EUROPEAN **S**YNCHROTRON **R**ADIATION **F**ACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

ESRF

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 report should be submitted electronically to the User Office using the **Electronic Report Submission Application:**

http://193.49.43.2:8080/smis/servlet/UserUtils?start

Reports supporting requests for additional beam time

Reports can now be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

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.

ESRF	**Experiment title:** Synchrotron Stereotactic Radiation Therapy (SSRT) efficiency on glioblastoma or oligodendroglioma spontaneously developed in adults rats in response to *in utero* exposure to ethyl-nitrosourea (ENU).	**Experiment number**: MD270
Beamline: ID17	**Date of experiment**: from: 14 Mar 2007 8:00h to: 15 Mar 2007 8:00h and from: 7 Jul 2007 8:00h to: 10 Jul 2007 8:00h	**Date of report**: 20 Aug 2007
Shifts: 12	**Local contact(s)**: Manuel Fernández	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

* Manuel Fernández, Inserm U836-6.

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* Helene Elleaume, Inserm U836-6.

Report:

The goal of this experiment was to assess the effects of the therapeutic protocol based on stereotactic synchrotron radiotherapy enhanced by photon-activation of platinum on the development of ethyl-nitrosourea *in utero* induced rat brain tumors. The tumoral model used presents some particular difficulties for the treatment and the follow-up. This is due to the fact that the position, type and grade of the tumors is quite disparate from one animal to another. Nevertheless, it is known that about 80% of the tumors developed are oligodendrogliomas-like, and the rest mostly glioblastoma-like. Extracranial tumors may also be found in some animals. These challenges make it an interesting case, closer to the clinical problem than other models.

A therapeutical protocol was designed for this model. It consists of an intracranial injection of cis-Pt in a large section of the brain and a hemispherical irradiation with monochromatic x-rays at an energy just above the K-edge absorption of the platinum (78.39 keV). A total of 46 animals were initially imaged in the MRI unit 2.35 T at the Inserm U836-5 facilities at CHU-Grenoble. The groups of animals for the ESRF protocol were prepared from the information of these MRI explorations. Four groups of N=8 animals were selected (total of 32 animals). They were chosen to have as homogeneous as possible pathologies within the groups. The first group was to be jus injected with cis-Pt, the second group to be just irradiated, the third to be both injected and irradiated and the fourth was to be kept as a control. Some of the animals were imaged by synchrotron computed tomography, after injection of iodinated contrast agent.

The intracranial injections were preformed with the aid of a stereotactic frame. The drug was delivered with a Hamilton syringe and 33-gauge needle. The injection was guided with an automatic pump, set to diffuse the drug in convection enhanced delivery conditions. The injections were performed in the labs of the BMF facility. The animals were then irradiated approximately 24h after the injections.

The irradiations were done in the optics hutch of ID17 in stereotactic synchrotron radiation therapy (SSRT) mode. The beam was tuned to an energy of 80 keV and collimated to have uniform intensity across its section. The slits were set to 1 mm thick, both for imaging and irradiation. Before irradiation, the head of the animals was imaged in tomographic mode, in order to get a reference for positioning the tumor in the center of rotation. The irradiation time was set to deliver a dose in the tumor of 15 Gy. The development of the tumors was followed-up at the CHU-Grenoble by MRI, before and after the experiment at the ESRF.

The volume of the tumor was measured from the MRI images to follow-up the temporal evolution of their size. In many cases, clear tumor regression was observed both in combined therapy (radio- and chemo-therapy) and in just radiotherapy. In some cases, a total disappearance of the tumor was observed. The analysis of the data shows an apparent diversity of results, due to the heterogeneity of the model itself, but some trends are clearly seen. As a general rule, the irradiated tumors tend to diminish its size (Fig. 1), and some disappear completely (Fig 2). The data analysis is under way and further study and interpretation of the results is needed.

Apparently, at this stage of the data analysis, there is no a clear difference between the effect on the tumors by simple irradiation or by combined chemo-radiotherapy. On the other hand, in the group just treated with chemotherapy there was no significant different with the control, untreated animals, and the tumors continued to grow. However, the good results in tumor regression are encouraging and further studies are required. For example, the tumors could be targeted directly with the CDDP instead of the whole hemisphere. This should help to differentiate the tumor types and its response to treatment and to assure an homogeneous diffusion of the drug inside some very heterogeneous tumors.

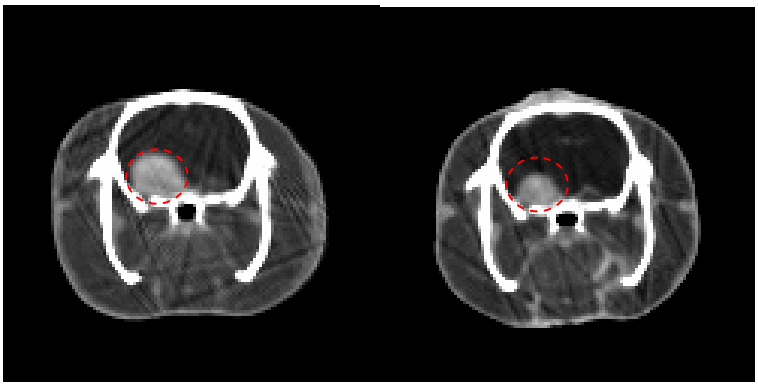

Figure 1. Computed tomography of a rat brain bearing a tumor (circled) , before and after the combined radio- and chemo-therapy. The reduction of the tumor size is evident.

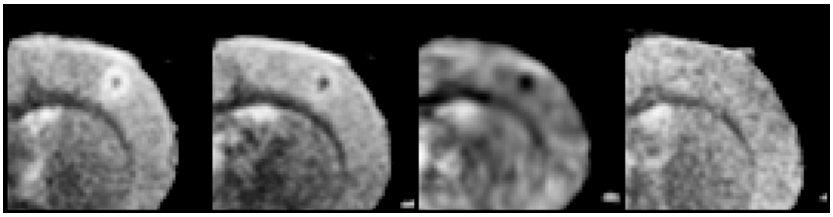

Figure 2. Magnetic resonance images of the size evolution of a tumor after an irradiation of the whole hemisphere at 15 Gy. The first image from the left is prior to the irradiation, the three following were acquired 4, 9 and 36 days after the irradiation.