PhD Thesis Title: Voxel-level dosimetry of ^{177}Lu-octreotate: from phantoms to patients

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ABSTRACT:

In radionuclide therapy, the patient is injected with relatively high amounts of therapeutic radiopharmaceutical which localises to target tissue and emits ionising radiation. Unfortunately, a perfectly targeting radiopharmaceutical has not been discovered and part of the radiopharmaceutical accumulates to healthy tissues, which are also thus irradiated. In order to ensure safe use, the absorbed dose of radiation-sensitive organs must be monitored.

The focus of this thesis is the patient specific dosimetry of Lutetium-177 (Lu-177) labelled somatostatin analogue Lu-177-DOTA-Tyr3-octreotate (Lu-177-DOTATATE) treatments and development of internal dosimetry software. Lu-177-DOTATATE is a radiopharmaceutical that binds to somatostatin receptors and is used to treat patients with metastatic neuroendocrine tumours. Recent studies have shown significant treatment outcome improvements with Lu-177-DOTATATE when compared to previously used somatostatin analogue treatments. However, the kidneys are the healthy organs that receive the highest amount of radiation dose from Lu-177-DOTATATE treatments and could be the organs that limit the number of treatments a patient can tolerate. In addition, absorbed dose to kidneys varies highly from patient to patient and thus patient specific dosimetry is recommended. Despite many years of dosimetry research and the existence of several published scientific dosimetry tools, there is no clinically validated kidney dosimetry software for Lu-177-DOTATATE treatments. The aim of this thesis was to study quantification accuracy of Lu-177 radionuclide using SPECT/CT imaging, and to study mean absorbed doses to kidneys, and dose distribution characteristics of Lu-177-DOTATATE. A streamlined voxel level absorbed dose software for clinical practice was developed and validated for kidney dosimetry of Lu-177-DOTATATE treatments.

The effect of reconstruction methods on Lu-177 quantification accuracy was studied using an anthropomorphic phantom with known Lu-177 sources [1]. Acquired data were reconstructed using different image compensation methods and results were compared with known source activities in the phantom. It was found that Monte Carlo simulation-based scatter compensation and SPECT detector response compensation improved Lu-177 quantification accuracy considerably. Similar findings were also observed with data from patients treated with Lu-177-DOTATATE.

A Monte Carlo simulation study was carried out to investigate absorbed dose distribution of Lu-177 [2]. Two main findings were that electrons emitted by Lu-177 can be assumed to be absorbed locally when the resolution of the imaging system is taken into account and the photon cross-irradiation can contribute significantly to total absorbed dose especially in the vicinity of highly active volumes.

Using Lu-177-DOTATATE patient data, two different kidney absorbed dose calculation methods were compared [3]. Comparing the mean kidney absorbed dose with the estimated maximum absorbed dose, it was observed that Lu-177-DOTATATE accumulates unevenly to kidneys causing significantly heterogeneous dose distribution within kidneys. In addition, a simplified imaging protocol was found to be adequate for dosimetry purposes and was later adopted clinical practice.

Combining previous findings new voxel level dosimetry software was developed. The clinical feasibility of the proposed software was tested with digital phantom simulations and reanalysing patient data from Lu-177-DOTATATE treatments [4]. The software was found to be reliable and to speed up and simplify the dosimetry workflow.

References to author publications that relate specifically to the dissertation:

1. **Hippeläinen, E**, Tenhunen, M, Mäenpää, H, Sohlberg, A. "Quantitative accuracy of Lu-177 SPECT reconstruction using different compensation methods: phantom and patient studies." EJNMMI Research 2016;6:16.

2. **Hippeläinen, E**, Tenhunen, M, Sohlberg, A. "Fast voxel-level dosimetry for Lu-177 labelled peptide treatments." Physics in Medicine and Biology2015;60:17:6685-6700.

3. Heikkonen, J, Mäenpää, H, **Hippeläinen, E**, Reijonen, V, Tenhunen, M. "Effect of calculation method on kidney dosimetry in Lu-177-octreotate treatment." Acta Oncologica 2016;55:9-10:1069-1076.

4. **Hippeläinen, ET**, Tenhunen, MJ, Mäenpää, HO, Heikkonen, JJ, Sohlberg, AO. "Dosimetry software Hermes Internal Radiation Dosimetry: from quantitative image reconstruction to voxel-level absorbed dose distribution." Nuclear Medicine Communications 2017;38:5:357-365.