Internship in nuclear instrumentation

Dosimetry for *in vitro* assessment of targeted alpha therapy

Targeted alpha therapy (TAT) is a treatment modality in which a labelled α-emitting radioisotope is injected to the patient. The labelled molecules specifically target biomarkers of the tumour cells. Consequently, the dose deposition, produced by the radioisotopes decay is concentrated at a close distance of tumour cells, especially in the case of α-emitters. The favourable characteristics of α particles (short range, high linear energy transfer, potent cytotoxicity), explain the increasing development and use of TAT [1].

As any new treatment, TAT requires preclinical investigations to evaluate the efficiency of new molecules and compare the results to other existing modalities. *In vitro* experiments are part of these investigations. They consist in exposing cells cultured in a dish to labelled radioisotopes diluted in culture medium. In this kind of experiments, biological effects (such as survival fraction for example) are usually compared to the injected activity. Even if this is relevant for β-emitters (due to the millimetre range of β-particles), it is not adapted to the quantitative evaluation of α-emitting radioisotopes. Moreover, to compare the efficiency of TAT to other treatments such as external beam radiotherapy or β-emitting targeted radiotherapy [2], the knowledge of the absorbed dose in cells is much more relevant. The determination of this quantity is given by the MIRD formalism [3-5] and, in the case of *in vitro* experiments, depends on the spatial distribution of the radioisotopes in the culture medium and the thickness of the cells.

An innovative method has been successfully tested during a preclinical evaluation of ^{212}Pb-VCAM-1 [6] to provide reliable and accurate dose measurements during *in vitro* experiments [7]. This method primarily relies on the measurement of the energy spectrum of α-particles emitted from the culture medium trough a 2.5 µm mylar wall by silicon detectors. The deconvolution of the experimental spectrum using Monte Carlo simulations provides the spatial distribution of the radioisotopes in the culture medium that is necessary for the dose determination.

The goal of this internship is to implement and characterise a dosimetry prototype adapted to *in vitro* experiments.

The prototype implementation will be based on silicon detectors of appropriate surface (determined by cell culture constraints) and thickness (determined by α particles range), charge preamplifiers and a FASTER acquisition system. Customized culture wells will have to be designed to be compatible with the detection of α-particles (mylar base of µm thickness).

The whole detection system will have to be light-shielded due to the use of the silicon detector and compatible with biology experimental conditions (principally temperature, humidity and oxygen concentration stabilization).

Once the prototype implemented, its geometry will be tested with alpha sources and its geometry with be reproduced in Monte Carlo simulations to analyse its response.

This project will be done at GANIL, in the framework of the research program on the production of innovative medical radioisotopes funded by ANR (REPARE project). GANIL has also important skills in nuclear instrumentation and preclinical dosimetry [8-13] and already developed collaborations with other laboratories (LPC Caen, Cyceron, ISTCT…) in interdisciplinary domains.

This internship leads to a PhD thesis.

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