Predicting response to anti-angiogenic chemotherapy in patients with high-grade glioblastomas using MR perfusion imaging

R. Sawlani[1,2], J. Raizer, MD[3], S. W. Horowitz[1], W. Shin[1,2], S. A. Grimm[3], J. P. Chandler[4], R. Levy[4], C. C. Getch[4], M. Shah[1,2], and T. J. Carroll[1,2]

[1]Radiology, Northwestern University, Chicago, IL, United States, [2]Biomedical Engineering, Northwestern University, Evanston, IL, United States, [3]Neurology, Northwestern University, Chicago, IL, United States, [4]Neurosurgery, Northwestern University, Chicago, IL, United States

PURPOSE

Currently, response to anti-angiogenic therapy is variable, but durable responses are seen. Using MR perfusion imaging, the success of this therapy can be predicted for individual patients. *We hypothesize that change in tumor perfusion due to angiogenic inhibition can serve as an independent measure of patient response to anti-angiogenic chemotherapy in recurrent high-grade glioblastomas (GBMs).*

METHOD AND MATERIALS

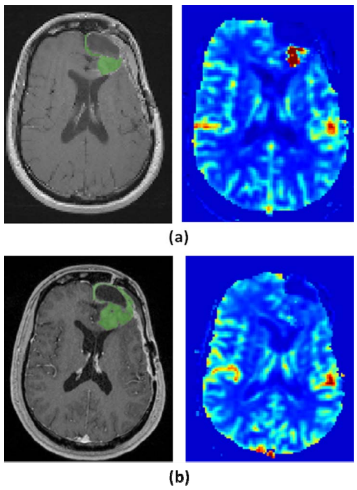

Figure 1. Images for one patient at (a) baseline and (b) six weeks later. T1 post-gadolinium images are on the left and CBV maps are on the right, with tumor ROIs in green on the T1 images. T1 images show slight growth in tumor size while perfusion images show a significant drop in tumor perfusion.

Twelve patients with pathologically proven recurrent high-grade GBMs were evaluated. All patients received Bevacizumab every 3 weeks at 15 mg/kg. Baseline images were acquired before drug administration and every 6 weeks thereafter until tumor progression or death. This interval between the start of treatment and tumor progression or death is defined as time to progression (TTP). MR perfusion images were acquired by tracking a bolus of contrast agent through the tissue and then analyzed to create cerebral blood volume (CBV) maps both with and without correction for contrast agent leakage. ROIs were then drawn using a partially-automatic segmentation algorithm to select the bright tumor voxels on an axial T1 post-Gd image, and relative CBV (rCBV) values were determined by normalizing to contralateral white matter.

We then measured the change in tumor perfusion between the baseline and first follow-up scans. The following parameters were used to define perfusion: Mean rCBV, Mean K2 (Leakage), or "hyper-perfusion volume" (HPV). We define the HPV as the percentage of pixels in the enhancing volume with an rCBV greater than a predetermined threshold. We used thresholds ranging from 1.00 to 3.00 in increments of 0.25 in order to determine the optimal value. The predictive value of each perfusion parameter was assessed by plotting them against TTP, and each plot was fitted using a least squares exponential regression to with the following equation:

$$TTP = A_0 e^{-\alpha(\Delta HPV)}$$

Where ΔHPV is the % change in HPV, TTP is time to progression in days, and A_0 and α are the constants being iterated for the regression. The correlation coefficient of each fit was used as a measure of the perfusion parameter's predictive power.

RESULTS

Figure 1 demonstrates how perfusion can change significantly over a period of 6 weeks, while tumor size remains similar. Tumor size yielded no correlation to TTP (R=0.30). Comparing TTP to each perfusion parameter, % change in HPV with rCBV > 1.75 yielded the optimum exponential correlation both with and without leakage correction, as shown in Figure 2 (n=12, R=0.92, p<0.01 for both plots). The data shows a longer TTP as the % change in HPV becomes more negative. Correlation coefficients were better without leakage correction than with correction for most perfusion parameters.

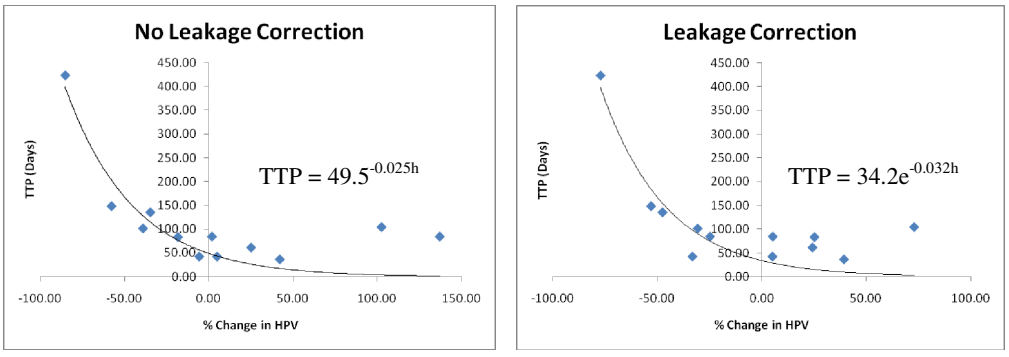

Figure 2. Plot of TTP vs. % change in HPV both without (left) and with (right) leakage correction. Both show exponential curve fits with R=0.92, p>0.01, indicating a statistically significant correlation between the two parameters. As % change in HPV becomes more negative, TTP rises indicating better response to therapy, following clinical reasoning.

CONCLUSION

The strength of the correlation between TTP and change in HPV indicates that using MR perfusion imaging and the above method, we can successfully predict patient outcomes to anti-angiogenic chemotherapy, thus allowing for better clinical use of this treatment.