

## A multiparameter DSC study demonstrates the best predictor of brain tumor grade.

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### Introduction

The study of brain tumor angiogenesis for the diagnosis of glioma has potential benefits in therapeutic management. In this study we employed a noninvasive imaging technique, dynamic susceptibility contrast (DSC) MRI to estimate various parameters such as relative cerebral blood volume (rCBV), cerebral blood flow (CBF), mean vessel diameter (MVD) and mean transit time (MTT). The main objective of this study is to determine which of these parameters best predicts glioma tumor grade.

### Methods

All MRI studies were performed on either a 1.5T GE Signa System fitted with a 12" local gradient coil and a quadrature transmit-receive birdcage RF coil (IGC-Medical Advances, Milwaukee, WI) or a 1.5T GE CV Scanner. A 0.10 mmole/kg dose of Gadodiamide (Omniscan; Nycomed Amersham, Princeton, NJ) was administered to diminish T1 effects that might result from agent extravasation. Next, simultaneous GE/SE-EPI images were acquired for 1 minute before and 2 minutes after a 0.2 mmole/kg bolus injection. Five, 7 mm slices were acquired at TE(GE)/TE(SE) = 30ms/109.1ms with fat suppression, TR=1s, a FOV=24cm and matrix = 64x64. Finally, conventional post-contrast T1-weighted images were acquired (SE, TE/TR = 11ms/500 ms, matrix = 256x256).

Analysis of functional neuro-images (AFNI) tool was used for data analysis. The rCBV maps were estimated as the area under the concentration-time curve following rapid injection of a paramagnetic contrast agent calculated using trapezoidal numerical integration method over the entire concentration-time curve and T1 leakage correction method previously described.<sup>1</sup> Voxel-wise estimates of rCBV were normalized to their average uninvolved white matter rCBV. Using singular value decomposition, the intravoxel tissue residue function was derived by deconvolving the tissue concentration time curves with the AIF. CBF estimates were determined as the maximum point of the residue function. Mean transit time (MTT) was estimated as  $MTT=CBV/CBF$ . Mean vessel diameter (MVD) was estimated as the ratio of the GE and SE concentration-time curves,  $(\Delta R2^*)/(\Delta R2)$ .

To evaluate the DSC parameters, 49 subjects with confirmed diagnosis of glioma and tumor grade were studied. Out of 49 subjects 2 were diagnosed with grade I tumor, 8 with grade II tumor, 8 with grade III tumor and 31 with grade IV tumor. ROIs were drawn for uninvolved white matter, tumor, and normal-appearing contralateral brain. Statistical analysis was performed using GraphPad Prism version 4.0a for Mac OS X (GraphPad Software, San Diego, CA). A Spearman rank correlation test was performed to compare the CBV, CBF, MTT, and MVD to tumor grade. A *P*-value less than or equal to 0.05 was considered statistically significant.

### Results and Discussion

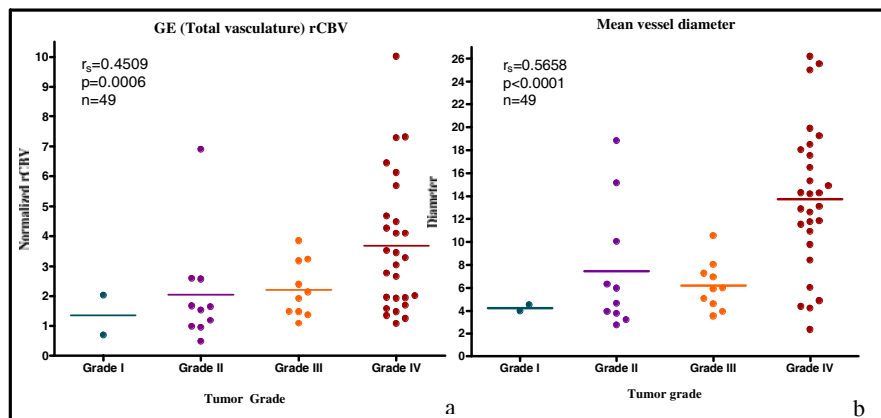


Figure 1: Normalized GE rCBV vs Tumor Grade and Mean Vessel Diameter vs Tumor Grade

Figure 1a displays the results of average normalized GE rCBV versus tumor grade. GE rCBV, a representation of the total blood volume present in the tumor vasculature, was found to be highly correlated with grade, with a *p* value = 0.006. Figure 1b displays the results of the average MVD versus tumor grade. MVD also was highly correlated with tumor grade, with a *p* value < 0.0001. These results confirm our previous studies that have shown that the DSC parameters most predictive of tumor grade are GE rCBV and MVD.<sup>2</sup> MTT, CBF, and microvascular blood volume were also evaluated but did not show a significant correlation with tumor grade. The results of this study support the hypothesis that monitoring changes in DSC MRI parameters, such as GE rCBV and MVD, could be useful in determining therapy effectiveness in patients with malignant brain tumors. Further studies are planned to investigate this potential.

### References

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