Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05.

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Abstract

PURPOSE: To determine the maximum tolerated dose of single fraction radiosurgery in patients with recurrent previously irradiated primary brain tumors and brain metastases.

METHODS AND MATERIALS: Adults with cerebral or cerebellar solitary non-brainstem tumors $\leq$ 40 mm in maximum diameter were eligible. Initial radiosurgical doses were 18 Gy for tumors $\leq$ 20 mm, 15 Gy for those 21-30 mm, and 12 Gy for those 31-40 mm in maximum diameter. Dose was prescribed to the 50-90% isodose line. Doses were escalated in 3 Gy increments providing the incidence of irreversible grade 3 (severe) or any grade 4 (life threatening) or grade 5 (fatal) Radiation Therapy Oncology Group (RTOG) central nervous system (CNS) toxicity (unacceptable CNS toxicity) was < 20% within 3 months of radiosurgery. Chronic CNS toxicity was also assessed.

RESULTS: Between 1990-1994, 156 analyzable patients were entered, 36% of whom had recurrent primary brain tumors (median prior dose 60 Gy) and 64% recurrent brain metastases (median prior dose 30 Gy). The maximum tolerated doses were 24 Gy, 18 Gy, and 15 Gy for tumors $\leq$ 20 mm, 21-30 mm, and 31-40 mm in maximum diameter, respectively. However, for tumors $\leq$ 20 mm, investigators' reluctance to escalate to 27 Gy, rather than excessive toxicity, determined the maximum tolerated dose. In a multivariate analysis, maximum tumor diameter was one variable associated with a significantly increased risk of grade 3, 4, or 5 neurotoxicity. Tumors 21-40 mm were 7.3 to 16 times more likely to develop grade 3-5 neurotoxicity compared to tumors $< 20$ mm. Other variables significantly associated with grade 3-5 neurotoxicity were tumor dose and Karnofsky Performance Status. The actuarial incidence of radionecrosis was 5%, 8%, 9%, and 11% at 6, 12, 18, and 24 months following radiosurgery, respectively. Forty-eight percent of patients developed tumor progression within the radiosurgical target volume. A multivariate analysis revealed two variables that were significantly associated with an increased risk of local progression, i.e. progression in the radiosurgical target volume. Patients with primary brain tumors (versus brain metastases) had a 2.85 greater risk of local progression. Those treated on a linear accelerator (versus the Gamma Knife) had a 2.84 greater risk of local progression. Of note, 61% of Gamma Knife treated patients had recurrent primary brain tumors compared to 30% of patients treated with a linear accelerator.

CONCLUSIONS: The maximum tolerated doses of single fraction radiosurgery were defined for this population of patients as 24 Gy, 18 Gy, and 15 Gy for tumors $\leq$ 20 mm, 21-30 mm, and 31-40 mm in maximum diameter. Unacceptable CNS toxicity was more likely in patients with larger tumors, whereas local tumor control was most dependent on the type of recurrent tumor and the treatment unit.

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