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<tr><td> </td><td>Experiment title: Photon Activation Therapy trial on cells cultures with intranuclear stable iodine or platinum: dose enhancement and DNA damages measurement produced by Auger effect induced by monochromatic photons of synchrotron radiation.</td><td>Experiment number:
LS-1392</td></tr>
<tr><td>Beamline:
ID17</td><td>Date of experiment:
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Report:

It is now recognized that Auger electrons emitters like ^{123}I can be useful for treatment applications of nuclear medicine, since many progresses have been made in their intranuclear vectorisation. Nevertheless, the use of such radioactive isotopes remains hazardous, because of their fixation on any rapidly dividing tissues (bone marrow for instance). Conventional radiotherapy seems to be a safer treatment, because of multiple beams convergence on tumor localization and high accuracy of recent treatment planning system. However, for some particular tumor types, as cerebral gliomas, dose enhancement is a proven and unique way to enhance tumor local control, but is strongly limited by healthy tissue tolerance.

Even if external stimulation of Auger cascades on stable iodine has already been studied, our idea was to redo Brookhaven's experiments, just to **validate our experimental protocol**. According to RG Fairchild, iodinated deoxyuridine should be the best 'activable' compound and consequently the more efficient. At NSLS (Brookhaven) R. Fairchild and B. Laster used ^{127}IUdR on V79 hamster cells to study possible enhancement of the radiation induced cell toxicity by Auger effect on iodine irradiated just above and below its K-edge. They found an Auger effectiveness factor of 1.4 and a promising therapeutic gain factor of 3 related to 17 % of ^{127}I incorporation in DNA.

During our first experiment, 112 cell culture flasks, treated or not with iododeoxyuridine were maintained into growing conditions until irradiation time. These flasks were brought at ESRF, and deposited into cell culture incubators (37°C, 5% CO_2,

humidified atmosphere) until the time of irradiation of each sample. Samples were placed on a special support, which allowed irradiation of 4 flasks in the same time. The angiography chair positioning system was used for vertical scanning of these samples, but was clearly not adapted. According to our beam calibration, delivered doses were between 1 and 8 Gy. In practice, the flasks stood presenting the wall bearing the monolayer of cultured cells directly toward the beam, and on the other side, thermoluminescent detectors were put to control given doses. There was a good correlation between doses, we wanted to deliver and doses read by these detectors. But few months later, it appeared that the ion chamber calibration factor, used to measure the dose rate and the TLD's calibration factor during these experiments, was overestimated by a factor of 70%; consequently the real given doses compared with the planned doses were in fact reduced by this factor…

Nevertheless feasibility of irradiation procedure has been proved during this experiment: no real technical problems appeared at the ESRF. Our 112 cell culture flasks were brought back to our cell biology laboratory for low-density subculture. Each flask was trypsinized and a known number of cells was seed as triplicate in Petri dishes. As a result of the bad quality of our trypsin, that avoided us to create monocellular suspension, we decided to estimate the global toxicity of our treatment by growing curves method, instead of cells colony forming ability. One week after, almost 350 Petri dishes were trypsinized and should have been counted without break. But as a simple time saving procedure, all samples were frozen in DMSO added medium and their count with automatical cytometer reported few days later. Unfortunately, the freezing occurred cell aggregation and precludes any cell count. It was impossible to obtain information concerning number of cells present any longer. Our samples are still frozen and we hope that a DNA extraction and its quantification by spectrometry could give us sufficient information to evaluate the experiment. Nevertheless, errors made concerning doses delivery would probably prevent us from achieving accurate informations.

To summarize, the results of this preliminary experiment are the following:

1) the demonstration of the technical feasibility of PAT devoted irradiation on ID17;
2) the necessity to obtain a motorized support devoted to the scanning irradiation of the cell culture vials which has been implemented for platinum PAT experiment in November 1999;
3) it showed the weak points of the procedure as dosimetry, duration of irradiation, risk of delay, needs in human power , and allow a better handling for future experiments.
4) the necessity to use a more classical end point for survival, as colony forming assay providing that the quantification could be assessed more objectively than in the standard application of the method.