Radiation Options for High-Grade Gliomas

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High-grade gliomas (HGGs) include World Health Organization (WHO) grade 3 anaplastic astrocytoma and grade 4 glioblastoma multiforme (GBM). Although HGG rarely results in distant metastasis, the condition's seemingly relentless local microproliferation renders its cure impossible (at least in the current technology). Even with the latest imaging and surgical technologies, the exact demarcation of the tumor and its proliferation cannot be determined. This makes the localization of the target an unachievable task. Another unique nature of brain tumor is that the brain is an unforgiving organ that contains many vital structures that many a time HGG involves. The outcome for HGG remains grim despite advancing multimodality treatments, including surgery, chemotherapy, and radiotherapy.

The exact mechanism of radiotherapy is still uncertain. However, the majority supports the notion that double-stranded breaks of the nuclear DNA are the most important cellular effect of radiation. This breakage causes an irreversible loss of reproductive integrity of the cell and eventual cell death. Radiotherapy also uses ionizing radiation to interact with water molecules within the cell, which releases free radicals, whereby causing additional DNA damage.¹ Soon after the discovery of x-rays by Roentgen in 1895,² there were reports that patients with cancers were being successfully treated with radiotherapy.³

Frankel and German⁴ published one of the earliest reports on radiotherapy for glioblastoma in 1958. The investigators reviewed 219 cases of GBM. Forty-seven patients received radiation doses varying between 2700 and 5900 rads (cGy), and 21 of these patients completed radiotherapy within 60 days after operation. When compared with 62 patients who underwent surgery alone and were alive 60 days after operation, the investigators found that there was a significantly greater percentage of survivors in the irradiated group during the first 12 months. This difference disappeared after the first year. The investigators concluded that routine postoperative radiation effectively prolonged the palliative effects of surgery and proposed a more general usage of radiotherapy. In terms of surgery, they found that a more radical removal offered the best prognosis with regard to operative mortality and survival time.

Radiotherapy is now routinely used as part of the treatment regimen for HGG. Its efficacy and

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