Volume of Bolus Tracking Perfusion Abnormality Predicts Emergence of Contrast Enhancement in Glioblastoma Multiforme

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Introduction: External beam radiation therapy (XRT) is the most effective adjunctive therapy to control rapid tumor progression in high-grade gliomas following initial surgical resection. Due to the infiltrative nature of glioma growth, it is often difficult, if not impossible, to remove the entire tumor volume; hence subtotal resection is common. For radiation therapy planning, often the residual contrast enhancement, depicted on the immediate post-operative scan, and its immediate surroundings are targeted [1]. Contrast enhancement, however, represents an area of blood-brain barrier breakdown and may not be synonymous with malignancy or angiogenesis. Bolus tracking perfusion MR imaging has shown a potential role in assessing tumor angiogenesis indirectly [2,3] and may provide additional information on changes in tumor characteristics during irradiation. The purpose of our study was to correlate pre-irradiation bolus tracking perfusion abnormality with the post-irradiation contrast enhancement pattern in patients with glioblastoma multiforme (GBM). We hypothesized that larger residual volume of perfusion abnormality prior to irradiation would result in larger volume of contrast enhancement following irradiation.

Methods: MR imaging was performed on 14 patients (age 27-76, median age 60) with untreated GBM using conventional anatomical imaging and bolus tracking T2*-weighted echo-planar MR imaging. All patients underwent subtotal resection with minimal residual contrast enhancement. The patients were imaged serially immediately before and after surgery, 4 weeks after surgery but before irradiation, at the completion of irradiation, and at 2 months interval thereafter. The raw image data were transferred to a computer workstation and regions of interest (ROIs) were drawn on anatomic images to calculate the volume of contrast enhancing regions. During the first pass of the paramagnetic Gd-DTPA bolus, signal intensity drops on T2*-weighted images. The T2* signal intensity time series was converted to the change in relaxation rate or T2* relaxivity ($\Delta R2^*$), using the equation $\Delta R2^*(t) = [-\ln(S_{(t)}/S_{(0)})]/TE$. Peak height and percent recovery of the post bolus signal from the maximum $\Delta R2^*$ signal were calculated for each voxel. A model curve function was derived from averaging the time series data from normal appearing brain. The model curve was then used to generate the peak height and percent recovery maps. Peak height maps were thresholded to include only those voxels with peak heights greater than twice that of the model function.

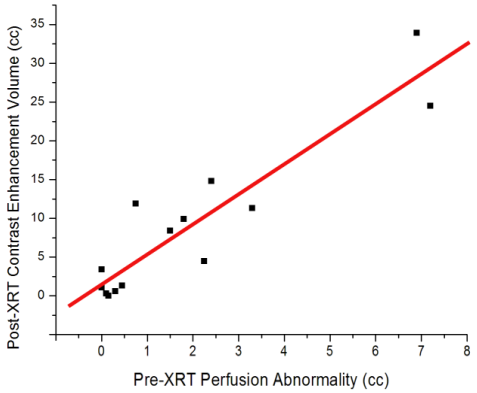

Figure 1: Volume of perfusion abnormality after pre-XRT vs. volume of contrast enhancement post-XRT (n=14, R^2=0.854).

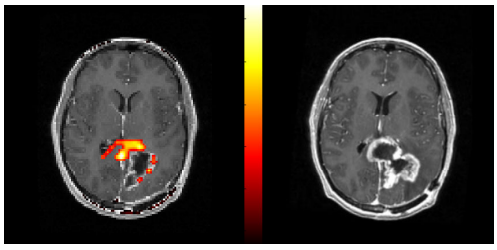

Figure 2: Left: Post-contrast SPGR image with perfusion abnormality map overlaid. Right: Post-contrast SPGR image post-XRT demonstrates increasing volume of CE in the regions of perfusion abnormality seen on the pre-XRT scan.

Results: The volume of residual perfusion abnormality before irradiation, defined as peak height of greater than twice the height of the normal model function peak, correlates with the volume of contrast enhancement on T1-weighted images on both the immediate post-XRT scan (n=14,R^2=0.854) and at two months post-XRT (n=8,R^2=0.934). There was poor correlation (n=10,R^2=0.178) between pre-XRT contrast enhancement and post-XRT contrast enhancement. For all 14 patients, the mean volume of perfusion abnormality was 1.9cc, and the mean volume of contrast enhancement in the immediate post-XRT scan was 9.0cc. For the eight patients with a two-month post-XRT scan, the mean volume of contrast enhancement for this scan was 12.6cc. Figure 1 illustrates the linear relationship between the volume of residual perfusion abnormality and immediate post-XRT contrast enhancement volume. Figure 2 shows a perfusion abnormality color map overlaid on a pre-XRT post-contrast SPGR image and the corresponding slice one month later in the post-XRT scan.

Discussion: The results of our study suggest that (a) there is a strong correlation between pre-XRT perfusion abnormality and emergence of contrast enhancement post-XRT in patients with GBM, and (b) there is no correlation between pre-XRT contrast enhancement volume and post-XRT contrast enhancement volume within a given tumor. We postulate that since most of the contrast enhancing portion of the tumor was removed during surgery, the residual perfusion abnormality prior to irradiation represented residual tumor that is vulnerable to XRT–induced microvascular damage. The emergence of contrast enhancement within the pre-existing perfusion abnormality following XRT probably represents dynamic changes in tumor microvasculature as opposed to true emergence of recurrent tumor or failure of therapy. The lack of correlation between pre-XRT and post-XRT contrast enhancement volume can be attributed in part to the fact that the contrast enhancement on a pre-XRT scan is nonspecific and may represent not only residual tumor, but also post-surgical granulation tissue. It is reasonable to assume that progression of contrast enhancement would be expected in regions of tumor but not in regions of post-operative scarring. Therefore, the pre-XRT residual perfusion abnormality may serve as a more accurate assessment of residual tumor than the immediate post-operative scan. Further investigations to correlate residual perfusion abnormality with time to progression and survival in patients with high-grade glioma may strengthen the validity of perfusion abnormality as a better target for radiation therapy planning.

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References:

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