

Evaluating Radiation-Induced White Matter Changes in Patients with Recurrent Malignant Gliomas under Treatment of Stereotactic Radiosurgery Using Diffusion Tensor Imaging: Initial Results

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Introduction

Radiation therapy is commonly used for the treatment of brain tumors. However, radiation-induced injury to normal tissue limits the dose that can be delivered. More specifically, radiation may cause detrimental effects on central nervous system, resulting in neurologic side effects. For example, white matter (WM) in the brain is generally vulnerable to radiation, which may compromise sensory and neurocognitive functions. In the past years, radiation-induced WM damage has been investigated [1-3]. MR diffusion tensor imaging (DTI) has been found as a potential biomarker of white matter damage [3-5]. Among radiotherapy, stereotactic radiosurgery (SRS) has been an effective treatment for the management of brain metastases and other brain diseases, which often delivers high radiation dose in a single fraction [6-7]. SRS differs from conventional radiotherapy in its much greater fractional dose and its hypofractionation scheme. As a result, SRS can have different effects on biological response from conventional radiotherapy. SRS has been a valuable treatment tool for patients with brain tumors [6-7]. There are however few data available regarding radiation-induced white matter change caused by SRS. In this work, MR DTI is used to investigate radiation-induced changes in white matter following SRS.

Methods

Patients

In this study, 7 patients with recurrent, unifocal malignant gliomas up to 5-cm in maximum dimension were enrolled. The study was approved by institutional review board. Patients with lesions <3-cm diameter would be treated with single-fraction SRS; patients with lesions 3- to 5-cm diameter would receive five 5-Gy intensity-modulated SRS treatments. The prescription dose received by the patients ranged from 16Gy to 26Gy. Patients would be scanned with MRI 1-4 days prior to SRS and 7 days and two months following the final SRS treatment.

MRI studies

All MRI scans including DTI were acquired on a 1.5T clinical scanner (GE Healthcare, Milwaukee, WI) using a standard quadrature birdcage head coil. The imaging protocol included T1- and T2-weighted imaging, post-contrast T1-weighted, and DTI. DTI scans were acquired in the axial plane using a spin-echo echo-planar imaging sequence (TR = 9,100 ms, TE = 98 ms, field of view = 30x 30 cm², matrix size = 128x128, slice thickness = 5-mm, no average). Diffusion-sensitized gradient encoding with a diffusion weighting factor of $b = 1,000 \text{ s/mm}^2$ was applied in six directions, and one set of images without diffusion-sensitized gradient encoding (e.g. $b = 0 \text{ s/mm}^2$) was also acquired. The acquired DTI data were then processed as follows.

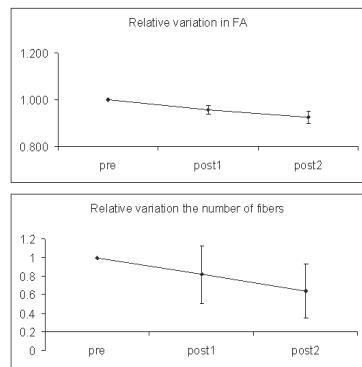
DTI Image registration and processing

Diffusion tensors were calculated and fiber tracking was performed using a commercial software known as iPlan 4.1 (BrainLAB, Feldkirchen, Germany). All the DTI images were registered with a set of high-resolution T1-weighted images. Generally, the course of a fiber is defined by following the direction of the maximum diffusion. Before tracking is initiated, the user can adjust the FA threshold and the minimum fiber length. In this study, the default FA threshold is 0.30, and the minimum fiber length is 80 mm. Tract seeding is performed within a defined volume of interest (VOI). In the study, the volumes of normal-appearing white matter

receiving dose > 5Gy were contoured and are used in the study as the VOIs.

Statistical analysis

Statistical analysis was performed using a commercial software known as Statistical Package for Social Sciences program (SPSS Software Products, Chicago, IL). Descriptive statistics of apparent diffusion coefficient denoted as $\langle D \rangle$ and fractional anisotropy (FA), the number of fibers tracked were obtained for the volumes of interest. The Wilcoxon signed-rank test was used to assess the differences. Statistical significance was considered at $p < 0.05$.



Results

The above figure shows the representative images of one patient: (a) 3D view of tumor in pink in the T1-weighted MRI; (b) tumor outlined in pink in the $\langle D \rangle$ map of one slice; (c) 3D view of tumor in pink with fiber tracking that passing through the VOI receiving >5Gy; (d) tumor outlined in pink in the FA map of the same slice of (b). The effects of radiation in the normal-appearing white matter were assessed by changes in $\langle D \rangle$, FA and the number of fibers that can be tracked after SRS. We performed quantitative analysis of the temporal changes in these parameters from 7 patients. After two months of the SRS, $\langle D \rangle$ increased slightly by about 3.9% ($p = 0.610$), and FA decreased significantly by 7.8% ($p = 0.02$) with nearly 40% decline of the number of fibers tracked ($p = 0.11$). The results are illustrated in the plots on the left for easy visualization.

Discussion and Conclusion

In this study, DTI data indicated compromise of white matter fiber integrity after SRS. The radiation-induced white matter damage shall not be ignored. These preliminary results suggest that dose sparing to white matter should be considered in SRS, particularly when the target is close to white matter fiber bundles such as genu and splenium.

References

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