MEDIRAD

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Midterm recruitment report for radiopharmaceutical dosimetry study

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D2.11 Midterm recruitment report for radiopharmaceutical dosimetry study

Introduction

An essential component of Subtask 2.3.2.2 (Estimation of patient organ doses from two commonly used PET and SPECT tracers) relies on data collected within a clinical study). The patient study aims to collect state-of-the-art biodistribution data from both ^{99m}Tc-HMDP and ^{18}FDG (tracers identified in subtask 2.3.1) by means of sequential quantitative SPECT/CT and PET/CT acquisitions respectively. This is one of the rare prospective studies developed within the frame of MEDIRAD.

Pharmacokinetics extracted from SPECT/PET and media density from CT will be used as input for the patient-specific Monte Carlo absorbed dose modelling. The aim is to provide updated administered activity-to-organ-dose conversion factors (Deliverable 2.17 – M45).

Status

The medical ethics committee approval of the Ghent University Hospital for both radiopharmaceutical biodistribution studies was received on *November 6th, 2019*. Image data acquisition protocols, patient information and informed consent documents were prepared.

Recruitment of patients was started at the beginning of *December 2019* among patients referred to nuclear medicine in routine clinical practice. At the time patients contact the nuclear medicine department to schedule their ^{99m}Tc-HMDP and ^{18}FDG scans, the patients are informed by phone about the study and asked whether they wish to participate in the study. Interest of participating in this study is low. The important (time) effort requested of these patients is the main reason to decline. As a result, patient recruitment strategy was optimized and now mainly focusses on patients that are in the hospital at the time of making the appointment.

Due to the COVID-19 crisis, no patients could be recruited as from begin of *March 2020* clinical studies were put on hold in the hospital. Only urgent scans were/are planned in the nuclear medicine department and for those patients it was/is considered as unacceptable to stay longer in the hospital as strictly needed for the actual clinical scan. Patient recruitment at Ghent University Hospital could take place again from *mid-June 2020*.

Unfortunately, no patients willing to participate in this study were found so far.

Main reasons given were:

(1) time effort: study takes too much of patients' time or is in conflict with other appointments,
(2) COVID-19 crisis: less patients go to the hospital and are 'afraid' to stay longer than necessary in a hospital environment, and
(3) a few patients indicated that they did not want to get additional irradiation (which is the case in this study).

Nevertheless, patient recruitment will carry on, thanks to the motivation of medical staff involved in the project. The (relatively) low number of patients considered for the study should be achievable in the remaining time allotted to the project.

If, after all, patient recruitment is too low, available 3D biodistributions of 2 new PET and SPECT tracers (^{99m}Tc-labelled S-HYNIC certolizumab pegol in rheumatoid arthritis patients and ^{18}F-PSMA-11 for prostate cancer patients) will be used.

The latter data are acquired with state-of-the-art methods and can be used to evaluate different methods of individualized dosimetry for diagnostic radiopharmaceuticals as developed by INSERM (D2.17). We expect approval of the Ghent University Hospital ethics committee in the coming weeks.

Yet, at this stage of the project, given the fact that the duration of tasks and deadlines for providing the results was already extended, the question is that of the feasibility of the task (i.e. performing the dosimetric study) within the remaining time, using clinical data not yet available.

Aside from patient recruitment, preparatory work for the patient-specific dosimetry simulations was conducted in anticipation, in order to speed up the overall process.

A patient-specific radiopharmaceutical dosimetry package was built within CRCT (INSERM). This software is at the intersection of WP2 and WP3. First, both WP include radiopharmaceutical dosimetry studies, in Subtask 2.3.2.2 and Task 3.3. Second, the development of the imaging and radiation dose biobank – IRDBB - (Task 2.4) triggered fructuous discussions between consortium members.

A 'chicken and egg' situation was identified for nuclear medicine dosimetry:

- no specific tag exists to give account of the dosimetric workflow. For example, there are no specific tags to document the time-activity-integration procedure – or even the results of that procedure (time integrated activity or time integrated activity coefficient). The 2 INSERM partners (LTSI and CRCT) therefore collaborated to develop the required ontology and integrate that in the IRDBB structure.
- yet, the second issue is that since no specific tags exist, no software is able to deal with specifically designed nuclear medicine dosimetry tags. As entering manually these tags at the end of the clinical dosimetry process was considered unrealistic (no clinical department would do that), it was therefore decided to *integrate this requirement within the development process of the nuclear medicine dosimetry software*.

We decided to build a nuclear medicine dosimetry software based on 3D Slicer (www.slicer.org). 3D Slicer is an *open source* software platform for medical image informatics, image processing, and three-dimensional visualization. Therefore, some of the steps included in a clinical dosimetry procedure, such as data import (in the DICOM format), image registration or segmentation are already present, documented and validated.

This led us to develop (only) missing modules such as:

- Calculation of absorbed dose (rate) from 3D maps of density and cumulated activity (activity) according to different algorithms (local energy deposition, convolution or Monte Carlo).
- Integration of time-dependent parameters such as activity (to provide cumulated activity or time-integrated activity), or absorbed dose rates (to provide the absorbed dose).

In addition, the *assembly of modules in a structured way* led to a global application that allows consideration of the calibration step as part of the dosimetry procedure (*a missing feature in all existing software*), and the storage and possible input/output of intermediary stages of the dosimetry procedure. This will not only allow processing data in different sessions if needed, but also to compare the intermediary results obtained using different approaches/software.

Last, the results and relevant dosimetric variables can be exported in the IRDBB, thereby populating the database and allowing further retrospective analysis of the results based on a range of dosimetric parameters.

The development of the software (OpenDose3D) has been structured from the start as an open source project and participates to the OpenDose collaboration (www.opendose.org). This means free access to the sources via a gitlab project (https://gitlab.com/opendose/opendose3d), and association of partners for the development, debugging and validation. It is believed that this is a way to ensure sustainable development – and provide the software a life expectancy that goes beyond the MEDIRAD project duration.

The development phase is globally completed and the software is currently being validated on test-cases provided by clinical centres (Fig. 1). The transfer from clinical centres to the IRDBB and from IRDBB to the dosimetry processing centre is now validated for different centres and data formats. Obviously, we could not test the software on patient data from Subtask 2.3.2.2, therefore clinical data from Task 3.3 patients were used instead. The validation phase should be completed on time to perform the dosimetric analysis as soon as clinical data become available.

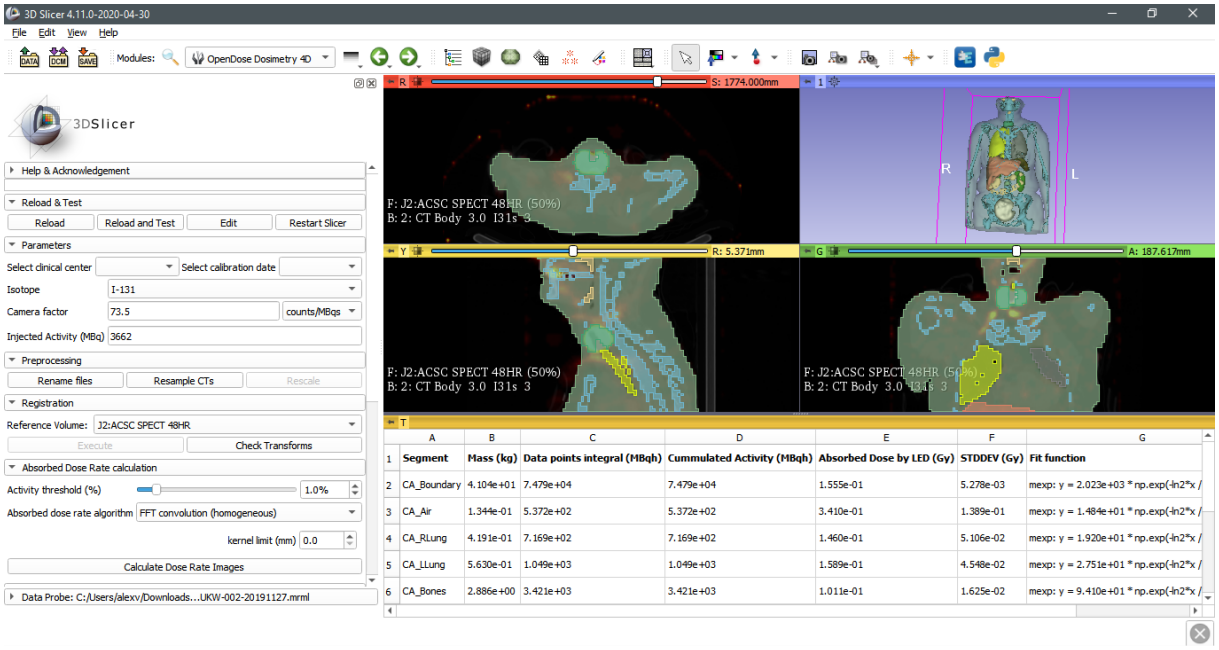

Fig 1: Presentation of the dosimetric software interface for a MEDIRAD WP3 patient.

Conclusions:

- Recruitment was delayed, not only but also due to COVID-19.
- The completion of the task is still possible, as planned with clinical data from a prospective clinical trial or alternatively by performing a retrospective analysis of already existing clinical data
- The processing of dosimetry will be optimised thanks to the development of a specific software.