

Clinical Cancer Research



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Imaging, Diagnosis, Prognosis

Regional Hypoxia in Glioblastoma Multiforme Quantified with [¹⁸F] Fluoromisonidazole Positron Emission Tomography before Radiotherapy: Correlation with Time to Progression and Survival

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Purpose: Hypoxia is associated with resistance to radiotherapy and chemotherapy and activates transcription factors that support cell survival and migration. We measured the volume of hypoxic tumor and the maximum level of hypoxia in glioblastoma multiforme before radiotherapy with [¹⁸F] fluoromisonidazole positron emission tomography to assess their impact on time to progression (TTP) or survival.

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Experimental Design: Twenty-two patients were studied before biopsy or between resection and starting radiotherapy. Each had a 20-minute emission scan 2 hours after i.v. injection of 7 mCi of [¹⁸F]fluoromisonidazole. Venous blood samples taken during imaging were used to create tissue to blood concentration (T/B) ratios. The volume of tumor with T/B values above 1.2 defined the hypoxic volume (HV). Maximum T/B values (T/B_{\max}) were determined from the pixel with the highest uptake.

Results: Kaplan-Meier plots showed shorter TTP and survival in patients whose tumors contained HVs or tumor T/B_{\max} ratios greater than the median ($P \leq 0.001$). In univariate analyses, greater HV or tumor T/B_{\max} were associated with shorter TTP or survival ($P < 0.002$). Multivariate analyses for survival and TTP against the covariates HV (or T/B_{\max}), magnetic resonance imaging (MRI) T1Gd volume, age, and Karnovsky performance score reached significance only for HV (or T/B_{\max} ; $P < 0.03$).

Conclusions: The volume and intensity of hypoxia in glioblastoma multiforme before radiotherapy are strongly associated with poorer TTP and survival. This type of imaging could be integrated into new treatment strategies to target hypoxia more aggressively in glioblastoma multiforme and could be applied to assess the treatment outcomes.

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