Temporal Blood Flow Changes in High-Grade Gliomas During Early Stages of Radiotherapy For Prediction of Tumor Response to Treatment

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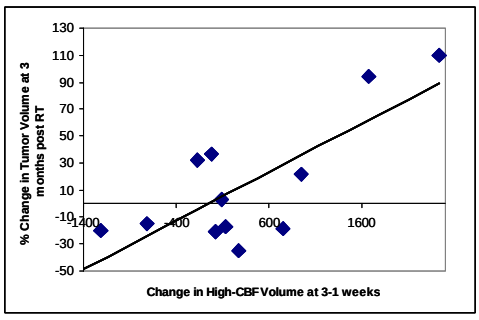
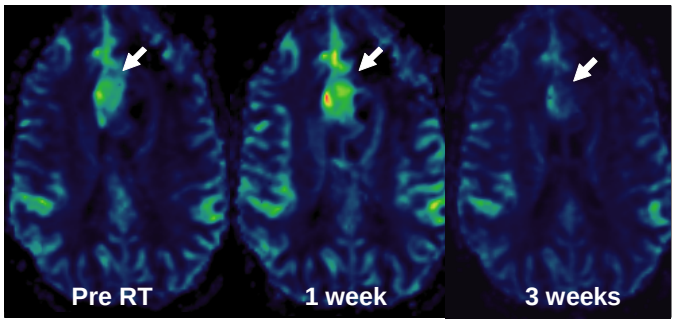
Introduction: The ability to use non-invasive imaging to assess tumor early response to fractionated radiation therapy (RT) could provide an opportunity to optimize individual patient treatment strategy. In this study, we investigated whether a change in tumor blood flow during early stages of RT could be used as a surrogate marker for early prediction of treatment response in high-grade gliomas.

Methods: Twelve patients with Grade III or IV supratentorial malignant gliomas underwent 3D conformal RT with a median dose of 70 Gy. The patients underwent anatomic MRI, and dynamic contrast enhanced (DCE) T2* weighted imaging before RT, and at weeks 1-2 and 3-4 during RT, in a prospective, internal review board approved, clinical study. Gross tumor volume (GTV) was defined using post-operative, post-contrast T1 weighted and/or FLAIR images. Cerebral and tumor blood volume and flow were computed from DCE T2* weighted images(1, 2). All MRIs were registered to a treatment planning CT scan using a mutual information algorithm. Via this alignment process, the total accumulated planned radiation dose was also co-registered with the MRIs. CBV and CBF images across different time points were normalized using white matter regions contralateral to tumor and received less than 30 Gy accumulated dose. Using means and standard deviations of CBF in normal white matter and grey matter, blood flow in the gross tumor volume was graded to three categories: low (10-50), intermediate (50-120), and high (>120 ml $(100g)^{-1}$ min^{-1}). Changes in the volume with low, intermediate or high blood flow over the first three weeks of RT were analyzed and tested for correlation with changes in the GTV 3 months after completion of RT using linear regression.

Results: After receiving approximately 10 Gy radiation (1 week), seven patients had an increase in the tumor volume with high BF (>120 ml $(100g)^{-1}$ min^{-1}), four had a decrease, and one had no change. However, this early change in high BF was not correlated with the GTV changes at 3 months after completion of RT ($p>0.9$). After receiving ~30 Gy (3 weeks), three patients had a decrease in the volume with high BF, and the remaining patients had an increase. Changes in the volume with high BF at week 3 of RT vs pre RT and at week 3 vs week 1 were correlated with changes in the GTV at 3 months after completion of RT ($R=0.64$ and $p<0.02$, and $R=0.76$ and $p<0.004$, respectively). In two patients who had the largest GTV decrease at 3 months post RT, the high-BF volume increased initially at week 1 subsequently decreased by third week. In two patients who had the largest GTV increase, the high-BF volume increased continuously during the first 3 weeks of RT.

Discussion: The temporal change of BF in tumor is complex. BF changes after ~10 Gy radiation might be too early to predict later tumor volume changes. However, after ~ 30 Gy radiation, a change in high BF predicts the change in the tumor volume at 3 months after RT. This early prediction could provide an opportunity for boosting or alternating the treatment plan for patients who did not respond to the therapy.





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