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# Contrast-enhanced synchrotron radiation therapy: From bench to bedside

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Radiation therapy remains a fundamental tool for cancer treatment, but selective dose deposition within a targeted-tumor, while sparing surrounding structures, remains a challenge. This objective can be achieved by loading the tumor with high-Z elements prior delivery of radiation therapy. Synchrotron sources are ideal sources since they provide high-intensity and tunable monochromatic X-rays within the optimal energy-range.

We evaluated the ability of various high-Z elements, either as molecular agents (iodine [1-4] or gadolinium [5, 6] contrast agents) or in the form of nanoparticles [gold [7] or gadolinium [5, 6], to act as radiation dose-enhancers through theoretical and experimental studies.

Clonogenic assays were first used to quantify cell survival after irradiation in the presence of the dose-enhancers using monochromatic X-rays from a synchrotron or 1.25 MeV photons from a 60Co source. Preclinical studies were then performed on rats bearing F98 glioma after administration of either iodine as contrast agent or AuNPs. In parallel, Monte Carlo simulations were performed to evaluate the dose for comparisons.

Finally, a clinical study was performed using an iodinated contrast-agent as the radiation doseenhancer [8-11]. Fourteen Patients with brain metastases received one fraction of the overall radiotherapy treatment at the synchrotron, the additional fractions were delivered using a
conventional Linac at the Grenoble university hospital. Radiosensitization was demonstrated with all agents in combination with X-irradiation at low energies. The radiation dose-enhancements were found to be highly energy-dependent for all agents. Secondary-electron-emission generated after photoelectric events appeared to be the
primary mechanism by which Iodine and Gd contrast agents or AuNPs act as dose-enhancers. Increase of the animal's survival was observed after iodine systemic injection or intracerebral infusion of AuNPs. The phase I-II clinical studies demonstrated the feasibility of this technique. Our overall experience will be summarized, pointing out the advantages and difficulties of applying this method for the treatment of brain tumors.

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