Diffusion Tensor Imaging and Contrast Enhanced MRI of Rat Brain Gliomas

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Introduction

Clinical identification of the presence and extent of brain tumors is typically carried out using T2-weighted and/or contrast enhanced (CE) MRI. With aggressive cell types, e.g. high-grade gliomas, the borders indicated using these techniques do not show the full extent of cancer cell invasion, which is critically important for surgical and radiation treatment planning. Recently, studies using diffusion tensor imaging (DTI) have been applied in humans to evaluate whether DTI demonstrates abnormalities distal to borders obtained using conventional MRI [1]. One difficulty with such studies is that since the brain being studied has already been affected by the tumor, defining the location and values of normal anisotropy parameters is somewhat problematic. We have applied DTI, T2-weighted MRI and CE-MRI to study implanted rat brain gliomas to determine whether maps of diffusion, diffusion anisotropy, and contrast enhancement demonstrate similar or differential regions of tissue abnormality. Such models are an important complement to clinical studies because imaging can be carried out in normal brain prior to implantation and throughout the development of the tumor.

Methods

MRI was carried out on Wistar rats (3 females) before and after implantation of C6 glioma cells using a Bruker Biospec 4.7T instrument. C6 glioma cells (~10^5 cells in 10 μl) were injected stereotaxically in the right caudate nucleus of the rats. Animals were anesthetized by isoflurane gas and placed into a homemade rat holder. An 18 mm OD circular surface coil, used as the MR signal receiver, was placed on top of the rat head and rats were placed into a 72 mm volume excitation coil. Body temperature was monitored using a fiber optic rectal probe and maintained using a circulating water bath. Rat brains were imaged in the axial plane with 1 mm slice thickness (no gap) with a 4 × 4 cm field of view. DTI imaging was carried out using a diffusion-weighted radial-FSE sequence [2] with the following parameters: TR = 2s, Prep Time = 36 ms, echo spacing = 12 ms, ETL = 4, matrix 256 × 256, Δ = 13 ms; δ = 5 ms. Images were obtained without (b = 0 s/mm^2) and with (b = 961 s/mm^2) diffusion weighting in six non-colinear gradient directions [3]. CE-MRI was carried out following the injection of gadolinium using a spin-echo sequence with the following parameters: TR = 80ms, TE = 6.5 ms, matrix 128 ×128. Images were acquired every 30 seconds for 30 minutes following the injection of contrast (0.1 mmol/kg Omniscan). Maps of diffusion anisotropy (FA, RA, ADC) and contrast enhancement (maximal enhancement and time to max) were generated for each slice (10 slices) using standard algorithms written in IDL.

Results and Discussion

Fig.1 shows maps of a) apparent diffusion coefficient (ADC), b) directional diffusion, c) fractional anisotropy (FA) and d) maximal contrast enhancement (MCE) obtained 6 days post implantation of tumor cells. Disruption of white matter tract in the cingulum of the right hemisphere is visible in the anisotropy maps (indicated by arrows) and correlates directly to the region of enhancement. The values of FA in this region (0.45 ± 0.08) are significantly lower than those on the contralateral side (0.78 ± 0.06) and values obtained prior to tumor implantation (0.86 ± 0.04). No significant regional difference in ADC is observed.

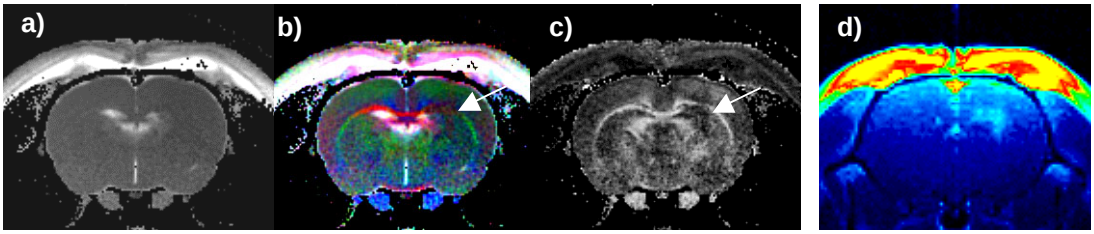

Fig.1. (a) ADC, (b) directional diffusion (red/green/blue = x/y/z-directional diffusion), (c) FA and (d) maximum intensity maps of rat brain 6 days after implantation of C6 cells in the caudate nucleus. R/L direction in image corresponds to R/L in mouse.

Data obtained in the same rat 11 days post implantation are shown in Fig.2. In addition to the previous observations, there is a beginning of a necrotic core indicated by an increase in ADC (Fig. 2a) and hyperintensity in T2-weighted images (not shown). Anisotropy measures with the tumor, as defined by these changes, are somewhat reduced compared to the contralateral side, but there are still regions of significant anisotropy within the tumor. This is likely evidence of the tumor growing into existing white matter structures as apposed to pushing them aside.

These results are common to the animals we have studied and indicate that DTI offers unique and useful information on tumor growth. Pre clinical investigations such as these can play an important role in understanding these tumor models and in critically assessing the utility of DTI to measure the extent and spread of brain tumors.

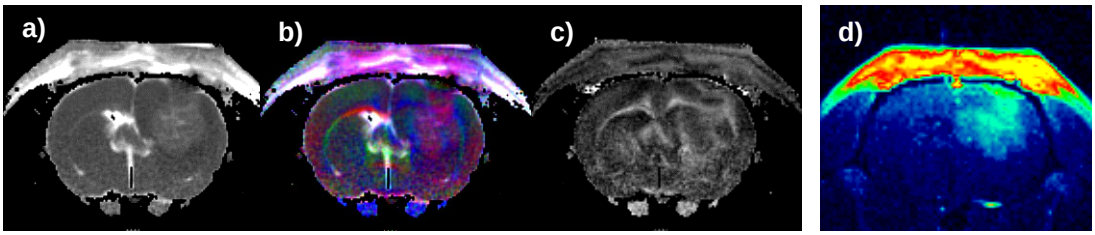

Fig.2. (a) ADC, (b) directional diffusion (red/green/blue = x/y/z-directional diffusion), (c) FA and (d) maximum intensity maps of rat brain 11 days after implantation of C6 cells (same animal as in Fig. 1)

References

[1] Price, *et al.*, *Clinical Radiology*, 58:455 (2003), [2] Trouard, *et al.*, *MRM.*, 42:11 (1999), [3] Hasan, *et al.*, *JMRI*, 13:769 (2001).