Heavy-atom enhanced synchrotron stereotactic radiotherapy of brain tumors: from DNA to preclinical studies

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Gliomas are the most frequent primary brain tumors in adults. Despite multimodality treatment strategies that combine surgery, chemotherapy and radiotherapy, high grade gliomas are almost uniformly fatal. Heavy-atom-enhanced synchrotron stereotactic radiotherapy (SSR) is a novel therapeutic modality proposed to increase the toxicity to the tumor while protecting the surrounding healthy tissue. It consists in selective accumulation of high-Z elements in tumor followed by stereotactic irradiation, in tomography mode, with monochromatic X-rays from a synchrotron source, tuned at an optimal energy. Two complimentary SSR approaches have been successfully developed in the past 5 years, and may be promising in high-grade glioma management: iodine-enhanced SSR , with an iodinated contrast agent; and Pt-enhanced SSR , , a concomitant radio-chemotherapy treatment with locoregional injection of platinated chemotherapy drugs. Several in vitro and in vivo experiments have been carried out at the European Synchrotron Radiation Facility, either with iodine or platinum. In vivo experiments are performed on F98 glioma-bearing rats. The F98 glioma model simulates several characteristics of human glioblastoma including lethality following treatment with a variety of therapeutic modalities. Recently, we have shown that a significant increase in survival time is obtained when the platinated drug (cisplatin or carboplatin) is infused intratumoraly followed by X-rays irradiation. Furthermore, a significant percent of animals are cured. To optimise the treatment, work is in progress in order to determine and increase the incorporation of heavy-atoms in tumoral cells and also to improve the intracerebral drug distribution by developing new injection methods and using different chemotherapeutic drugs including oxaliplatin, chlorotertpyridineplatinum and 5-iodo-2'-deoxyuridine. In addition, efforts will be made to have a better understanding of the biological consequences at the molecular and cellular level of the SSR treatment.

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