THE EXTENT AND SEVERITY OF VASCULAR LEAKAGE AS EVIDENCE OF TUMOR AGGRESSIVENESS IN HIGH-GRADE GLIOMAS

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Purpose: MRI reveals heterogeneous regions within high-grade gliomas, such as a contrast-enhanced rim, a necrotic core, and non-contrast enhanced abnormalities. It is unclear which of these regions best describes tumor aggressiveness. We hypothesized that the vascular leakage volume, which reflects disorganized angiogenesis typical of glioblastoma, would be the best predictor of clinical outcome.

Method: Twenty patients with newly diagnosed high-grade gliomas underwent an IRB approved clinical MRI protocol prior to radiation therapy. MRI included anatomic imaging, and dynamic contrast enhanced (DCE) T2* weighted imaging during intravenous injection of a singe dose bolus of Gd-DTPA. Using an iterative algorithm (1), transfer constant of Gd-DTPA from plasma to tissue was estimated from DCE T2* weighted images, see Figure. The FLAIR tumor volume, post-Gd T1 tumor volume, tumor vascular leakage volume determined by DCE imaging, and volume of the contrast-enhanced rim seen on post-Gd T1-weighted images were defined. The potential for imaging characteristics to improve prediction of survival and time to progression over clinical parameters was tested in using a Cox multivariate regression model.

Results: We found that the vascular leakage volume of the tumor estimated by DCE imaging was the strongest predictor of survival ($p<0.012$) than the other tumor subvolumes, such as the FLAIR tumor volume ($p=0.09$), post-Gd T1 tumor volume ($p>0.6$), and the volume of the contrast-enhanced rim ($p>0.5$). When clinical parameters, the vascular leakage volume, and the mean vascular permeability were tested for prediction of survival, only the vascular leakage volume was selected as a significant predictor. However, when time to progression was tested as a dependent variable both the volume of vascular leakage and the mean of vascular permeability were selected as co-predictors, along with surgical status ($p<0.001$).

Discussions and Conclusion: Our findings suggest that for patients with high-grade glioma, time to progression after radiation therapy is influenced both underlying biological aggressiveness (vascularity) and spread of disease. In contrast, survival depends chiefly on the spread of disease at the time of presentation. The vascular leakage volume of the tumor appears to be a better marker for the extent of disease than the FLAIR tumor volume, post-Gd T1 tumor volume or the volume of the contrast-enhanced rim seen on the post-contrast T1 weighted images.

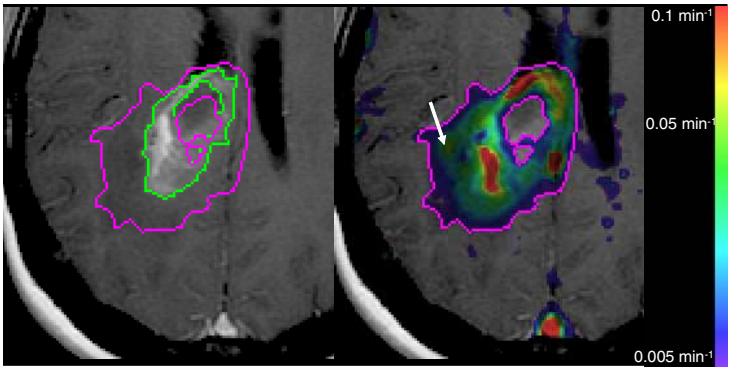

Figure. Post-contrast T1-weighted image (left) and the color-coded permeability map (right) overlaid on the post-contrast T1-weighted image. Green contours enclose the contrast-enhanced rim seen on theT1-weighted images while dark pink contours enclose the volume that has the vascular permeability to Gd-DTPA greater than 0.005 per minute.

1. Y. Cao, et al. JMRI (in press).