DIFFERENTIATING BETWEEN RECURRENT TUMOR AND POST-TREATMENT RADIATION EFFECTS USING HIGH-ORDER DIFFUSION IMAGING

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Introduction: Resolving the regions of recurrent tumor from post-treatment radiation effects (PTRE) can be challenging, because both can appear enhancing on the contrast enhanced T1 imaging, as shown in Fig. 1a and 1e. Diffusion-weighted Imaging (DWI) was shown to correlate with tumor cellularity [1]. Recently, DWI with a higher b-value was found to have greater sensitivity to the changes in tumor cellularity [2, 3]. While the complications of treatment-bed changes involve tumor growth, radiation- and operation-induced lesions [4, 5], the intra-voxel diffusion heterogeneity measured by the high b-value DWI may be useful in differentiating between pathological mechanisms. In this study, two multiple b-value diffusion models: the stretched exponential model (α-DWI) [6] and diffusion kurtosis imaging (DKI) [7] were used to assess recurrent tumor and PTRE. Their fitted parameters: α and Kapp quantify the diffusion heterogeneity without information about the number of water compartments.

Method: With the Institutional Board Approval and the informed consent obtained from each patient, we studied 11 recurrent WHO grade III and IV gliomas patients, who had undergone previous multimodality therapy, including chemo-radiation. We obtained pre-operative imaging and correlated with histopathology, which showed 9 patients to have recurrent tumor and 2 patients with PTRE. Patients with tissue samples containing both tumor and PTRE were considered as tumor cases. Echo planar imaging (EPI) sequences were implemented on a GE 3T scanner with 40 mT/m gradients. DWI images were acquired with directions: X, Y, and Z axes using maximum b-value: 2500 in increments of 500 s/mm^2. Other imaging parameters were: SENSE: 2, TR/TE = 4000/104 ms, NEX = 4, slice thickness = 4.5 mm, FOV = 240 × 240 mm^2, and matrix = 128 × 128. Three ROIs were defined [8] (Fig.1): enhancing region on T1, peri-enhancing region defined on the T2 abnormal signals outside of the enhancing regions, and the normal appearing white matter (NAWM), which was segmented on T1 images using SPM. α-DWI and DKI models were fitted to the data using the Levenberg-Marquardt algorithm in MATLAB (Mathworks, Inc.). Data below the noise floor were excluded from the data fitting. The ADC values were calculated for comparison. The fitted parameters were normalized by those of NAWN for each person, and were compared using the unpaired one-tailed Student's t-test with significance level: $p < 0.05$.

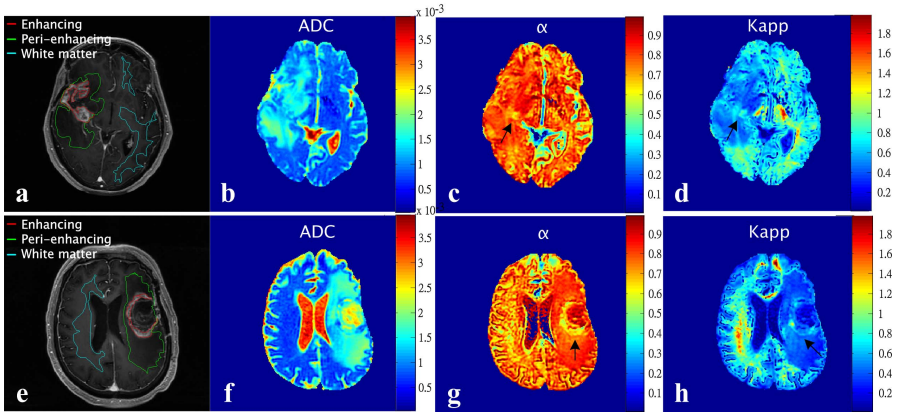

Figure 1 Illustration of the ROIs selection and the calculated parametric maps of one case of recurrent tumor (1a-1d) and PTRE (1e-1h).

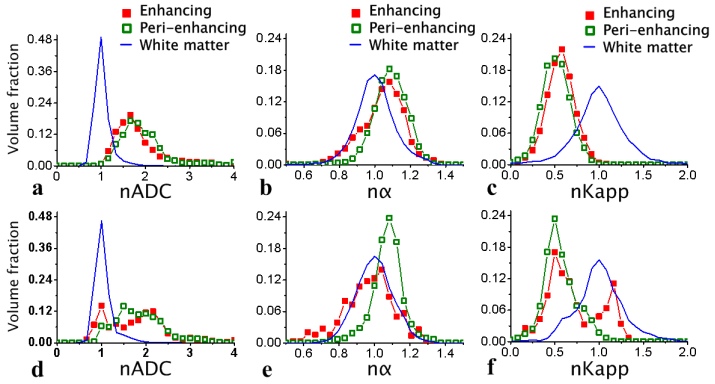

Figure 2 The histogram of normalized ADC, α, and Kapp in three selected ROIs of recurrent tumor group (a-c) and PTRE group (d-f).

Results: The enhancing regions in one case of recurrent tumor and PTRE showed an increased diffusional heterogeneity (arrow in Fig. 1). Figure 2 shows the comparisons of the normalized parametric histogram between recurrent tumor and PTRE groups. The nADC in the enhancing ROI of recurrent tumor group was significantly lower than the nADC in the peri-enhancing ROI ($p = 0.035$). The difference between the nADC of recurrent tumor and the nADC of PTRE groups was not significant ($p = 0.124$). The nα in the enhancing ROI was significantly lower than the nα in the peri-enhancing ROI of both recurrent tumor ($p = 0.003$) and PTRE ($p = 0.002$) groups. The nα of recurrent tumor group was significantly higher than the nα of PTRE group ($p = 0.011$). The nKapp in the enhancing ROI was significantly higher than the nKapp in the peri-enhancing ROI of both recurrent tumor ($p = 0.022$) and PTRE ($p = 0.03$) groups. The nKapp of recurrent tumor group was significantly lower than the nKapp of PTRE group ($p = 0.04$).

Discussion & Conclusion: The results indicated that the diffusional heterogeneity measured by α and Kapp of PTRE was significantly higher than that of recurrent tumor, whereas the diffusivity measured by ADC showed no significant difference. Further tissue study must identify the mechanisms that explain the increased diffusion heterogeneity. Although the fitted parameters showed a significant difference between the enhancing and peri-enhancing regions in the recurrent tumor group, the apparent overlap may suggest the cell infiltration of high-grade brain tumors [9]. This work demonstrated the potential of using the high b-value diffusion models to differentiate the pathologies during the treatment of brain tumor.

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