Differentiation of Tumor Recurrence from radiation-induced Necrosis Using Diffusion Tensor Imaging

Q. Dong¹, P. Sundgren¹, P. Weybright¹, S. K. Mukherji¹, R. C. Welsh¹, T. L. Chenevert¹

¹University of Michigan, Ann Arbor, MI, United States

Purpose: To evaluate the ability of diffusion tensor imaging (DTI) in distinguishing between radiation necrosis and brain tumor recurrence in patients after radiotherapy.

Introduction: Surgical resection and chemotherapy alone have proven to be insufficient in treatment of patients with primary and metastatic brain tumors. As a result, the various forms of radiotherapy, such as external-beam radiation, radiosurgery have become important therapeutic adjuncts. The appearance of a new enhancing lesion after radiation treatment may represent tumor recurrence, radiation-induced demyelination, or radiation necrosis of the brain. Differentiation among these possibilities can be difficult with conventional MR imaging. Diffusion-weighted imaging (DWI) has been reported to be helpful in distinguishing tumor recurrence and radiation damage (1). Our study was designed to explore the ability of DTI in assessing new contrast enhancing lesions as tumor recurrence or non-neoplastic therapy related change.

Methods: We reviewed 16 patients (7 males, 9 females, 5-56 years old, mean age 35 years) who developed new contrast-enhancing lesions 3-36 months after radiation treatment of the original tumor. Histologic diagnoses of the original tumors in these 16 patients were astrocytic tumors (11 patients), metastases (3 patients), medulloblastoma (1 patient), and ependymoma (1 patient). The final differentiation between tumor recurrence and non-neoplastic necrosis of the new enhancing mass found after radiotherapy was decided based on either histological findings or follow-up MR examinations and clinical conditions. In 4 patients who received histologic verification (by either surgical resection or stereotactic biopsy), there were 2 cases of tumor recurrence and 2 of radiation necrosis. In the remaining 12 patients who did not undergo surgical intervention, the lesions were considered to non-neoplastic therapy related changes if the enhanced lesions disappeared (n=3) or decreased in size (n=2) in subsequent MR examinations. Otherwise, tumor recurrence was entitled if the enhancing lesions increased extensively in size on follow-up serial MR examinations (n=5), and the patient's clinical condition deteriorated progressively during that period (n=2).

In addition to a standard anatomical imaging protocol which includes routine T1-weighted, T2-weighted, FLAIR and, contrast-enhanced T1-weighted sequences, diffusion tensor imaging was obtained using a single shot spin-echo EPI technique along nine different directions with a b value of 1000s/mm². All examinations use a 1.5T system with the manufacturer-supplied birdcage, quadrature head coil. Image post-processing was performed to generate ADC and FA maps with vendor-provided software. Initially, images were preprocessed to remove image distortion that arises from the echo planar readout (EPI): shear, compression and shift were corrected. To further reduce artifactual values, a noise threshold was applied. Finally, a tensor data set for each voxel (including eigenvalues and eigenvectors) was generated. The region of interest (ROI) was placed in solid part of the enhancing lesions according to contrast-enhancing T1 images and T2 weighted (b0) images. ADC, FA values and the standard deviation were then calculated. Two-sample t test was used for statistic analysis.

Results: Conventional MRI T1 post contrast and T2-weighted images demonstrated contrast-enhancing lesions surrounded by various degrees of edema in all the patients. ADC values for tumor recurrence (range = $1.16-1.29 \times 10^{-9} \text{mm}^2/\text{s}$, mean $\pm \text{SD} = 1.21 \pm 0.12$) were significantly higher (p<0.05) than those for radiation-induced cerebral necrosis (range= $1.05-1.15 \times 10^{-9} \text{mm}^2/\text{s}$, mean $\pm \text{SD} = 1.10 \pm 0.12$). A decreased FA also was demonstrated in both groups related to normal white matter with ranges of 0.10-0.32 (mean $\pm \text{SD} = 0.19 \pm 0.05$) for tumor recurrence, and 0.15-0.5 (mean $\pm \text{SD} = 0.27 \pm 0.06$) for necrosis. Representative images from a tumor recurrence case and a radiation necrosis case are illustrated in Fig. 1 and Fig.2, respectively.

Discussion: Diffusion imaging has been increasingly used to investigate various tumor components, and assess tumoral invasion from normal tissue or edema. ADC maps have shown to be helpful in recognizing solid enhancing tumor and non-enhancing tumor, peritumoral edema, necrotic and cystic regions, and normal white matter. Our findings of higher ADC values in tumor recurrence compared to radiation necrosis are consistent with previous reports (1,2). The higher ADC values found in the areas of tumor recurrence may be due to micronecrotic changes in treated brain tissue in these patients. On the other hand, the lower ADC in radiation necrosis patients may be a result of scarred tissue that retards water movement. Deceased FA value in both groups can be explained by the destruction of white matter. However, this is not specific enough to distinguish the difference between tumor recurrence and necrotic change. Our initial results suggest that DTI can potentially provide a non-invasive means to distinguish between tumor recurrence and radiation necrosis.

Acknowledgment: Support in part by NIH Grant #CA 85878.

References:

- 1. Le Bihan D, et al., Top Magn Reson Imag. 1993;5:25-31.
- 2. Tung GA, et al., AJR Am J Roentgenol. 2001;177:709-712.

