Glioma Grading: Comparison of Parameters from Dynamic Contrast-enhanced (DCE) MRI, Apparent Diffusion Coefficient (ADC), and Fractional Anisotropy (FA)

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Purpose: The purpose of this study is to evaluate permeability parameters such as transfer constant (K^{trans}), extravascular extracelluar space (v_e), rate constant (K_{ep}), and blood plasma volume (v_p), ADC value, and FA value in glioma grading.

Methods: This retrospective study was waived for patient's consent from institutional review board. Forty one patients (53.12±18.62 year-old) with pathologically proven gliomas were included in this study. There were 12 low-grade gliomas (WHO grade 1 and 2) and 29 high-grade gliomas (WHO grade 3 and 4). Preoperative MRI was taken using 3.0-T system and 8-channel SENSE head coil. Dynamic contrast enhanced MR images, ADC maps, and 32-directional FA maps were obtained in all of the patients and they were all applicable to the analysis. For dynamic contrast-enhanced (DCE) MRI, precontrast T1-weighted images were obtained with those parameters: FOV=240mm; Matrix 192x192; slice thickness=3mm. After precontrast scan, 60-dynamic contrast enhanced T1-wighted images were taken with same MR parameters and injection of Gadovist (0.1mL/Kg) at a rate of 2mL/sec. Total scan time for dynamic contrast-enhanced (DCE) MRI was less than 7 minutes. Permeability parameters were calculated by off-line Pride tools provided by Philips Medical System, which is based on the pharmacokinetic model of Tofts[4]. Region of interest (ROI) for arterial input function was drawn on M1 segment of middle cerebral artery, ipsilateral to the glioma. ROI for permeability parameters was drawn at the area of maximal enhancing solid portion of the tumor, which was considered the highest grade of the tumor. ADC values and FA values were measured at the same ROI as DCE-MRI. FA value was also measured in contralateral normal-appearing white matter for calculating FA ratio (tumor to contralateral normal-appearing white matter). Mann-Whitney U test was used to analyze those parameters (K^{trans}, v_e, K_{ep}, v_p, ADC value, and FA ratio) between low-grade gliomas (WHO grade 1 and 2) and high-grade gliomas (WHO grade 3 and 4). Variables with *P* value less than 0.1 in Mann-Whitney U test were chosen for multivariate logistic regression analysis to find the most predictive variable to differentiate the high grade gliomas from the low grade ones. Statistical significance was set at $P < 0.05$.

Results: High-grade gliomas showed higher value of transfer constant (K^{trans}) and higher value of extravascular extracelluar space (v_e) compared with low-grade gliomas (*P* value<0.05). Transfer constant (K^{trans}), extravascular extracelluar space (v_e), and ADC value (table 1) were chosen for multivariate logistic regression analysis. When multivariate logistic regression analysis was performed, the most predictive parameter for differentiating gliomas between high and low grade was extravascular extracelluar space (v_e) (*P* value<0.05).

WHO grade	K^{trans} (min^{-1})	v_e	k_{ep}	v_p	ADC ($*10^{-3}mm^2/s$	FA ratio[+]
High grade[*]	0.088±0.087	0.207±0.125	0.392±0.259	0.039±0.041	1.089±0.296	0.505±0.362
Low grade[*]	0.053±0.085	0.100±0.151	0.337±0.280	0.032±0.017	1.231±0.249	0.534±0.274
P value	0.023	0.007	0.810	0.921	0.088	0.506

Discussion: DCE-MRI has strong points in quantification of permeability parameters regardless of the biologic situations and better spatial resolution within reasonable imaging time. Transfer constant (K^{trans}) from dynamic contrast-enhanced (DCE) MRI has shown efficient in glioma grading. In contrast to transfer constant (K^{trans}), extravascular extracelluar space (v_e) has been underused for glioma grading. Extravascular extracelluar space (v_e) has been considered an index of tumor necrosis and an inverse index of tumor cellularity. A recent longitudinal research using in-vivo glioma imaging in mouse model showed a progression of tumor vascularization, permeability, and increased extravascular extracelluar space (v_e) with tumor growth[2]. Marked increase of extravascular extracelluar space (v_e) in the latter growth stage of high grade glioma has been observed in this study. Another DEC-MRI based study in human glioblastoma multiforme about a candidate biomarker of extravascular extracelluar space (v_e) in comparison of apparent diffusion coefficient (ADC) demonstrated no correlation between ADC and v_e. However, the study suggested the different aspects of the parameters about tumor microenvironment[3]. Therefore, comprehensive evaluation about permeability parameters should be considered.

Conclusions: Transfer constant (K^{trans}) and extravascular extracelluar space (v_e) can be used in differentiating high-grade and low-grade gliomas. Extravascular extracelluar space (v_e) was the most predictive parameter using DCE-MRI in our series. Further investigation of extravascular extracelluar space (v_e) is needed in this stage.