Development, validation, and implementation of a patient-specific Monte Carlo 3D internal dosimetry platform

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Targeted radionuclide therapy is emerging as an attractive treatment option for a broad spectrum of tumor types because it has the potential to simultaneously eradicate both the primary tumor site as well as the metastatic disease throughout the body. Patient-specific absorbed dose calculations for radionuclide therapies are important for reducing the risk of normal tissue complications and optimizing tumor response. However, the only FDA approved software for internal dosimetry calculates doses based on the MIRD methodology which estimates mean organ doses using activity-to-dose scaling factors tabulated from standard phantom geometries. Despite the improved dosimetric accuracy afforded by direct Monte Carlo dosimetry methods these methods are not widely used in routine clinical practice because of the complexity of implementation, lack of relevant standard protocols, and longer dose calculation times. The main goal of this work was to develop a Monte Carlo internal dosimetry platform in order to (1) calculate patient-specific voxelized dose distributions in a clinically feasible time frame, (2) examine and quantify the dosimetric impact of various parameters and methodologies used in 3D internal dosimetry methods, and (3) develop a multi-criteria treatment planning optimization framework for multi-radiopharmaceutical combination therapies. This platform utilizes serial PET/CT or SPECT/CT images to calculate voxelized 3D internal dose distributions with the Monte Carlo code Geant4. Dosimetry can be computed for any diagnostic or therapeutic radiopharmaceutical and for both pre-clinical and clinical applications. In this work, the platform's dosimetry calculations were successfully validated against previously published reference doses values calculated in standard phantoms for a variety of radionuclides, over a wide range of photon and electron energies, and for many different organs and tumor sizes. Retrospective dosimetry was also calculated for various pre-clinical and clinical patients and large dosimetric differences resulted when using conventional organ-level methods and the patient-specific voxelized methods described in this work. The dosimetric impact of various steps in the 3D voxelized dosimetry process were evaluated including quantitative imaging acquisition, image coregistration, voxel resampling, ROI contouring, CT-based material segmentation, and pharmacokinetic fitting. Finally, a multi-objective treatment planning optimization framework was developed for multi-radiopharmaceutical combination therapies.