J Neurooncol. 2023 May 31. doi: 10.1007/s11060-023-04340-4. Online ahead of print.

## Re-irradiation for recurrent high-grade glioma: an analysis of prognostic factors for survival and predictors of radiation necrosis

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PMID: 37256526 DOI: 10.1007/s11060-023-04340-4

## **Abstract**

**Purpose:** Recurrent high-grade glioma (rHGG) is a heterogeneous population, and the ideal patient selection for re-irradiation (re-RT) has yet to be established. This study aims to identify prognostic factors for rHGG patients treated with re-RT.

**Methods:** We retrospectively reviewed consecutive adults with rHGG who underwent re-RT from 2009 to 2020 from our institutional database. The primary objective was overall survival (OS). Secondary endpoints included prognostic factors for early death (< 6 months after re-RT) and predictors of radiation necrosis (RN).

**Results:** For the 79 patients identified, the median OS after re-RT was 9.9 months (95% CI 8.3-11.6). On multivariate analyses, re-resection at progression (HR 0.56, p = 0.027), interval from primary treatment to first progression  $\geq$  16.3 months (HR 0.61, p = 0.034), interval from primary treatment to re-RT  $\geq$  23.9 months (HR 0.35, p < 0.001), and re-RT PTV volume < 112 cc (HR 0.27, p < 0.001) were prognostic for improved OS. Patients who had unmethylated-MGMT tumours (OR 12.4, p = 0.034),  $\geq$  3 prior systemic treatment lines (OR 29.1, p = 0.022), interval to re-RT < 23.9 months (OR 9.0, p = 0.039), and re-RT PTV volume  $\geq$  112 cc (OR 17.8, p = 0.003) were more likely to die within 6 months of re-RT. The cumulative incidence of RN was 11.4% (95% CI 4.3-18.5) at 12 months. Concurrent bevacizumab use (HR < 0.001, p < 0.001) and cumulative equivalent dose in 2 Gy fractions (EQD2,  $\alpha/\beta$  = 2) < 99 Gy<sub>2</sub> (HR < 0.001, p < 0.001) were independent protective factors against RN. Re-RT allowed for less corticosteroid dependency. Sixty-six percent of failures after re-RT were in-field.

**Conclusion:** We observe favorable OS rates following re-RT and identified prognostic factors, including methylation status, that can assist in patient selection and clinical trial design. Concurrent use of bevacizumab mitigated the risk of RN.

**Keywords:** Corticosteroid dependence; Glioblastoma; Pattern of failure; Radiation necrosis; Reirradiation; Recurrent high-grade glioma.

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