

Study of dosimetry based on MRI and autoradiography in Targeted Radiotherapy

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 tumour cell biomarkers. As a result, particles emitted during the decay of the radioisotope deliver the dose locally, close to tumour cells, especially in the case of α -emitters. The favourable properties of α -particles (short range, high linear energy transfer, potent cytotoxicity) explain the increasing development and use of TAT [1]. This project is therefore part of the willingness to evaluate and implement new radiopharmaceuticals based on alpha-emitting radioisotopes: ^{223}Ra , ^{211}At , ^{212}Pb , ^{225}Ac .

Like any new treatment, TAT requires research to evaluate the efficiency of new molecules and to compare results with other existing modalities. These studies include in vivo experiments to assess the efficiency of the treatment on tumours and the toxicity to healthy tissues. The accuracy of this evaluation and the understanding of the biological effects depend in particular on the knowledge of the dose absorbed by the different organs.

Three-dimensional dosimetry for internal radiotherapy in general and TAT in particular is more complex than for external beam radiotherapy and is described in **Figure 1**. It involves the acquisition of the biodistribution of the radiopharmaceutical, usually by positron emission tomography (PET) or Single Photon Emission Tomography (SPECT) imaging and the calculation of the absorbed dose by Monte Carlo or kernel convolution.

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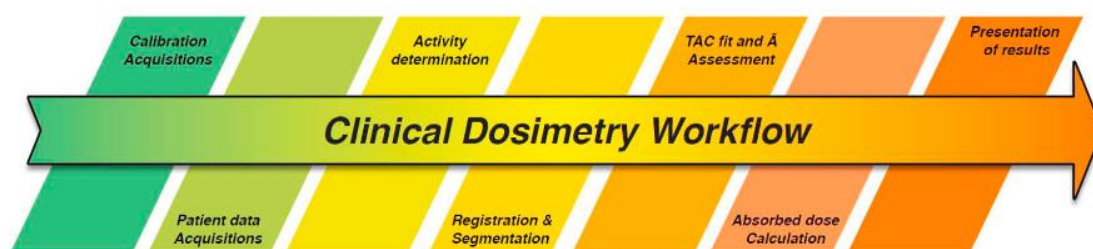


Fig 1. The basic steps to performing and recording an absorbed dose from radiopharmaceuticals.

The objective of this internship is part of the preclinical study of a new TAT treatment for brain metastases being carried out by ISTCT, CLCC Baclesse, INTHERES and GANIL. At this stage, the efficiency of the treatment with a vector labelled with an alpha-emitting isotope on metastases and its toxicity on normal tissues must be evaluated and quantified in relation to the absorbed dose in small animals.

To address this aim, a dosimetry process has been implemented and tested with preclinical and clinical SPECT and PET acquisitions. Nevertheless, these modalities lack of spatial resolution in the case of brain metastases in small animals.

To address this issue, complementary *ex vivo* autoradiography measurements were performed using an antibody labelled with ^{125}I . These measurements provide 2D distributions of the antibody in several layers of the brain.

The objective of the internship is thus to integrate autoradiography measurements in the dosimetry process developed prior to this internship, to determine the dose



delivered to the metastases and the healthy tissues in the brain. The internship will rely on several steps:

1. Bibliography on the integration of autoradiography in dosimetry
2. Characterization and calibration of autoradiography acquisitions
 - Characterization of the background
 - Calibration of autoradiography films in terms of activity
 - Analysis of the activity distribution in the metastases and the healthy tissues
 - Analyse du nombre et des tailles de métastases -> rapprochement avec CPOP (cross-fire) + à partir de quelle taille/nb de cellules on détecte l'activité

Autoradiography measurements, including known activity drops and ex vivo samples, have been performed prior to the internship.

3. Modelling of the activity distribution in 3D and registration with anatomic data acquired in MRI (homogeneous vs. heterogeneous distribution, distribution geometry, spatial resolution...)
4. Implementation of the anatomy and modelled activity distribution in Monte Carlo simulation (OpenGate v10) and simulation of different beta and alpha-emitting isotopes
5. Analysis of the dose distributions corresponding to the different activity distribution models and isotopes.

The internship will be -supervised by the GANIL but will include close collaboration with ISTCT, LITO, LPCC, CLCC François Baclesse, INTHERES.

References:

[1] F. Guerard, J. Barbet, J.-F. Chatal, F. Kraeber-Bodere, M. Cherel and F. Haddad, "Which radionuclide, carrier molecule and clinical indication for alpha-immunotherapy," *Q J Nucl Med Mol Imaging*, vol. 59, pp. 161-167, 2015.

Expected skills

The student should have a formation in medical physics with a good knowledge of radiation-matter interactions, radiotherapy and dosimetry. Knowledge in Monte Carlo simulation (OpenGATE), 3DSlicer and Python would be a plus.

This work does not lead to a PhD-thesis.

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