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Patterns of Progression in Patients with Newly Diagnosed Glioblastoma Treated with 5 mm Margins on a Phase I/II Trial of 5 Fraction Stereotactic Radiosurgery with Concurrent and Adjuvant Temozolomide

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Abstract

Background: In patients with newly diagnosed glioblastoma (GBM), tumor margins of at least 20 mm are the standard of care. We sought to determine the pattern of tumor progression in patients treated with 5 fraction stereotactic radiosurgery (SRS) with 5 mm margins.

Methods: Thirty adult patients with newly diagnosed GBM were treated with 5 fraction SRS in escalated doses from 25 Gy to 40 Gy with a 5 mm total treatment margin. Progression was scored as 'in-field' if the recurrent tumor was within or contiguous with the 5 mm margin, 'marginal' if between 5 and 20 mm, and 'distant' if entirely occurring greater than 20 mm. As geometric patterns of progression do not reflect the biologic dose received, we calculated the minimum equieffective dose in 2 Gy per day (EQD2) at the site of tumor recurrence. Progression was 'dosimetrically in-field' if covered by a minimum EQD2 of 48 Gy_{10}.

Results: From 2010 to 2016, 27 patients had progressed. Progression was in-field in 17 (63%), marginal in 3 (11%) and distant in 7 (26%) patients. In the 3 patients with marginal progression, the minimum EQD2 to recurrent tumor were 48 Gy_{10}, 56 Gy_{10} (both considered dosimetrically in-field) and 7 Gy_{10} (i.e., dosimetrically out-of-field). Median overall survival (OS) was 12.1 months for in-field (95%CI 8.9-17.6), 15.1 months (95%CI 10.1-not achieved) for marginal and 21.4 months (95%CI 11.2-33.5) for distant progression. Patients with radiation necrosis were less likely to have in-field progression (1 of 7; 14%) compared to those without radiation necrosis (16 of 20; 80%; p = 0.003); those with necrosis had a median overall survival of 27.2 months (95%CI 11.2-48.3) compared to 11.7 months (95%CI 8.9-17.6) for patients with no necrosis (p = 0.077).

Conclusion: In patients with newly diagnosed GBM treated with a 5 mm CTV margin, 3 patients (11%) had marginal progression within 5-20 mm; only 1 patient (4%) may have dosimetrically benefitted from conventional 20 mm margins. Radiation necrosis was associated with in-field tumor control.

Keywords: clinical trial; disease progression; glioblastoma; prospective study; radiation dose hypofractionation; radiosurgery; radiotherapy; temozolomide.

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