A Marker of Vascular Tortuosity (Relative Recirculation) in Gliomas: Comparison with Blood Volume and Tumor Grade

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Introduction
The relationship between regional blood volume (rBV) measured by MRI and the grade of tumor was first established for glioma [1]. Similar relationships between blood volume and grade or prognosis have since been described for many tumor types. This relationship is believed to reflect the increased angiogenic drive in high-grade tumors and there is considerable interest in using such measures to provide prognostic information and to study therapeutic responses in both clinical practice and therapeutic trials. Angiogenic activity is associated with several pathological features that can be studied with MRI based techniques. These include microvascular density, increased endothelial permeability and vascular tortuosity. We have recently described a new metric known as relative recirculation (rR), which provides an indicator of vascular tortuosity [2]. Parametric maps of rR show elevation in aggressive tumors such as glioma but not in less aggressive tumors such as meningioma. This study examines the relationship between rR, rBV and tumor grade in patients with glioma.

Methods
Imaging was performed on 10 patients with suspected cerebral glioma. All patients had had an enhancing mass diagnosed on previous CT or MRI. All diagnoses were subsequently histologically confirmed from resection or multiple biopsy specimens. Diagnoses were grade III astrocytoma (n=5), anaplastic astrocytoma (n=2) and glioblastoma (n=3). All imaging was performed prior to biopsy or definitive treatment although all patients were receiving steroids to reduce intracranial pressure. Imaging was performed using a 2D FFE-EPI sequence with heavy T2* weighting (TR 262, TE 30, FA 35°, Matrix 128x128). The acquisition collected 9 x 5mm thick slices and the temporal resolution was 1.89s per acquisition. Contrast agent (0.1mmol/L, Gd-DTPA-BMA, Omniscan, Nycomed) was injected 10 minutes prior to scanning in order to remove residual relaxivity effects [1]. A further dose of contrast agent was administered during image acquisition. Images were transferred to an independent workstation for analysis. Perfusion data sets were used to calculate T2* rate changes (ΔR2*) and the resulting maps were used to generate parametric maps of rBV and rR as we have described previously [1]. Tumors were manually segmented from post-contrast images and the resulting volumes of interest (VOI) were applied to parametric maps of rBV and rR.

The distribution of volume of interest data was tested for asymmetry using analysis of skewness (S) where:

\[ S = \frac{\text{mean-mode}}{\text{Standard Deviation}} \]

Mean values of rR and rBV were plotted against tumor grade and compared using analysis of variance. Measures of the shape of the distribution including the position of 95th - 75th centiles and skewness were also compared to grade.

Results
Measurements of rCBV from the VOI ranged from 357-3096 arbitrary units (AU) with a mean of 1877 and standard error of 910. The range of measurements for rR was 0.098-0.257 AU with a mean of 0.179 and standard error of 0.049. Values of rBV varied with tumor grade with higher mean values seen in higher-grade tumors (p<0.01). Mean values of rR did not vary significantly with tumor grade although a trend to lower values in high grade tumors was noted. Use of the 95th-75th centile points for rBV and rR, as an indicator of distribution shape, showed no significant difference between different grades of tumor. However the skewness of the distributions of rR was considerably different between grades with considerably greater skew seen in higher grade tumors. Although the number of patients in the study is small a plot of the skewness of rR against mean rCBV values suggests that these parameters provide complementary information about tumor microvasculature both of which are independently related to tumor grade.

Discussion
The relationship between rBV and tumor grade is well recognized and was first described by Aronen and colleagues in 1994. The measurement of vascular tortuosity using rR has been reported in only one previous publication [2] and was not compared to tumor grade. The results of this study suggest that rR provides an independent indicator of microvascular composition which is related to tumor grade. The use of the distribution skew as a surrogate measure is novel but is in keeping with the findings of previous workers that the shape of the distribution can reveal significant features not evident from simple parametric analysis.

References