In Vivo DTI-Based Tractography of Intra-Cranial Rat Brain Tumors

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Introduction: Fiber tractography based on diffusion tensor images has been widely used to reconstruct white matter axonal projections of the brain [1]. While this technique is commonly applied to the human brain, there have been only a limited number of reports on tractography of the rat brain for both *in vivo* [2] and *ex vivo* [3] experiments. Furthermore, the white matter tracts in the rat brain using fiber tracking have not been defined in a systematic way. The availability of DTI-based tractography of rat brain *in vivo* could be particularly useful to investigate changes in the white matter tracts during brain development or due to the presence of a pathology, such as intra-cranial gliomas. These studies could then be corroborated with invasive measurements that are not feasible in the clinic. Thus, in this study, we have developed a DTI data acquisition and tractography method for in vivo rat brain and have demonstrated its application in a model of rat glioma.

Method: 9L glioma (10 μl, 5×10^4) cells suspended in PBS were inoculated into the brain of 4 syngenic female Fisher rats stereotactically (3 mm lateral and 3mm posterior to bregma; depth 3 mm from dura). The animals were scanned at four time points (day-3, 11, 18, and 25) after tumor cell implantation using a 4.7 T, 40 cm horizontal bore magnet with a dual coil system; a 7 cm microstrip volume coil to transmit and a surface coil to receive the rf signal. General anesthesia was induced by 1.5% isoflurane in air. The animal was mounted on a cradle and the head was secured in a specially designed nose cone with a restraining device to minimize motion artifact. Subdermal needle electrodes and a rectal thermister were placed and connected to a small animal vital signs monitoring device to monitor ECG and core body temperature. The animal body temperature was maintained at 37 (±1) °C during the scan. A pulse gradient spin echo sequence was modified to acquire 2D multi-slice images with diffusion weighting along six directions optimally selected for anisotropy measurement [4]. The scan was repeated with opposite direction diffusion gradients to reduce the cross-term effect from the imaging gradients by taking geometric average [5]. The imaging parameters were TR = 2 s, TE = 35 ms, FOV = 3 cm, slice thickness=1 mm, and matrix size = 128 x 128. The strength and duration of gradients were 12 G/cm and 7 ms, respectively, and diffusion time was 20 ms, resulting in a b-value close to 891 s^2/mm. Twenty slices were selected to cover most of the cerebral cortex. The data was acquired with cardiac gating with delay of ~70 ms, which corresponded to acquisitions between two R peaks. The diffusion tensor was computed in each voxel and diagonalized to compute eigenvectors, eigenvalues and fractional anisotropy (FA) [6]. Fiber tracking was performed as suggested by Mori et al. [7], with termination condition of FA=0.25 and angular distance of 70 degrees. Two ROIs were selected based on FA-weighted directional encoded color map. Fiber tracking was launched from both ROIs with 25 seeding points per voxel. Reconstructed tracts passing both ROIs were selected afterwards.

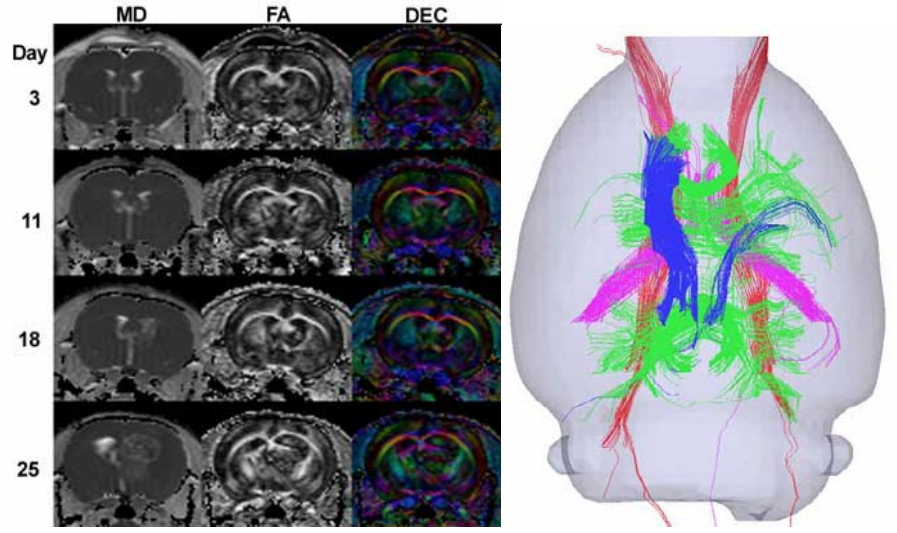

Fig.1 Growth of 9L glioma in rat brain observed by DTI-derived measures (left); MD, FA, and DEC maps. A representative example of white matter tracking is shown on the top view of the rendered brain (right); red: optic tract, green: corpus callosum, pink: fimbria, blue: cingulum.

Results and Discussion: Fig.1 shows the growth of 9L tumor in one of the rats. The tumor starts growing in the hippocampus (between the corpus callosum and fimbria). The tumor is easily discernable on mean diffusivity (MD) maps since normal brain parenchyma has a homogeneous intensity. Additionally, both FA-map and the directionally encoded color (DEC) map provide more detailed information on the displacement and changes of surrounding tissues. An example of white matter fiber tracking is also shown in Fig.1. A gradual reduction of reconstructed fiber tracts was observed as the tumor growth progressed for most of the fiber tracts (e.g. fiber count for the forcep minor = 155, 76, and 59, for day 3, 18, and 25, respectively in this example). To conclude, we have demonstrated that DTI of *in vivo* rat brain provides useful information regarding morphological and biophysical changes due to a tumor in the brain noninvasively.

References: [1] Le Bihan et al., JMRI 13:534-546, 2001. [2] Xue et al., MRM 42:1123-1127, 1999. [3] Huang et al., MRM 52:559-565, 2004. [4] Jones et al., MRM 42:515-525, 1999. [5] Neeman et al., MRM 21:138-143, 1991. [6] Basser and Pierpaoli, JMR B 111:209-219, 1996.

Acknowledgement: This study was funded by a grant from the University Research Foundation.