EUROPEAN SYNCHROTRON RADIATION FACILITY

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:** Evaluating microbeam radiation therapy (MRT) for malignant brain tumors and vascular malformations: an animal experimental study	**Experiment number**: MD 131-1
Beamline: ID 17	**Date of experiment**: from: April 27 to: May 1, 2004	**Date of report**: February 2, 2005
Shifts: 12	**Local contact(s)**: Dr. Elke Bräuer-Krisch, Dr. Alberto Bravin	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Dr. Elisabeth SCHULTKE*, Walton Medical Centre, University of Liverpool, U.K.
Khalid ATAELMANNAN*, Department of Surgery, University of Saskatchewan, Canada
Hans BLATTMANN*, Jean A. LAISSUE*, Department of Pathology, University of Bern, Switzerland
Elke BRAEUER-KRISCH*, Alberto BRAVIN*, ESRF
Dean CHAPMAN, Bernhard JUURLINK*, Department of Anatomy & Cell Biology, University of Saskatchewan, Canada
Daryl FOURNEY*, Robert GRIEBEL*, Division of Neurosurgery, University of Saskatchewan, Canada

Report:

MRT was performed two weeks after implantation of 100,000 tumor cells, in bidirectional mode, with 350 Gy both. The TECOMET collimator at ID 17 was used to produce ~1 cm wide arrays of microbeams with beamwidths of 25 micrometer and c-d-c of 200 micrometer. Because the original collimator configuration would allow only c-d-c of 400 micrometer, the animls mounted on the stage were translated vertically through the beam, after which the the stage moved back into start position. The stage was then translated laterally and the animal was translated vertically through the beam a second time, with a resulting c-d-c of 200 micrometer in the horizontal plane. The animals were then rotated around the vertical axis, and the irradiation process was repeated to achieve c-d-c 200. The beam arrays intersected at the location of the tumor assumed based on the burr hole and the stereotactic coordinates used for tumor cell implantation.

A total of 122 animals were used for these experiments. Brain tumor cells were stereotactically implanted for the following small animal models:

1. **C6 glioma cells in Wistar rats**

   Groups treated:

   A) Short-term experiment (24 hrs survival):

      5 animals with tumor, irradiated / 4 animals with tumor, non-irradiated / 3 healthy controls, irradiated

B) Long-term experiments (endpoint: dead of the animal or euthanasia when dead was inevitable).

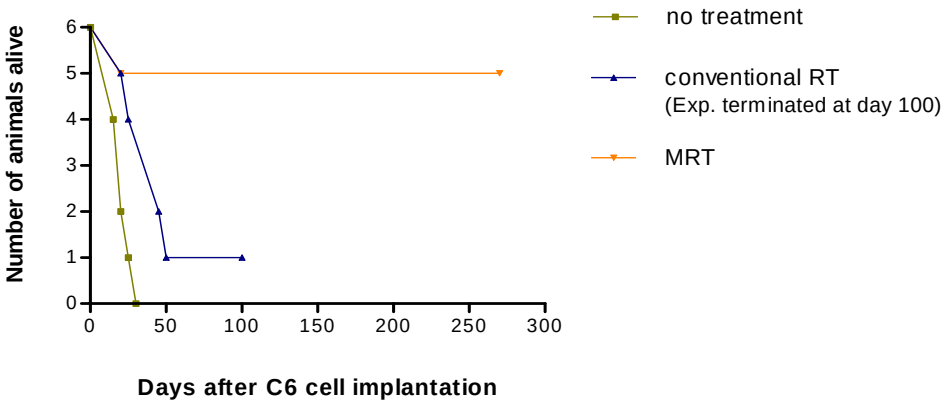
Survival status by end of January, 2006 (9 months after MRT):

Of the animals with tumor, the survival status is as follows:

No treatment: all dead (between days 12 and 21)

MRT treatment only: 2 dead (day 18 and 2.5 mo)

MRT + BSO: 2 dead (days 31 and 46)



The conventional radiotherapy (CRT) experiment, using a 10 Gy (6 MeV) administered in one single session at the University of Saskatchewan, was terminated at 100 days after tumor cell implantation.

2. F 98 cell glioma in Fischer rats

Groups treated:

C) Short-term experiment (24 hrs survival):

5 animals with tumor, irradiated / 4 animals with tumor, non-irradiated / 3 healthy controls, irradiated

D) Long-term experiments (endpoint: dead of the animal or euthanasia when dead was inevitable).

Group distribution as above.

Survival status by end of January, 2006 (9 months after MRT):

This is a model of an extremely aggressive and advanced tumor. It correlates well to patients seen in clinical practice with large brain tumors and in severely compromised general condition. In those situations, the physician is confronted with telling the patient either that nothing can be done anymore to improve his condition or offer palliative treatment, usually radiation therapy.

In our model, death occurred

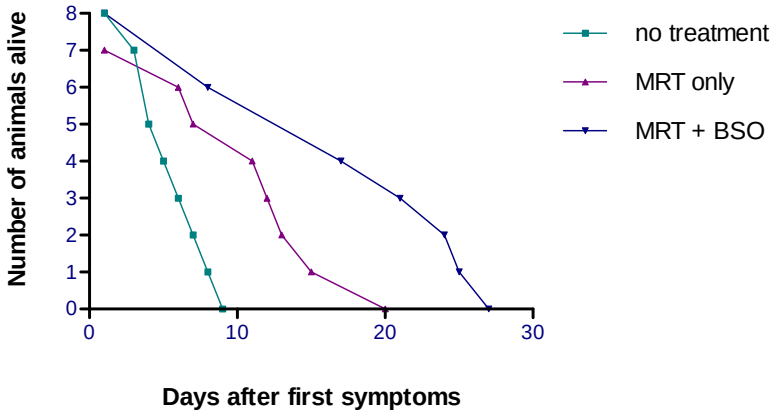
· between days 12 and 16 after tumor cell implantation when untreated

· between days 15 and 24 after tumor cell implantation when treated with MRT only and

· between days 15 (2) and 36 after tumor cell implantation when treated with MRT + BSO.

Summary: even in these animals modeling 'terminal patients' at the time of treatment, both general survival time and symptom-free survival time were increased by both treatment modalities. The

combination of MRT and BSO (used to decrease the glutathione content in the tumor, which in turn results in loss of cytoprotective potential within the tumor cells) resulted in the higher survival gain, when compared to MRT alone.



The animals that had not been implanted with brain tumors were used as controls (healthy, BSO injection only, MRT only etc.) and for small group trials of higher irradiation doses (450 and 500 Gy bidirectional).

Three animals died spontaneously from their tumor before the beginning of the MRT. This agrees with our previous experience of spontaneous deaths from tumor growth. Eight animals died under anaesthesia for MRT. One of these animals was a Wistar rat, while the remaining 7 animals were Fischer rats with F 98 glioma. This is most like ly due to the much more advanced stage of tumor growth in the Fischer rats with F 98 gliomas. Therefore, the intracranial pressure in these animals is significantly increased, resulting in autonomous instability. We therefore decided that, in future experiments with Fischer rats, we will irradiate on day 12 after tumor cell implantation instead of day 13, to reduce losses due to anaesthesia.

Twenty-six animals were used for short-term experiments. They were sacrificed 24 hrs after irradiation to be used for histology studies. 65 animals were, after the end of the experiments at ID 17, shipped as airfreight to Saskatoon, Canada, for observation in the animal facility at the University of Saskatchewan. All animals arrived alive and well, considering their disease. Weight loss between 10 and 18 g, compared to the weights recorded on the day before shipping, was noticed in most animals (even in healthy controls). Animals that were deemed unfit for shipping remained at the animal facility of ID 17.

We would like to thank Mr. Dominique Dallery and his colleagues for the continuing superb support in all matters pertaining to animal care. We also would like to thank everybody involved in solving the transport problem for those animals. And, finally, we would like to thank everybody from the ID 17 team who helped to make our experiments successful as well as enjoyable.