AbstractID: 1591 Title: Synchrotron monochromatic radiation associated with cis-platinum: molecular and preclinical results

Conventional radiotherapy of high-grade glioma is unsuccessful since less than 50 % of patients survive at 9 months. We propose a new radiotherapy procedure, the *photon activation therapy* (PAT), associating synchrotron radiation with a chemotherapy agent, cisdiamminedichloroplatinum (II) (CDDP). This binary treatment takes advantage of the beam monochromaticity for selective excitation of a high-Z compound introduced in tumor cell DNA. Recent results show that monochromatic synchrotron irradiation of CDDP at 78.8 keV, just above the 78.4 keV platinum absorption K-edge leads to an enhanced photoelectric effect and an increased local toxicity[1] In order to verify this hypothesis, we irradiated CDDP-treated rat F98 glioma cells with synchrotron X-rays at different energies and assessed yields of DNA double-strand breaks (DSBs) by using pulsed-field gel electrophoresis.
In vivo treatments combining synchrotron radiation and intra-cerebral CDDP were thereafter performed on rats bearing F98 glioma. CDDP concentrations in rat brain were mapped by synchrotron X-rays micro-fluorescence. The molecular results show that an irradiation at 78.8 keV induces an extra-number of more slowly repaired DSBs. The *in vivo* survival curves show a dramatic increase in life span for the rats treated with 3 μg CDDP and 15 Gy (median survival time 206 days). After one year, about 34% of treated rats were still alive. This preclinical finding supported by molecular analysis, represents the most protracted survival reported with this radioresistant glioma model and opens new perspectives brain tumor treatment.

[1]Corde, S. et al Cancer Res. 63: 3221-3227; 2003