. Following data acquisition, diffusion-tensor elements were computed on a pixel-by-pixel basis for every slice using a least-squares algorithm. The diffusion tensor was then diagonalzed and converted to RDA index using custom software developed within FuncTool (GE Medical Systems, Milwaukee, WI).

Results and Discussion

The results from the eight patients are summarized in Table 1. Six out of the eight patients (patients 1-6) revealed a noticeably decreased RDA value in the white-matter fiber tracts close to the tumor when compared to the RDA value at the contra-lateral side, suggesting tumor cell infiltration into the tracts (Fig. 1a). After tumor resection, two patients in this group exhibited decreased RDA value (by 44% and 27%, respectively) in the corpus callosum adjacent to the surgical cavity as compared to the RDA value in the contra-lateral side (Fig. 1b). Tumor recurrence was observed in both patients after surgery, suggesting that a correlation may exist between the reduced RDA values and tumor recurrence.

Pre-surgical DTI scans on the remaining two patients (patients 7 and 8) did not show significant decrease in RDA values. The white-matter fiber tracts near the tumors were primarily distorted and compressed by the tumor mass (Fig. 1c). Following tumor resection, no substantial change in RDA value was observed in these fiber tracts, and no tumor recurrence was detected.

Our preliminary results indicate that tumor cell infiltration along the white-matter fiber tracts can be evaluated using the RDA index. A decrease in RDA value can be an indicator of tumor cell migration through the fiber tracts, which may result in tumor recurrence. With further validation, DTI may play a significant role in malignant glioma management.

Table 1. Diffusion Anisotropy in Fiber Tracts

Patient No.	RDA tumor side	RDA contra-lateral side
1	0.35±0.03	0.73±0.05
2	0.18±0.05	0.68±0.03
3	0.23±0.07	0.62±0.03
4	0.42±0.03	0.77±0.04
5	0.24±0.05	0.56±0.05
6	0.46±0.03	0.64±0.05
7	0.74±0.03	0.70±0.04
8	0.76±0.04	0.78±0.05

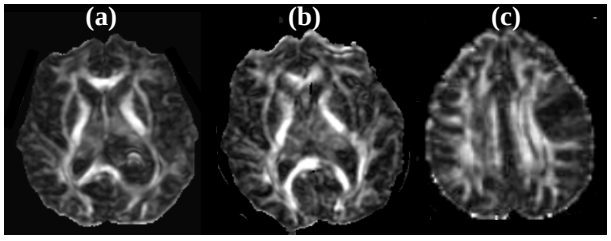

Fig.1 RDA maps of malignant gliomas.

References

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