Stereotactic radiosurgery for pediatric brain tumors

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Abstract Six papers from the recent literature are reviewed for outcomes after stereotactic radiosurgery used to treat pediatric brain tumors. Results indicate that radiosurgery is feasible in children with brain tumors. The efficacy is approximately 80% local control for benign astrocytomas. The local control is less effective in malignant tumors. Only 4 of 15 children with recurrent ependymoma were controlled. The complication rate of all the papers combined is approximately 11%. Permanent neurologic complication owing to stereotactic radiosurgery is approximately 5%. These complications are discussed.

Key words Radiosurgery · Radiation therapy · Pediatric brain tumors · Stereotactic radiosurgery

Introduction

Radiation therapy is frequently used for the treatment of pediatric brain tumors. The use of radiation is limited primarily by normal tissue toxicity, especially when large areas of the brain are irradiated. Stereotactic radiosurgery allows more accurate treatment of the target volume with minimal doses to the surrounding normal tissues. This is especially useful in lesions that are inaccessible to surgical intervention, in eloquent areas of the brain, or with residual disease post-operatively.

The use of a single large dose of irradiation may be associated with a constellation of deleterious effects that are different from those seen with standard, fractionated, external beam irradiation. With fractionated radiation therapy, the normal tissues have an opportunity to repair potentially lethal damage or sublethal damage between treatments. The repair mechanisms for normal tissues are typically better than for tumor tissues, and thus a protracted course of fractionated irradiation will improve the therapeutic ratio. The effects of larger doses per treatment are more pronounced in neural tissue than in other normal tissues. These effects are especially important in children and may be more pronounced especially in very young children. These factors are the rationale for extended-course treatment, including hyperfractionated irradiation. Stereotactic radiosurgery (SRS) uses a single large dose of radiation, which may increase the risk of normal tissue complications in the high-dose volume. The advantage of SRS is that the high-dose volume is much smaller than with conventional external beam radiotherapy. The impact of this treatment technique may be better local control with fewer global central nervous system (CNS) side effects but at the cost of a higher rate of necrosis. The situations in which SRS is beneficial have not been clearly delimited, nor has the optimal treatment dose and volume. These articles provide some basis for establishing guidelines for the optimum use of SRS.
**[1] Gamma knife radiosurgery in children**


**Information.** The goal of this paper is to review 52 children treated with gamma knife stereotactic radiosurgery of which 25 had brain tumors. Seven children were treated for recurrent disease. Most of the children with recurrent disease had high-grade gliomas. The patients had received prior external beam radiotherapy (16 patients), interstitial implants (2), prior SRS (2), or chemotherapy (16). The average volume treated was 8.1 cm³ with a dose of 16.7 Gy to the 50% isodose surface. Local control was noted in 5 of 7 children with low-grade gliomas, 3 of 3 children with sarcomas, and 4 of 5 children with craniopharyngiomas, but only 5 of 14 children with high-grade gliomas. Twelve of 25 patients had progressive disease after SRS, with progression in the SRS field in 9 of those children.

Three patients had CNS necrosis at 9–16 weeks, with an actuarial incidence of 12% at 1 year; all of these children had been previously treated with external beam irradiation and chemotherapy, plus brachytherapy or radiosurgery. One patient had brain stem injury at 8 months following a dose of 10.8 Gy with SRS; this patient had previously received 70 Gy external beam irradiation. The neurologic deficits resolved with corticosteroids. One patient had permanent visual loss from optic chiasm injury. This patient had received external beam irradiation and then SRS twice (3.3 Gy and 4.2 Gy to the chiasm), with a total dose of 69.6 Gy to the optic chiasm. A univariate analysis was performed, and prior focal radiotherapy boost (implant or previous SRS) was the factor most predictive of necrosis after SRS.

**Analysis.** This paper highlights several important points about stereotactic radiosurgery. The brain stem and cranial nerves (including the optic chiasm) are very sensitive to the dose per fraction of irradiation. Higher doses per fraction can cause injury to these areas at a much lower total dose than would be seen with conventionally fractionated external beam radiotherapy. As an example, optic chiasm injury is rarely seen with external beam doses of <50–55 Gy in conventional 1.8–2.0 Gy fractions. In contrast, single doses of >8 Gy have caused optic chiasm or optic nerve deficits. This can be a problem with stereotactic radiosurgery, where single large doses of radiation are given. The brain stem and optic pathways should be excluded from SRS treatment whenever possible and the dose limited when exclusion is not possible.

The risks of re-radiation are well documented in many tissues, although the results are better known for tissues outside of the CNS. Because of the fear of potentially devastating side effects, re-irradiation of the brain has been performed with relative infrequency. In situations where high-dose re-irradiation has been performed, the risk of radionecrosis has been significant (for example, with interstitial brachytherapy for recurrent high-grade gliomas). In this series reported by Baumann et al., the risk of necrosis or other complications was strongly associated with prior high-dose radiotherapy.

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**[2] Stereotactic radiosurgery for glial neoplasms of childhood**

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**Information.** Grabb et al. present their results in 25 children with unresectable glial neoplasms who were treated with stereotactic radiosurgery using the gamma knife. Thirteen of the patients had “benign” tumors (pilocytic astrocytoma or non-pilocytic low-grade astrocytoma) and were treated with single doses of 11–20 Gy to the periphery of the tumor. All 13 children remain alive, although 2 had tumor progression after SRS. Four children had complete resolution of disease at 10–25 months after treatment. Three patients with tumors in the brain stem or cerebellar peduncles had transient neurologic toxicity after treatment, but all of these were reversed with corticosteroids. All 3 of these children had evidence of increased peritumoral edema at 1–6 months after SRS.

In the twelve children with “malignant” brain tumors, the diagnoses were anaplastic astrocytoma (3), glioblastoma multiforme (2), and ependymoma (7). Five of these children are alive 12–72 months after SRS, including 2 children with progression after SRS. Of the 9 patients with progressive disease after SRS, 7 had local progression only (4 patients) or progression associated with disseminated disease (3 patients). Toxicities were relatively uncommon, with only 1 patient (4%) experiencing a permanent long-term neurologic complication: 1 patient had delayed neurologic toxicity with a mild restriction of upward gaze.

The patients with ependymoma fared especially poorly. All 7 patients had progression of disease...