EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF. Once completed, the original report should be sent, together with 5 reduced (A4) copies, to the User Office.

In addition, please send a copy of your file as an e-mail attachment to reports@esrf.fr**,** using the number of your experiment to name your file. This will enable us to process your report for the ESRF Annual Report.

Reports accompanying requests for additional beam time

If your report is to support **a new proposal**, the orginal report form should be sent with the new proposal form, and a copy of your report should be attached to each copy of your proposal. The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.
- bear in mind that the report will be reduced to 71% of its original size. A type-face such as "Times", 14 points, with a 1.5 line spacing between lines for the text, produces a report which can be read easily.

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ESRF	**Experiment title:** *Photon Activation Therapy 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*	**Experiment number**: LS-1698
Beamline: ID17	**Date of experiment**: from: *18/09/2000 to 23/09/2000*	**Date of report**: 01/09/2001
Shifts:	**Local contact(s)**: Tropres Irène	*Received at ESRF:*

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Report:

Background

Dose enhancement in human radiotherapy is a proven way to improve tumor local control, but it is limited by healthy tissue tolerance. Continuing researches are done to improve tumor lethal damages with respect of surrounding tissues (drug sensitization; contrast mediated dose enhancement, …). Two approaches are particularly attractive, the use of high RBE* ion beams and tumor targeted irradiation sources as classical brachytherapy$ or metabolic radiation therapy£. The Photon Activation Therapy (PAT) is a combination of these two approaches: a selective excitation of high-Z compound fixed inside DNA tumor should allow radio-toxicity enhancement, thanks to the increase of local dose deposition. Actually, photon-stimulation of these heavy elements induces ejection of an internal electron by photoelectric effect. The following electronic rearrangement may lead to Auger electrons cascades. This phenomenon, predominant with light elements, occurs with lower probabilities with high-Z atoms; nevertheless, energies needed for their resonant excitation are higher and consequently suitable for external radiotherapy. Because of their very short range, these Auger electrons could be very toxic for tumor cells, but only if they are released in the close vicinity of their DNA.

Material and methods

Radiobiological and microanalysis experiments have been made on ID17 beamline (LS1698) and ID22 (LS1714) in order to study sensibility modifications of human cancerous cells (SQ20B), treated or not with different concentrations (1 µM 12h, 3 µM 6h or 12h, 30 µM 6h) of cis-diaminedichloroplatinum (II) (CDDP). For the radiobiological assays, these cells have been irradiated with monochromatic X-rays, whose energies were either above or below the K-absorption edge of platinum (78,39 keV). Delivered doses range was 1 to 16 Gy. After irradiation, low-density subcultures of treated cells have been carried out for evaluation of the treatment toxicity by standard colony forming assay. Microanalysis of platinum loaded in cells and trace elements have been done on the same cell line by X-ray fluorescence quantitative microscopy, and compared with induced charged coupled mass spectrometry results. DNA double strand breaks have been studied by pulsed field electrophoresis of whole cellular DNA. Quantification and repair kinetics have been established and compared for above and below K-edge irradiations.

Results

Our results show that more DNA double strand breaks are induced in the cells pre-treated with cisplatinum (CDDP) when irradiated above platinum K-edge than below. Moreover, the DNA repair kinetic study shows that damages induced with the Above K absorption edge of platinum radiation are less easily repairable (more DSB due to Auger effect?). This radio-induced toxicity of CDDP appears like a small sensitization on survival curves, for a drug exposure of 0.1 µM of CDDP during 48 hours. The increase of CDDP cell loading seems to have little effect on this radio-sensitization, whereas chemical toxicity of the drug is drastically increased (only 10% of the cells treated with 1 µM of CDDP during 6 hours survive after 15 days. Do they have enough platinum covalently bound to DNA?). The analyze of SQ20B cells by synchrotron light micro-imaging shows an homogenous distribution of CDDP within the whole cell compartment, directly correlated with potassium one's. Nevertheless, at the time of irradiation, platinum is present in cells in rather low quantity (few ppb in our experimental conditions). Next step of this study will be to test new experimental conditions, in particular different cell line, with higher affinity to CDDP and different platinum carriers, with lower chemical toxicity