

Intracerebral Delivery of Carboplatin in Combination with Photon Irradiation for the Treatment of Rats Bearing F98 Glioma

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Up until recently, the overall median survival of patients with high-grade gliomas usually has been less than one year after diagnosis. Standard treatment consists of surgical resection of the tumor followed by radiation and chemotherapy. Although such treatment has generally increased lifespan by several months, the tumor inevitably recurs. Among all chemotherapeutic agents available, platinum-derived drugs (such as carboplatin) have played an important role in the treatment of solid tumor, but their systemic administration has been limited by their toxicity. Strategies have been developed to improve drug delivery, such as the disruption of the blood brain barrier or local administration of drug within the central nervous system by the mean of implantable pumps, biodegradable polymers and convection-enhanced delivery (CED). In this study, carboplatin was administrated intracerebrally by CED to F98 glioma-bearing rats, 13 days following stereotactic implantation of 1000 tumor cells. The following day, photon irradiation was carried out using either a conventional (6 MV) linear accelerator (LINAC) or a (80 keV) monochromatic synchrotron source at the European Synchrotron Radiation Facility (ESRF). The primary endpoint of this study was overall survival. A subset of long-term survivors (>200 days) were observed in both chemo-radiotherapy groups, and their median survival times were increased compared to irradiated, chemotherapy, and untreated controls.

KEYWORDS: F98 rat glioma, carboplatin, convection-enhanced delivery, radiotherapy