Quantitative Correlation of Volume Transfer Coefficient Ktrans with Histopathologic Grades of Gliomas

N. Zhang[1,2], Z. Deng[2], L. Meng[3], X. Wang[3], W. Liao[3], and B. L. Hou[4,5]

[1]Paul C. Lauterbur Research Center for Biomedical Imaging,Paul C. Lauterbu, Chinese Academy of Science, Shenzhen, Guangdong, China, People's Republic of, [2]1Institute of Biomedical Engineering, School of Info-physics and Geomatics Engineering, Central South University, Changsha, Hunan, China, People's Republic of, [3]Department of Radiology, XiangYa Hospital of School of Medicine, Central South University, Changsha, Hunan, China, People's Republic of, [4]Radiology, West Virginia University, Morgantown, WV, United States, [5]Central South University, Changsha, Hunan, China, People's Republic of

Introduction

The breakdown of blood-brain barrier (BBB) in gliomas results in the increment of microvascular permeability: a surrogate marker to assess malignant degree of gliomas [1]. The volume transfer coefficient of contrast agent (CA) from a plasma space to an extravascular extracellular space (EES), as defined K^{trans}, has been used to characterize the microvascular permeability quantitatively [2-3]. Since knowing the grades is very important for the tumor treatments, and applying T1 perfusion MRI data for evaluating the grades is becoming popular, we presented the results of K^{trans} for the gliomas with four grades by using a T_1-weighted dynamic contrast enhancement magnetic resonance imaging (DCE-MRI) technology and a modified Tofts' model, and also investigated to apply K^{trans} , K_{ep}, K_{el}, V_e, and V_p obtained from the T1 perfusion data analyses for evaluating the grades.

Materials and Methods

28 patients (10 females, 18 males; age range, 19–74 years with mean of 47.11±14.18 years) with gliomas were scanned by applying a 1.5 T Siemens Syngo MRI scanner. The histopathologic analyses of the tumors demonstrated there were 14 low grades (8 grade I and 6 grade II) and 14 high grades (6 grade III and 8grade IV). After a T1-weighted high resolution anatomical imaging scan (TR/TE=450/10ms, slice thickness=5mm, and 10 axial slices), each patient was injected intravenously by Gd-DTPA (0.1 mmol of the CA per kilogram of body weight) at 4 mL/sec., and a 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. We modified Tofts' model [4] by more accurately considering an artery input function (AIF), for which was derived from the time course of the DCE scan within the tumor artery of each patient. All the DCE data in the regions of interest (ROIs) of tumors and arteries were processed via a pharmacokinetic analysis and a nonlinear least square fitting method. Quantitative parameters K^{trans}, the flux rate constant of CA from extravascular extracellular space to plasma space (K_{ep}), the elimination rate of CA (K_{el}), EES volume fraction (V_e), and plasma volume fraction (V_p) were obtained from the modified Tofts' model. A Kruskal-Wallis H-test and a Mann-Whitney U-test for these parameters was performed with a value of $p<0.05$ regarded as significance for differentialting the grades of the tumors. The Mann-Whitney U-test was used to compare the two parameters between any two grades and between low grade and high grade.

Results

The images for the tumors with the grade I to IV (from the left to the right) and the tumors' ROIs (in red cycles) were showed in Figure 1, and the concentration-time courses (CTCs) and AIFs from the DCE data in the tumor ROIs and artery ROIs (not be shown here) were plotted in Figure 2. Mean ± standard deviation for K^{trans}, K_{ep}, K_{el} V_e, and V_p parameters in the four grades were listed in Table 1. K^{trans} and V_e increase with the tumor grades, and the increase is statistical significance since the results of the Kruskal-Wallis H-tests on the five parameters expose only the K^{trans} and V_e values have p values less than 0.05 (Table 2). The results from the Mann-Whitney U-tests for comparing any two parameters between any two grades or between low grade (I and II) and high grade (III and IV) were listed in Table 3. Normalized K^{trans} and V_e values verse the grades were plotted in Figure 3.

Discussions

In current study, the modified Tofts' model was applied to analyze the DCE data for establishing the relationships between K^{trans}, K_{ep} , K_{el} V_e, and V_p parameters and the tumor grades. It was known that K^{trans} depends on both blood flow and the product of capillary wall permeability-surface area, and the parameter of V_e is the ratio of quantity of CA leaked into the EES to that returned to the plasma space. As shown in Table 1 and Fig.3, K^{trans} and V_e increase with the increase of the grades, indicating that higher of malignant degree is, higher leakage of the CA into EES is. The data in the Table 2 suggest that there are no statistical significances for K_{ep}, K_{el}, and V_p between any two grades ($p>0.05$). K^{trans} and V_e (Table 3) are good parameters for distinguishing any two histopathologic grades except for the group III and IV. The normalized values for K^{trans} and V_e in Fig. 3 exhibit larger increment in the K^{trans} values form the grade Ⅱ to Ⅲ. Even both K^{trans} and Ve are capable of distinguishing the high grades (III and IV) with the low grades (I and II) (Table 2), and the K^{trans} seems a better parameter for evaluating the tumor grade, especially for differentiating high grades with the low grades (Fig 3).

References

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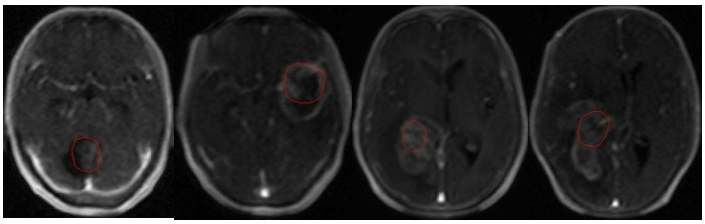

Fig.1 Gliomas I to IV (from left to right) and the tumor ROIs (red circles)

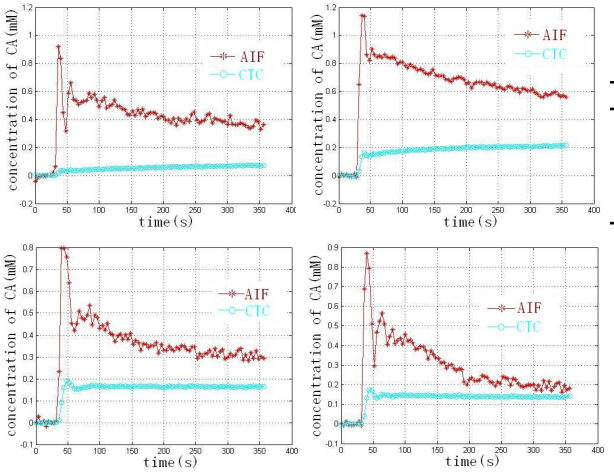

Fig.2 CTCs within the ROIs in the Fig.1 and AIFs for the tumors in Fig.1.

Table 1 Mean ± standard deviation for five parameters in the grades

grade	K^{trans}/min^{-1}	k_{ep}/min^{-1}	K_{el}/min^{-1}	V_e	V_p
I	0.02 ± 0.02	0.29 ± 0.10	0.42 ± 0.21	0.10 ± 0.14	0.05 ± 0.02
II	0.05 ± 0.03	0.21 ± 0.10	0.25 ± 0.15	0.29 ± 0.24	0.04 ± 0.02
III	0.18 ± 0.06	0.23 ± 0.06	0.35 ± 0.11	0.59 ± 0.17	0.03 ± 0.02
IV	0.22 ± 0.04	0.26 ± 0.04	0.43 ± 0.10	0.81 ± 0.21	0.04 ± 0.02

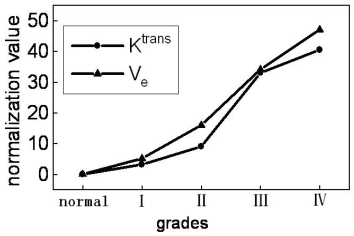

Fig. 3 normalizing values vs. grades

Table 3 Mann-Whitney U-test

grade	K^{trans}/min^{-1}	V_e
I vs II	0.039	0.039
I vs III	0.002	0.011
I vs IV	0.001	0.003
II vs III	0.010	0.033
II vs IV	0.002	0.006
III vs IV	0.245	0.136
low vs high	<<0.05	<<0.05

Table 2 Kruskal-Wallis H-test

parameter	χ^2	P
K^{trans}/min^{-1}	21.167	<<0.05
k_{ep}/min^{-1}	4.241	0.237
K_{el}/min^{-1}	6.398	0.094
V_e	16.677	0.001
V_p	0.881	0.830