EUROPEAN SYNCHROTRON RADIATION FACILITY

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Experimental Report MD1177

Nanoscintillators-induced photodynamic therapy upon synchrotron radiation for deep-seeded glioma tumors

Beamtime: From October 24th to October 27th 2018 – 9 shifts

Experiments performed:

We investigated the dose enhancement effect produced when LaF_3:Ce nanoscintillators are accumulated within the tumor prior to monochromatic synchrotron radiation radiotherapy.

We first investigated this effect *in vitro* on 3D models of glioma (spheroids grown in suspension). We compare the effects obtained on two types of cultures: F98 spheroids (rat cell line) and U87 spheroids (human cell line). We investigated the effect of the dose (2 Gy, 4 Gy and 8 Gy) on these cultures for a given radiation energy (50 keV), as well as the effect of the energy (30 keV, 50 keV and 80 keV) for a given dose (4 Gy).

In parallel to these *in vitro* experiments, we performed an *in vivo* study. Rats bearing F98-glioma were randomized in 6 groups (n=10/groups): a control group, a group receiving the injection of nanoscintillators intravenously, a group receiving the nanoscintillator by convention enhanced delivery (CED) infusion directly in the brain, and three treatment groups: one group receiving the radiotherapy only and two groups receiving the nanoparticles (intravenously or by CED) and the radiations. The radiation dose delivered to the animals was 10 Gy, delivered by a monochromatic beam with an energy of 50 keV, 30 min after the nanoparticle injection. In addition, as nanoscintillators injected by CED induced enough contrast on tomography images, we acquired images 30 min, 24 hours and 48 hours after injection. Using these images, we were able to quantitively compare the amounts of nanoparticles present in the tumor 30 min, 24 hours and 48 hours after injection. All the animals were then imaged by MRI every 7 days and monitored for survival upon reaching a humane endpoint. After euthanasia, the brains were collected to perform immunohistochemistry and elementary analysis.

Summary and impact :

This study is the first one ever performed that demonstrate the radiation dose enhancement effect induced by nanoscintillators accumulated within a tumor prior to radiation therapy. This study performed *in vitro* and *in vivo* provided results that are currently being prepared for publication. In addition, these results were already presented to several international conferences including during three conferences were the main proposer was an invited speaker:

- *17th International Photodynamic Association World Congress* - Boston, USA - 06/2019
- *2019 ESP-IUPB World Congress* - Barcelona, Spain - 08/2019
- *15th International Conference on Scintillating Materials and their Applications* - Sendai, Japan - 10/2019