Suppression of Peritumoral Edema for Improved Demarcation of Brain Tumor Lesion with T_1 over T_2 (T_1/T_2) Mapping

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Introduction

Multi-parametric (ADC, T_1 and T_2) MRI has been used to monitor tumor progression and treatment response, yet unambiguous demarcation of tumor from peritumoral edema is often difficult due to diffuse tumor boundary [1-2]. Given that both T_1 and T_2 of tumor and edema alter to different extent, we here postulated that a T_1 and T_2 ratio (i.e., T_1/T_2) could be useful in delineating tumor from surrounding edematous and normal brain tissues. The aim of our study was to compare T_1/T_2 map with commonly used multi-parametric MRI for demarcating tumor.

Materials and Methods

Brain Glioma Model: $2x10^5$ rat glioma (D74/HveC) cells were implanted intracranially in male Fischer 344 rats (160-230 g; *N* = 5). Tumors were grown for 11 days prior to MRI. Left femoral vein was cannulated for contrast agent injection.

Multi-parametric MRI: MRI experiments were performed on a 4.7T Bruker MRI scanner. Each animal was anesthetized, with both heart rate and blood pO_2 monitored online. In addition, body temperature was maintained within the normal physiological range. Multislice MRI (5 slices, slice thickness/gap = 1.8/0.2 mm, field of view = 25x25 mm^2, acquisition matrix = 64x64) was obtained with single-shot echo-planar imaging (EPI) (receiver bandwidth = 200 kHz). Specifically, isotropic diffusion-weighted imaging (DWI) was measured with two b-values of 250 and 1000 s/mm^2 (TR/TE = 3250/54 ms, NA = 16); T_1 images were acquired using an inversion recovery sequence, with seven inversion delays from 250 ms to 3000 ms (TR/TE = 6500/14.8 ms, NA = 4); T_2 images were obtained with two TE of 30 and 100 ms (TR = 3250 ms, NA = 16). In addition, contrast-enhanced T_1W FLASH images (acquisition matrix = 128x128, TR/TE = 100/5.5 ms, FA = 30°, NA = 4) were acquired after injection of gadolinium (Gd-BOPTA, ~0.2 mmol/kg) for visualizing contrast-enhanced tumor lesion.

Image and Data Analysis: ADC, T_1 and T_2 maps were obtained by least-square fitting of the signal intensities as a function of b-value, inversion time and echo time, respectively. T_1/T_2 ratio maps were computed by pixel-by-pixel. Region of interest (ROI) analysis was performed in one slice with considerable peritumoral edematous and tumor tissues in each animal. Specifically, ROIs were defined on Gd enhanced T_1W images for tumor lesion, and on ADC maps for peritumoral edematous tissue based on prolonged ADC compared to normal brain tissue, with care of excluding cerebrospinal fluid (CSF) and the defined tumor ROIs.

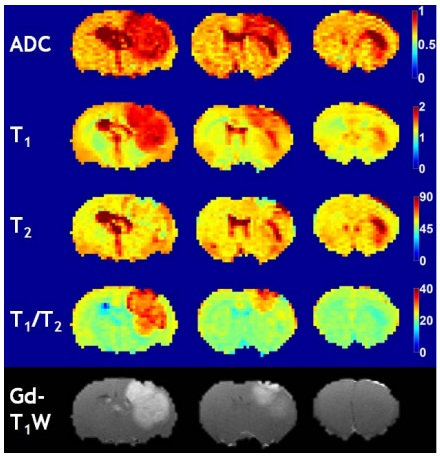

Fig. 1. ADC maps (in 10^{-3} mm^2/s), T_1 maps (in s), T_2 maps (in ms), T_1/T_2 ratio maps, and Gd contrast-enhanced T_1W images of rat brain with glioma tumor and peritumoral edema.

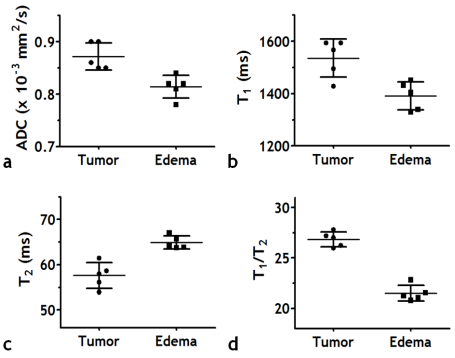

Fig. 2. ADC (**a**), T_1 (**b**), T_2 (**c**), and T_1/T_2 ratio (**d**) of tumor and peritumoral edematous tissues (*N* = 5). Error bar represents standard deviation.

Results and Discussions

Fig. 1 shows ADC, T_1, T_2 and T_1/T_2 maps, in addition to Gd-enhanced T_1-W images from a representative animal. For rat D74/HveC glioma tumor, we found it difficult to use ADC and T_1 maps to demarcate tumor from peritumoral edema, while T_2 showed very little contrast. In comparison, T_1/T_2 map was able to suppress contrast from peritumoral edema, thus better delineate tumor lesion from surrounding tissues. Noteworthily, ADC, T_1 and T_2 showed hyperintensity in the third slice, while neither T_1/T_2 nor Gd-enhanced MRI showed abnormality. Therefore, it appears that T_1/T_2 provides more specific characterization of tumor. In addition, T_1/T_2 ratio map exhibited low contrast for CSF, which has both high ADC and relaxation times, allowing improved definition of tumor boundaries adjacent to CSF regions. Most importantly, the delineation of tumor in the high contrast T_1/T_2 ratio maps well corresponded to the Gd contrast-enhanced tumor lesion, suggesting its capability to demarcate tumor tissue from surrounding tissues without injection of contrast agent. Similar to other parameteric maps, spatial heterogeneity could be observed within the tumor tissue in the T_1/T_2 ratio map, likely reflecting varying local pathophysiological properties such as cellularity of the tumor microenvironment.

Fig. 2 compares ADC, T_1, T_2, and T_1/T_2 ratio of tumor and peritumoral edematous tissues. Note that measurements of MRI parameters over the tumor ROI only reflected the average values of entire tumor lesion, which is often heterogeneous. It shows that T_1/T_2 ratio provided the best contrast between tumor and edema. The percentage differences of parameters between tumor and edematous tissue with tumor as reference (i.e., $(I_{tumor}-I_{edema})/ I_{tumor}$) were 6.6%, 9.4%, -12.7% and 19.9% for ADC, T_1, T_2 and T_1/T_2 ratio, respectively. It is interesting to note that T_1/T_2 ratio has been explored in discriminating hepatocellular carcinomas and metastases from benign hepatic lesions such as cysts and hemangiomas in a previous liver study [3], indicating distinct T_1/T_2 relaxation behavior in different pathologic structures. Further evaluation of T_1/T_2 ratio mapping in demarcating tumor from surrounding tissues is warranted in future studies with different brain tumor types.

Conclusion

In this study, T_1/T_2 ratio mapping was compared with commonly used multi-parametric MRI in characterizing rat glioma tumor. Our data showed that T_1/T_2 better depicted brain tumor region by suppressing signal from peritumoral edema and CSF, which typically show similar contrast to brain tumor lesion in conventional MRI parameter maps. Moreover, the delineation of tumor tissue in T_1/T_2 ratio map was in good agreement with that of Gd contrast-enhanced T_1W MRI. Given that T_1 and T_2 are widely used diagnostic imaging methods, the proposed T_1/T_2 mapping can be easily translated to clinics, which may assist differential diagnosis and treatment planning of brain tumors in clinical settings.

References [1] Eis M et al. MRM 1995;3:835-844. [2] Oh J et al. JMRI 2005;21:701-708. [3] Farraher SW et al. JMRI 2006;24:1333-1341.