craniotomy surgeries followed by adjuvant treatments (2005-2014) were derived from the National Cancer Database (NCDB). The time intervals (days) from the date of diagnosis to the initiation date of adjuvant treatment [radiation therapy only (RT), chemotherapy only, concurrent chemoradiation (CRT), or non-concurrent RT and chemotherapy] were categorized into quartiles (Q1-Q4). Kaplan-Meier method and Cox proportional hazards regression were applied for survival analysis. Multivariate logistic regression was performed to compare differences in treatment timing, intervention modalities, and secondary outcomes. The patients underwent biopsy obtained significant survival benefit by having delayed adjuvant treatment [comparing to Q1, Q2: HR (hazard ratio), 0.88; Q3: HR, 0.86]. For patients underwent resection, the prolonged waiting time of adjuvant treatment had 5-6% reduced risk of death [comparing to Q1, Q2: HR, 0.95; Q3: HR, 0.94]. Patients received more RT fractions [comparing to 10-29 fractions, 30-33 fractions: HR, 0.62 (biopsy), 0.62 (resection); ≥34 fractions: HR, 0.53 (biopsy), 0.62 (resection)] and high-dose RT [comparing to 34-46 Gy, 50-60 Gy: HR, 0.91 (biopsy), 0.95 (resection); ≥ 60 Gy: HR, 0.77 (biopsy), 0.88 (resection)] experienced significantly superior survival in both biopsy and resection groups. The impact of timing to adjuvant treatment on GBM survival varied by surgery procedures. Having adjuvant treatment initiated within 21 days for both biopsy and craniotomy groups may not guarantee a significant survival benefit. More RT fractions and high-dose RT are associated with better GBM survival.

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Altersations in the epigenetic profile of glioblastoma tumors within hypoxic tumor regions

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Glioblastomas are the most frequent and aggressive primary brain tumor in adults and despite recent therapeutic advances, they are resistant to treatment. Increasing malignancy of gliomas correlates with an increase in cellularity and a poorly organized tumor vasculature, leading to insufficient blood supply, hypoxic areas, and ultimately to the formation of necrosis. Hypoxia induces direct or indirect changes in the biology of solid tumor and their microenvironment through the activation of HIF transcription factors, leading to increased aggressiveness and tumor resistance to therapy. Not much is known about the epigenetic alterations induced by hypoxia and how they could alter tumor biology. In the present study, we have utilized PIMO as a specific marker of hypoxia in glioblastoma patients, treated with PIMO preoperatively. We have estimated PIMO positivity in each tumor (5-45%) and determined that it positively correlates with the hypoxia marker CA IX (r=0.57). In addition, 10 surgical PIMO cases were dissociated, immune labeled using PIMO antibody, followed by DNA isolation and methylation profiling. Our analysis of differentially top 4000 differentially methylated probes suggests that PIMO-positive (hypoxic) cells are differentially methylated compared to the PIMO-negative cells and these changes are associated with genes involved in hypoxic cellular response. We will validate these findings in additional glioblastoma cases and assess the mechanism of these epigenetic alterations in vitro in glioma stem cell culture conditions and upon exposure of the cells hypoxic conditions.

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CD271/p75NTR is a novel diagnostic marker, prognostic indicator and therapeutic target for SHH medulloblastoma

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The extensive heterogeneity both between and within the medulloblastoma (MB) subgroups underscores a critical need for variant-specific biomarkers and therapeutic strategies. We