Imaging parameters of high grade gliomas in relation to the MGMT promoter methylation status: diffusion tensor imaging, perfusion imaging and intravoxel incoherent motion imaging using 3.0-T MR

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Target audience: Radiologists, Physicians, and Neurologists

Purpose: High grade gliomas (HGGs) are rapidly progressive forms of primary brain tumors. Recent molecular investigations have revealed that the methylation status of the methyl-guanine methyl transferase (MGMT) gene promoter is associated with a favorable prognosis and prolonged survival for patients with HGGs treated with temozolamide[1]. We hypothesized that the MGMT promoter methylation status is associated not only with the imaging features as seen in MRI but also with the quantitative imaging parameters, which include the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) from diffusion tensor imaging (DTI), the regional cerebral blood parameters from perfusion-weighted imaging (PWI) and pseudodiffusion coefficients (D*) and perfusion fractions (f) from intravoxel incoherent motion (IVIM). The purpose of this study was to retrospectively evaluate the relationship between the MGMT methylation status and the quantitative imaging parameters of MR in HGGs.

Methods: Out of 38 consecutive patients with HGGs, 24 patients whose MGMT promoter methylation status was available [13 men and 11 women; median age, 52 years; age range, 26–79 years; WHO grade III (n = 7), WHO grade IV (n = 17)] were enrolled retrospectively. MR examinations (Achieva 3.0T TX, Philips, Best, The Netherlands) were performed before surgery. ADC and FA from DTI, and the regional cerebral blood parameters from PWI and parameters from IVIM were measured for enhancing tumors. Qualitative imaging features were also analyzed. The ADC, FA, and rCBV ratios were expressed as ratios relative to those in a region of interest of the same size in the contralateral homologous normal-appearing brain parenchyma. Mann–Whitney and Fisher's exact tests were used to evaluate relationships between MGMT promoter methylation status and imaging variables.

Results: ADC values tended to be higher in the methylated HGGs than in the unmethylated HGGs (p = 0.055), the ADC ratio was significantly higher in the methylated tumors versus the unmethylated tumors (p = 0.032). The FA and FA ratio showed significantly lower values in the methylated HGGs as compared with those in the unmethylated HGGs (p = 0.006 and p = 0.007). In contrast to the DTI parameters, the rCBV ratio from PWI did not reveal a significant difference between the methylated group and the unmethylated group (p = 0.380). The f values of methylated HGGs (0.156 +/- 0.039 [standard deviation]) were significantly larger than those of unmethylated HGGs (0.066 +/- 0.031) (P = .003). The D* values of unmethylated HGGs (21.99 x 10^{-3} mm^2/sec +/- 19.01) were significantly smaller than those of methylated HGGs (42.64 x 10^{-3} mm^2/sec +/- 20.17) (P = .022) (Figure 1). Regarding imaging features, only ill-defined margin was seen more frequently in the methylated group than in the unmethylated group (45.5% versus 7.7%, respectively, p = 0.048).

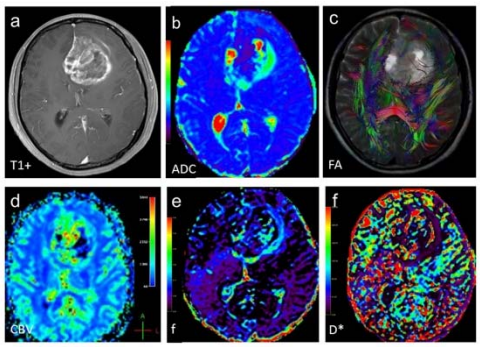

Figure 1: High-grade glioma with a methylated MGMT promoter. a: axial post-contrast T1WI, b: axial ADC map, c: axial FA map, d: CBV map, e: f map, f: D* map. Notice that the enhancing tumor is poor defined with moderate peritumoral edema and nodular enhancement. The pathological diagnosis is glioblastoma (WHO grade IV). The enhancing solid tumor shows higher ADC, lower FA and higher perfusion parameters as compared to the contralateral white matter.

Discussion: The differences of the ADC may mostly depend on the methylation status of the MGMT promoter rather than the tumor grading or proliferation. The tumors with a methylated MGMT promoter may have more heterogeneous or have lower cellularity as compared with the tumors with an unmethylated MGMT promoter [2]. Our study has suggested that the greater destruction of the white matter that occurred due to infiltrative neoplasm, the lower is the fractional anisotropy in the HGGs. However, the underlying mechanisms for the lower FA in tumors with a methylated MGMT promoter are unknown. Among several perfusion parameters, the regional rCBV derived from PWI and f and D* from IVIM are the most potent imaging parameters, and it is a surrogate marker for differentiation between the different MGMT promoter methylation status [3].

Conclusion: This study demonstrates that the MGMT promoter methylation status is associated with a specific imaging feature (an ill-defined margin) and several imaging parameters (a higher ADC, lower FA and higher perfusion parameters) of HGGs. Our results imply that preoperative imaging may predict the MGMT promoter methylation status, which is of paramount importance for predicting the treatment response to chemotherapy with an alkylating agent. Perfusion measurement with IVIM, because it is intrinsically local and quantitative, deserves more attention and further development.

References: [1] Stupp R, et al. N Engl J Med 2005; 352: 987-996. [2] Sunwoo L, et al. J Magn Reson Imaging 2012 (in press). [3] Moon WJ,et al. Neuroradiology 2012; 54: 555-563