Evaluating preclinical radionuclide therapy efficacy by imaging and dose-response modeling

To further develop Radionuclide therapy (RNT) there is a great need for quantitative measurements of treatment response in vivo and improved dosimetry models. This project aims to investigate Positron emission tomography (PET) as a tool to follow RNT tumor response during ongoing preclinical treatment and to model RNT dose response through Monte Carlo microdosimetry simulations. Measuring tumor characteristics with PET during RNT can enhance current dosimetry models by adding factors known to affect the therapy outcome to the model. Dosimetry models for in vitro irradiation of cancer cell cultures is a tool to better estimate the absorbed dose in the subcellular compartments of cells irradiated with high Linear Energy Transfer (LET) particles emitted by radionuclides used in RNT.

Project 1: We investigated the limitations to perform PET imaging during RNT on three preclinical PET-systems, by adding gamma emissions from a non-PET tracer source during PET acquisition (1). Gamma emissions comparable to those expected from a tumor bearing prostate cancer mouse model treated with $^{177}$Lu, distorted the PET tracer count rates detected, making quantitative measurements of PET tracer uptake impossible, and worsened the image spatial resolution. The systems sensitivity and count rate properties determined the systems limits for intratherapeutical PET imaging. The method in our paper was suggested as a method for researchers interested in investigating their PET-systems ability to perform intratherapeutic PET imaging.

Project 2: We investigated a method to enable intratherapeutic preclinical PET imaging on PET-systems otherwise unable to do so at high therapeutic radioactivity. Shields, made of Rose metal alloy, were used to attenuate the emissions from $^{177}$Lu when present in the PET-system simultaneously as a PET tracer during image acquisition. A GATE/Geant4 Monte Carlo simulation of the PET system was used to investigate the effect of the coincidence energy window on the coincidence count rates during intratherapeutic imaging. We found that a 2-4 mm Rose metal shield surrounding a mouse injected with $^{18}$F-FDG and a tumor-phantom filled with $^{177}$Lu activity, was sufficient to allow PET-data to be detected and produce PET images of good quality (2).

Future projects: We plan to examine the agreement of cell survival assays in vitro for cancer cell lines relevant in the field of RNT, when irradiated with high, low, and intermediate LET radiation. This will include the colony forming assay, MTT assay and growth assay. To guide the in vitro irradiations of cells, microdosimetric models of the irradiation geometries and cells will be built in GATE/Geant4 to calculate the absorbed dose on a subcellular level.