A Study of Correlation between Neovascularity and Tumor Infiltration of Gliomas Using Perfusion and Diffusion MRI

S. Yang[1], J. L. Villano[2], G. Srinivasan[1,3], K. R. Thulborn[1,4], and X. J. Zhou[1,5]

[1]Center for MR Research, Univ. of Illinois Medical Center, Chicago, Illinois, United States, [2]Department of Medicine, Univ. of Illinois Medical Center, Chicago, Illinois, United States, [3]Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, United States, [4]Departments of Radiology and Biophysics, Univ. of Illinois Medical Center, Chicago, Illinois, United States, [5]Departments of Neurosurgery, Radiology, and Bioengineering, Univ. of Illinois Medical Center, Chicago, Illinois, United States

INTRODUCTION

Neovascularity and tumor infiltration are important characteristics defining glioma growth and aggressiveness [1]. Although related, they reflect different pathological processes. With its capability of quantifying hemodynamic parameters, perfusion MRI has been widely used to investigate tumor neovascularity. However, it has had limited utilities in identifying tumor infiltration in peritumoral regions [2]. Over the past few years, diffusion tensor imaging (DTI) has demonstrated promise for revealing white-matter regions that are predominated infiltrated by tumors [3-5]. The goal of this study is to investigate the possible correlation between tumor neovascularity and infiltration of low-grade (LGGs) and high-grade gliomas (HGGs) by employing both perfusion and diffusion imaging techniques.

METHODS

Twenty-four patients with newly diagnosed LGGs (WHO grade II; n=13; age range: 18~65 years old; male/female: 7/6) and HGGs (WHO grades III and IV; n=11; age range: 19~74 years old; male/female: 10/1) underwent MRI scans prior to treatment. The MRI protocol included DTI and perfusion scans with dynamic susceptibility contrast (DSC), in addition to conventional scans consisting of pre- and post-contrast T1-weighted, pre-contrast T2-weighted, and FLAIR series. All MRI scans were performed on a GE 3.0 Tesla Signa HDx scanner (General Electric Healthcare, Waukesha, Wisconsin) with an eight-channel head coil. The DTI scan was carried out using a customized single-shot EPI pulse sequence with additional capability to compensate for residual eddy currents. The number of diffusion gradient directions was 27, and the b-value was 1000 s/mm^2. Other acquisition parameters included TR =5225ms, TE = 85.7ms, FOV = 20cm, and matrix size = 128× 128. The perfusion scan was performed with a gradient-echo EPI sequence, following a single dose of IV injection of gadodiamide (Omniscan, General Electric Healthcare) at a rate of 5ml/s. The key perfusion acquisition parameters were TR = 1200ms, TE = 30ms, flip angle = 60°, matrix size = 64×64, and scan time = 48s.

The images from the DTI scan were processed using DIVE (Diffusion Imaging Visualization Environment) software developed using IDL (ITT Visual Information Solutions, Boulder, Colorado) in our laboratory. Two DTI parameters, fractional anisotropy (FA) and regional fiber coherence index (r-FCI) [6], were evaluated at regions of interest (ROIs) selected from the peritumoral regions. For the HGG patients, ROIs were chosen in the white-matter fiber tracts suspected of tumor infiltration within a ~2cm zone outside the enhancing rim in the post-contrast T1-weighted images. For the LGG patients, ROIs were selected on the fiber tracts affected by the tumor as revealed by FLAIR and T1-weighted images. The perfusion images were analyzed using a commercial software package, FuncTool, provided by the scanner manufacturer. The selected ROIs in the perfusion images were co-registered with the corresponding ROIs used in the DTI analysis. The rCBV value in the ROIs was evaluated after an arterial input function was measured. A total of 66 ROIs in the peritumoral regions were analyzed for the HGG group, and 79 for the LGG group. For each ROI in the peritumoral regions, FA, r-FCI, and rCBV were also evaluated at the ROI located at the corresponding tract on the contralateral side, and used as controls. Correlations between the DTI parameters and the rCBV were evaluated by a linear regression.

RESULTS

Figure 1 shows representative anatomic, DTI, and perfusion images selected from the HGG (top row) and LGG (bottom row) groups. Data used for evaluating the correlations are shown as scatter plots in Fig. 2 for both patient groups. The correlation coefficients obtained from the linear regression, as well as other statistical parameters, are summarized in Table 1. A very weak (negative) correlation was observed between rCBV and r-FCI for HGGs (r= -0.31; P=0.01), while no statistically significant correlation was found for LGGs (P=0.72). No correlation was observed between rCBV and FA for either patient group (HGGs: P= 0.24, LGGs: P=0.7).

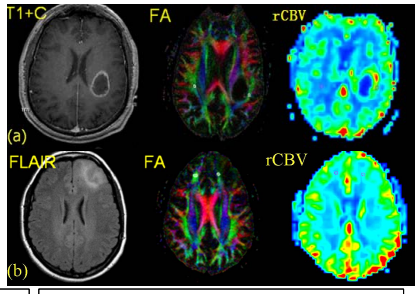

Fig.1 (right) Representative images of HGG (a) and LGG (b) patients.

Table 1. Correlations between rCBV and FA/r-FCI.

Correlation	rCBV					
	HGGs (N=66)			LGGs (N=79)		
	r	t	P	r	t	P
FA	-0.15	1.196	0.24	-0.04	0.392	0.7
r-FCI	-0.31	2.567	0.01	0.04	0.358	0.72

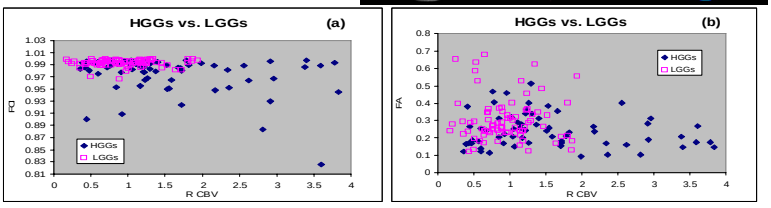

Fig. 2 Scatter plots of rCBVvs. r-FCI (a) and rCBV vs. FA (b) for patients with gliomas.

DISCUSSION AND CONCLUSIONS

Peritumoral regions of gliomas are known to harbor infiltrating tumor cells, vasogenic edema, and/or neovascularity [1]. Although a possible correlation between neovascularity and tumor cell infiltration has been suggested [2, 7], no such evidence of correlation between neovascularity and vasogenic edema has been established. Previous DTI studies indicate that reduced FA in the peritumoral regions is predominantly caused by vasogenic edema [3-5], which is consistent with the lack of correlations shown in Fig. 2b for both patient groups. Previous studies also suggest that r-FCI provides better specificity than FA for identifying fiber tracts predominantly infiltrated with tumor in the peritumoral regions [4, 6]. For the LGG group, the high r-FCI values suggested lack of tumor infiltration, and the relatively low rCBV values may indicate that there was no significant neovascularity. For the HGG group, the ROIs with reduced r-FCI values most likely reflected areas with significant tumor infiltration. Some of these ROIs exhibited correlations with the increased rCBV as shown in Fig. 2a. However, a significant number of ROIs did not show such correlation. This suggests that neovascularity and tumor cell infiltration may represent two interactive but relatively independent pathologic processes. This could also suggest that in some cases neovascularity and tumor cell infiltration may not occur at the same time during glioma growth and development. A time-course study would be needed to provide new insights into the temporal relationship between neovascularity and tumor infiltration. In summary, our results in general do not support a *spatial* correlation between neovascularity and tumor infiltration for both LGGs and HGGs. However, the combination of DTI and perfusion imaging may be useful to reveal the *temporal* relationship between neovascularity and tumor infiltration through a time-course study.

REFERENCES

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