EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

Experiment Report Form

	Experiment title: Enhancement of radiation effects by gold nanoparticles for Synchrotron steretotactic radiotherapy	**Experiment number**: MD440
Beamline:	**Date of experiment**: from: September 17th 2009 to: September 20th 2009	**Date of report**: October 4th 2010
Shifts:	**Local contact(s)**: Helene Elleaume	*Received at ESRF:*

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Report:

Aims of the experiment and scientific background:

The purpose of this study was to determine the dose-enhancement factor on F98 cells at 50 keV using 15 nm-diameter and 1.9 nm-diameter gold nanoparticles (AuNPs).

Cell survival studies were performed in the first part of the proposed experiment, in the second part, gold-enhanced Synchrotron Stereotactic Radiotherapy was performed on the F98 rodent glioma model, after intratumoral injection by convection-enhanced delivery methods of 15 nm AuNPs. These results could be compared with the results obtained in the previous *in vivo* study with smaller AuNPs (proposal MD-355).

In vitro results (17-20 September 2009):

The experiments were carried on F98 glioma cells. The cells were irradiated at 50 keV in media containing or not gold nanoparticles at a gold concentration of 10 mg/mL. A dose enhancement factor was observed for both the AuNPs of 1.9 nm and 15 nm (DEF=1.9 and 1.4 ,respectively). but a DEF more significant was noticed for the 15 nm AuNPs.

In vivo results (25-28 November 2009):

A preliminary study was carried out in February 2009, using intracerebral nanoparticles delivery in association with synchrotron stereotactic radiotherapy for the treatment of F98 glioma bearing rats (MD355). An important toxicity was observed with these gold nanoparticles. The present study was performed with 15 nm gold nanoparticles. For all irradiated groups, the irradiation was performed on day 14, following the irradiation set-up described in the previous study [1]. The gold nanoparticles were injected into the tumor by convection-enhanced delivery methods few minutes before irradiation, as described previously [2, 3].

The rats were divided into 6 experimental groups:
Group 1 : “untreated animals”,
Group 2 : “irradiation alone 15 Gy delivered in a single fraction”,
Group 3 : “gold alone 125 µg/ 5 µl”,
Group 4 : “gold alone 250 µg/ 5 µl”,
Group 5 : “gold alone 125 µg/ 5 µl + irradiation ”
Group 6 : “gold alone 250 µg/ 5 µl + irradiation ”.

No toxicity was observed after intracerebral injection of these AuNPs. An increase of median survival life span was observed for the rats treated with gold and irradiation in comparison with the “irradiation alone group”. The median survival time of group 2 was: 35 days, Group 5: 37 days, Group 6: 41 days. The differences were however not significant ($p>0.05$).

Conclusions:

These preliminary results demonstrate that dose-enhancement can be obtained in presence of gold nanoparticles, both *in vitro* and *in vivo*. However, this method will require further studies to obtain *in vivo* a more substantial survival improvement. The results of these experiement will soon be published and are part of Laure Bobyk’s PHD thesis (Grenoble University - November 10th 2010).

References:

1. Adam JF, Elleaume H, Joubert A, Biston MC, Charvet AM, Balosso J, Le Bas JF, Esteve F: Synchrotron radiation therapy of malignant brain glioma loaded with an iodinated contrast agent: first trial on rats bearing F98 gliomas. Int J Radiat Oncol Biol Phys 57: 1413-1426, 2003
2. Rousseau J, Boudou C, Barth RF, Balosso J, Esteve F, Elleaume H: Enhanced survival and cure of F98 glioma-bearing rats following intracerebral delivery of carboplatin in combination with photon irradiation. Clin Cancer Res 13: 5195-5201, 2007
3. Rousseau J, Boudou C, Esteve F, Elleaume H: Convection-enhanced delivery of an iodine tracer into rat brain for synchrotron stereotactic radiotherapy. Int J Radiat Oncol Biol Phys 68: 943-951, 2007