DCE and DWI in Evaluating Grades of Gliomas

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Introduction: Abnormal neovascularity is a biomarker of a brain tumor and alterations in the neovascularity with tumor grade result in hemodynamic changes (1). Hence rCBV calculated from DSC perfusion data has been successful applied to evaluate grades of gliomas (2). DCE perfusion is emerging as a powerful tool for differentiating the tumor grade because the technique provides several parametric information of tumor vascularity, such as Ktrans, Kep and ve (3). We hypothesized that micro vascularity changes related to the tumor grade can be reliably detected with DCE and that vessel permeability (i.e., leakage, ~Ktrans) of the brain tumors increase with the grade. In this study, we used DCE perfusion and diffusion weighted imaging (DWI) techniques on a group of patients with variable grades of gliomas. Our aims were to evaluate relationships between the tumor grade and perfusion and diffusion parameters and to seek out one of the most sensitive and specific parameters for demonstrating the changes in the tumor vascularity, capillary integrity and cell cellularity with the tumor grades.

Materials and Methods: 22 glioma patients (5GBMs(grade 4), 7astrocytomas(grade 3), 7astrocytomas(grade 2), and 3astrocytomas(grade 1), the high grades (4 and 3) N=12; the low grades (2 and 1) N=10) were studied by applying a 1.5 T Siemens Sonata MR scanner with a standard head coil. The imaging volume was first localized by using a T1 weighted SE pulse sequence (TR/TE=450/10ms, slice thickness=5mm, and 10 axial slices). DWI was performed by using a SE EPI pulse sequence (TR/TE=2300/72ms and b-factor=1000 s/mm^2). The DCE perfusion imaging dynamic series for the contrast bolus tracking was performed by using the multi slice 2D Turbo-flash with a 20° flip angle over a period of 6 minutes for a total of 90 volumes. The contrast agent was administered through a cannula that had been placed in the antecubital vein. After the acquisition of the first five volumes of the dynamic series (20 seconds), 0.1 mmol of Gd per kilogram of body weight was injected at 4 mL/sec. After the DCE scan, the T_1 weighted SE acquisition was performed to provide position matched high resolution images for comparison with the perfusion and diffusion maps. Ktrans (1/miute), Kep(1/miute), and ve (%) maps were generated by applying the NORDICIC software (4), and ADC (mm^2/s) values were obtained from DWI by using Siemens VE31G software. An unpaired T-test for Ktrans, Kep, ve and ADC values for tumor ROIs in the tumor grade groups was performed. A *P* less than 0.05 for a parameter was considered as statistically significant. Calculations of sensitivity and specificity for a parameter were performed by using the MEDCALC software (5).

Results: Mean ± standard deviation for Ktrans, Kep, ve and ADC in the tumor grades of 4 to 1 were listed in Table 1, and the *P* values for the Ktrans, Kep, ve and ADC values in the tumor grade groups were listed in Table 2. A threshold of Ktrans value for distinguishing the low (N=10) with high (N=12) grade gliomas was found as 0.8 and plotted as a straight line in Figure 1. The correlations between Ktrans or ADC and grades were fitted by linear lines and shown in Figures 2 a & b.

Discussion and Conclusions: The approximately four time increase in Ktrans and Kep (Table 1) of the high grade (3 &4) comparing with the ones of the low grade (1 &2) implies that blood vessels associated with the high grade gliomas were leaky. Considering the process of angiogenesis, the increased values of the Ktrans is consistent with the characteristics of decreased tumors' capillary integrity with the grades. There is a difference between the low and high grade gliomas for Ktrans, and differences between grade 1 and grades 2, 3 and 4 for Kep, and differences between grade 1 and grade 3 and 4 for ve (Table 2). Studies on applying DSC (2) and ASL (6) to predict grades of gliomas found rCBV and CBF can distinguish low with high grade gliomas. Our results of Ktrans are consistent with other studies. The threshold of Ktrans as 0.8 (Figure 1) for differentiating the low and high grade provided a sensitivity= 92 and a specificity=90. The increased permeability of gliomas suggested by Ktrans, increased lineally (R^2=0.5936) with the tumor grades (Figure 2a). ADC values for the variable grade tumors were not different between any two tumor grades (Table 2) suggesting that the change of tumor cellularity was not significant (R^2=0.0887) (Figure 2b). Our results from DCE and DWI suggest Ktrans (~permeability) is the most sensitive and specific parameter for separating the low from high grade gliomas, and the threshold of Ktrans values for distinguishing the low from high grade gliomas was found as 0.8 (sensitivity= 92 and specificity=90).

References: 1. Law, M, et al., Radiology, 2008, 247:490. 2, Jackson, A., BJR, 2003, 76:S159. 3, Cha. S, et al., AJNR, 2006, 27:409. 4. Nordic IC lab. 5. Mediclac com. 6. Chawla, S et al., AJNR, 2007, 28:1683.

Table 1. Tumor's mean Ktrans, Kep, ve & ADC values in 4 grades.

Grade	Ktrans(1/min)	Kep(1/min)	ve	ADC(mm^2/s)
4	1.37±0.34	6.28±2.50	0.26±0.16	111.64±7.57
3	1.08±0.35	6.84±3.10	0.22±0.08	119.48±18.13
2	0.48±0.16	2.85±3.18	0.14±0.16	144.97±6.79
1	0.15±0.05	0.074±0.07	0.03±0.14	132.8±4.6

Table 2. *P* values for Ktrans, Kep, ve & ADC values in grade groups.

Grade	*P* (Ktrans)	*P*(Kep)	*P*(ve)	*P*(ADC)
1 vs 2	0.116	0.033	0.116	0.651
1 vs 3	0.0001	0.006	0.027	0.631
1 vs 4	0.006	0.033	0.006	0.403
2 vs 3	0.003	0.052	0.156	0.243
2 vs 4	0.005	0.141	0.061	0.156
3 vs 4	0.115	0.266	0.267	0.666

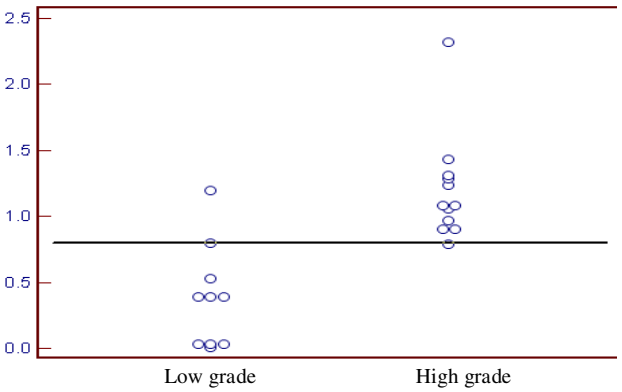
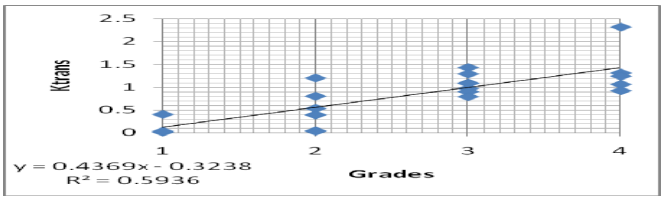


Figure 1. The threshold of Ktrans value (0.8) shown as the straight line for distinguishing the low (N=10) with the high (N=12) grade gliomas.



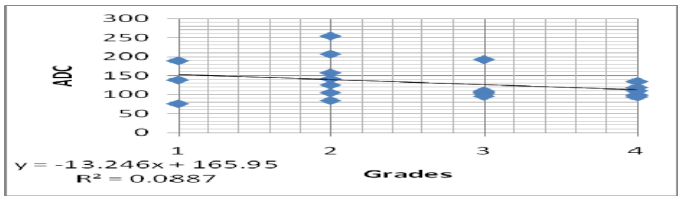


Figure 2. Ktrans vs grades (a) & ADC vs grades (b). (a) (b)