Evaluation of affected fiber structures in rat infiltrative glioma with Diffusion-Tensor MR fiber tracking method: immunohistochemical correlation

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Background and Purpose

Gliomas spread diffusely through the brain and infiltrate along white matter (WM) tracts (1). To evaluate WM fiber structure changes affected by the tumor could contribute glial tumor grading and treatment. Researchers have suggested change of anisotropy index derived from diffusion-tensor (DT) MR imaging can represent the WM fiber structural integrity and arrangements affected by gliomas (2). Fiber tracking methods using anisotropic indices derived from DT MR imaging have been tried to apply not only to visualization of WM tracts but also to tissue characterization. Especially, fiber tracking method which traces all possible fibers through the image set from all voxels having sufficiently high anisotropy (3) is an attractive tool for tissue characterization.

The purpose of our study is to correlate WM fiber structures discriminated by the fiber tracking method using DT MR imaging with histological distribution of neurofilaments (NF), which represent axon, in N-ethyl-N-nitrosourea (ENU)-induced infiltrative glioma of rat.

Material and Method

Animal Four Fisher-334 rats, which had been treated transplacentally with ENU, underwent in vitro MR imaging. All procedures met institutional Laboratory Animal Care and Use Committee approval.

MR imaging and Immunohistochemistry The experiments were performed on a horizontal 7T/40 cm magnet (Japan Superconductor Technology Inc., Kobe, JAPAN) equipped with a 12cm gradient set up to 400mT/m (Magnex Scientific Ltd., Abingdon, UK) interfaced to a UNITYINOVA NMR system (VARIAN Inc, Palo Alto, CA, USA). At postnatal day 231-258, the rats were sacrificed and the brains were removed from the skulls. After 3 days fixation, the brain was put into the tube filled with the buffer for MR imaging. Acquisition parameters were 2000/36/12-14 (TR msec / TE msec / averaging), 24 mm field of view, 0.5 mm slice thickness, and 256 x 256 scan matrix. The data set of diffusion-weighted images with b-value = 1027 sec/mm^2 in six different noncolinear directions and T2-weighted images (b0 images) were obtained. After MR imaging, histological sections with NF immunohistochemistry using the avidin-biotin-peroxidase complex method were obtained.

Postprocessing and Analysis The mean value of fractional anisotropy (mFA) and standard deviation (SD) were obtained from the region- of-interest which was positioned in the corresponding normal WM site of the opposite hemisphere to the tumor location. All possible fibers through the image set from all voxels above FA threshold of mFA, mFA-0.5SD, mFA-1SD, mFA-1.5SD, and mFA-2SD were reconstructed and superimposed on T2-weighted image (Fiber maps). Two authors (R.I. and K.B.) visually compared the reconstructed fiber structures in the tumor and the peritumoral area on the Fiber maps with NF distribution on the corresponding histological section, and determined the FA threshold with which fiber tracking described fiber structures best matching with the NF distribution. Fiber tracking and measurement were performed by using DTI-Studio software (processing tools and environment for DT MR imaging, version 2.3, H. Jiang and S. Mori, Radiology Dept, Johns Hopkins University, Baltimore, MD, USA).

Results and Conclusion

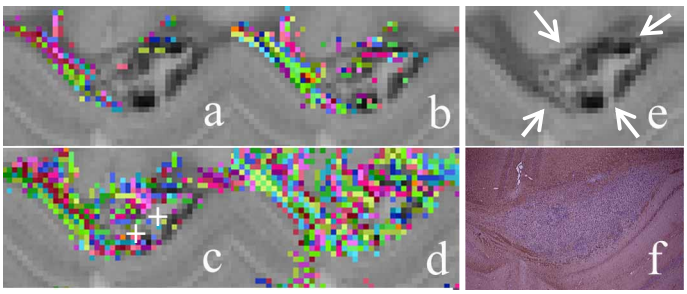
DT MR image sets and corresponding histological sections of five tumors involving in WM were obtained. On the each image section including tumor, the mFAs and SDs were 0.64-0.79 and 0.10-0.16, respectively (Table). Fiber tracking was successfully performed for the five tumors. The FA thresholds with which fiber tracking described the fiber structures best matching with NF distribution determined by histology were mFA-1SD in two tumors and mFA-1.5SD in three tumors (FAbest in Table). Fiber maps, T2-weighted image, and NF stained histological section of an example of infiltrative glioma (Tumor B of rat #115) are shown in Figure. Fiber tracking with the FA threshold ranging from mFA-1SD to mFA-1.5SD described the preserved fiber tracts in the peripheral zone of the tumor and few tracts in the necrotic tumor center, which was confirmed by corresponding histological section.

The fiber tracking method, which traces all possible fibers through the image set from all voxels, could characterize the residual fiber structures in the infiltrative glial tumor area. This approach may discriminate intact or only diluted fiber tracts from destroyed tracts within the infiltrative tumor area and may contribute glial tumor grading and treatment.

Table: mean FA and SD, FAbest

mean FA values and SDs in normal white matter FA best: a threshold with which fiber tracking described the best correlating fiber structures with NF distribution determined histology		
Tumor	Mean FA (SD)	FAbest
A (rat #111)	0.66 (0.12)	0.48 (mFA-1.5SD)
B (rat #115)	0.67 (0.14)	0.46 (mFA-1.5SD)
C (rat #115)	0.64 (0.16)	0.48 (mFA-1SD)
D (rat #116)	0.79 (0.10)	0.64 (mFA-1.5SD)
E (rat #221)	0.75 (0.12)	0.63 (mFA-1SD)

Figure: Fiber maps, T2-weighted image, and histological section of glioma (tumorB of rat#115)



a-d; reconstructed fibers on T2-weighted images with a FA threshold of 0.60, 0.53, 0.46, and 0.39, respectively
e; T2-weighted image
f; corresponding histological section stained with NF immunohistochemistry / haematoxylin & eosin

In e, ENU induced infiltrative glioma (arrows) in the corpus callosum is shown. In c, the reconstructed fiber tracts are preserved in the peritumoral area and peripheral zone of the tumor (colored dots). Few fiber tracts are reconstructed in the necrotic tumor center (++). The reconstructed fiber structures correlate with NF distribution in f.

References

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