Aim/Introduction: Quantitative measures such as the intratumoural activity distribution of a radiopharmaceutical and the corresponding absorbed dose distribution are useful information for radiopharmaceutical therapy (RPT) and radiopharmaceutical development. The ionizing-radiation Quantum Imaging Detector (iQID) is a scintillation-based detector able to image alpha particles, such as those emitted from tissue sections of mice injected with an alpha-emitting radiopharmaceutical. Quantitative imaging enables the determination of dose rates and time integrated activities within tumour sections. The aim of this work is to generate quantitative images of the activity distribution and dose rates within tumour sections of mice who were injected with an $^{225}$Ac labelled antibody. 

Materials and Methods: Small drops of a solution containing $^{225}$Ac with activities ranging from 0.8 Bq to 95 Bq were pipetted onto a silver-doped Zinc Sulfide (ZnS:Ag) scintillator and imaged with the iQID detector. The images were segmented and a calibration factor was calculated by generating a calibration curve and performing a linear fit. Four tumour bearing mice were injected with $18.4 \pm 2$ kBq of an $^{225}$Ac labelled antibody. Three days post injection, the tumours were collected, frozen, and sliced into 14 µm slices for autoradiography with the iQID detector. The calibration factor was used to convert the iQID images into units of activity (Bq). A dose kernel for $^{225}$Ac was created using GATE version 9.0 assuming water as the medium. The kernel was convolved with the iQID image to generate dose rate maps of each tumour slice. The tumour slices were segmented and the total dose rate within each slice was calculated.

Results: The measured calibration factor for the $^{225}$Ac isotope in the iQID camera was 0.33 cps/Bq. Using this factor, activity maps in units of Bq and dose rate maps in units of Gy/s were generated. Total activities within the slices range from 1.1 Bq to 2.7 Bq and total dose rates ranged from 0.6 to 1.5 Gy/s. Visually, activity distributions were heterogeneous.

Conclusion: We present a method to generate $^{225}$Ac quantitative images of the activity distribution and dose rates within mouse tissue sections using the iQID detector. This work has the potential to find correlations between dose, dose rates, and the degree of tumour heterogeneity with the therapeutic efficacy and other biological variables. Moreover, it will allow us to understand the distributions of different radiopharmaceuticals within tissue and correlate it with therapeutic outcomes.

References: None

References: None

**OP-0045**

The Impact of Cell Shape on the Doses Delivered to the Nucleus from $^{177}$Lu-labelled Radiotracers

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Aim/Introduction: Targeted radiopharmaceutical therapy (RPT) is a promising treatment option for various tumour types and metastases. While most dosimetry estimates in RPT are done on a macroscopic level, e.g. with PET or SPECT imaging, dosimetry on a cellular level is key to enhance our understanding of the mechanisms of RPT and to increase the chances of treatment success. Cellular dosimetry is often based on Monte Carlo (MC) simulations, however the choice of cell shape and distribution of the radiopharmaceutical within the cell may impact the calculated dose and therefore the accuracy of these methods. This work aims to compare S-values to the nucleus from $^{177}$Lu in two in vitro models of LNCaP (human prostate cancer cell line) cells: a spherical model and an ‘egg-white’ shaped model representing an adherent cell. 

Materials and Methods: A spherical and an ‘egg-white’ shaped cancer cell were modelled using GATE version 9.0 Monte Carlo software. Both models include a nucleus, nuclear membrane, cytoplasm, and cellular membrane. All cell regions were assumed to have the density of water (1g/cm$^3$). The total areas of both models were identical and were based on dimensions of LNCaP cells. The spherical cell was 13.5µm in diameter and the maximum dimensions of the egg-white cell was 39µm x 7µm x 14µm. $^{177}$Lu activity was homogeneously distributed either throughout the cytoplasm or at the cell membrane of each model to represent levels of internalization of the radioisotope. Absorbed dose was scored on a voxel level (0.04µm)$^3$ with GATE’s dose actor. S-values to the nucleus were calculated for each of the source regions and models. Results: The S-values to the nucleus of the ‘egg-white’ cell were 1.4x10$^{-4}$ Gy/Bq and 1.5x10$^{-4}$ Gy/Bq from the cytoplasm and membrane respectively. These values were 2.1 and 1.2 times lower than those from the spherical cell respectively.

Conclusion: The S-values to the nucleus of the spherical cell were larger than those from the ‘egg-white’ cell, likely due to the symmetrical distribution of activity. This indicates that the shape of the cell model influences the S-value and therefore the total dose to the nucleus of the cell. Consequently, absorbed dose simulations at a microscopic level must take
into account the cell size and shape and care should be taken to ensure the use of an accurate cell model referring to human cell lines. Future steps will include the comparison of different radionuclides on a cellular level. References: None

**OP-0046**

A physiologically-based pharmacokinetic model of $^{212}$Pb-labelled pharmaceuticals targeting neuroendocrine tumors in mice

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**Aim/Introduction:** $^{212}$Pb-labelled pharmaceuticals are promising in vivo sources of alpha particles through the short-lived $^{212}$Pb-daughter $^{212}$Bi. Cytotoxic alpha particles have a great potential in the treatment of aggressive neuroendocrine tumours that are resistant to beta radiation. Quantitative analysis of the distributed free radioactive products is challenging in targeted alpha particle therapy (TAT). Mathematical modelling allows for describing separately and simultaneously the pharmacokinetics of each of the decay products of alpha generators. Therefore, a first physiologically-based pharmacokinetic (PBPK) model was developed to describe the pharmacokinetics of $^{212}$Pb-$^{212}$Bi-DOTAMTATE targeting somatostatin receptor type2 (SSTR2) in mice. **Materials and Methods:** A whole-body $^{212}$Pb-PBPK model for mice was developed and implemented in both modelling software SAAM II (version 2.3) and Simbiology/MATLAB (MATLAB R2020a). All relevant physiological mechanisms are described in the $^{212}$Pb-PBPK model with parameter values from the literature. Another PBPK model for free $^{212}$Bi was developed, evaluated and integrated into the $^{212}$Pb-PBPK model. The pharmacokinetic parameters in the $^{212}$Pb-PBPK model were estimated using $^{212}$Pb-DOTAMTATE biokinetic data in AR42J-bearing mice after intravenous administration of 0.0013 nmol (0.185 MBq) of $^{212}$Pb-DOTAMTATE [1]. Absorbed dose coefficients (ADC) due to bound and unbound conjugated and released radionuclides were calculated. Results: The developed model successfully describes the experimental data. The fitted curves were good by visual inspection. The tumour plasma flow rate was (0.33±0.45) ml/min/g. SSTR2 densities in tumour, kidneys, liver, pancreas, spleen and lung were (5.94±1.04), (3.04±0.31), (0.33±0.45) ml/min/g. SSTR2 densities in tumour, kidneys, liver, pancreas, spleen and lung were (0.13±0.03), (4.05±1.48), (0.57±0.04) and (1.39±0.05) nmol/l. The calculated ADC in tumour, kidneys, liver, pancreas, spleen and lung were (5.94±1.04), (3.04±0.31), (0.33±0.45) ml/min/g.

**Conclusion:** The developed $^{212}$Pb-PBPK model describes the pharmacokinetics of a $^{212}$Pb-labelled pharmaceutical and the decay products in mice. The $^{212}$Pb-PBPK model can be used to determine the contribution of distributed free radionuclides to the absorbed dose in non-target tissues. Hence, the efficacy and safety of using $^{212}$Pb-labelled pharmaceuticals can be evaluated, reducing the time required for translation from bench to bedside. References: [1] Stallons, T. A. R., et al. (2019). Molecular Cancer Therapeutics 18(5): 1012-1021.

**OP-0047**

Therapeutic efficacy of heterogeneously distributed radiolabelled peptides: influence of radionuclide choice

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**Aim/Introduction:** To model dose-response relationships for in vivo experiments with radiolabelled peptides enabling therapeutic efficacy comparison. **Materials and Methods:** Distribution of somatostatin receptor type-2 (SSTR2) expression was imaged in NCI-H69 xenografts on mice, at 0,2,5,11 days after injection with $^{177}$Lu-DOTATATE. Realistic 3D heterogeneous activity distributions (5.7x5.7x10μm voxels) were reconstructed in tissue geometries of cancer and healthy cells. The resulting spatial absorbed dose rate distributions at each time-point were calculated using GATE and compared to homogenous dose rate distribution. Calculations were performed for the most commonly used radionuclides ($^{90}$Y, $^{16}$Tb,$^{177}$Lu, $^{212}$Bi), assuming comparable biodistributions. The added activity was in all cases 30 MBq, except for $^{212}$Bi with 10 MBq. The averaged absorbed dose on the mm-scale tissue sections delivered over the whole treatment (complete decay) was correlated to the modelled in vivo survival. Radiobiological parameters were derived from experimental data on $^{177}$Lu-DOTATATE: DNA-damage repair half-life ($T_{D}$) by fitting the in vitro DSBs over time and linear quadratic (LQ) model radiosensitivity parameters ($\alpha, \beta$) by comparison with cell death assay and volume response over time. The tumor doubling time $T_{D}$ was obtained by fitting the tumor volume data over time. An RBE of 3.4 was used for the calculations with $^{212}$Bi. The absorbed dose (0-2days) on μm-scale sections was correlated with DSBs induction, measured by yH2AX-foci for $^{177}$Lu-DOTATATE. Results: The average S-values for the initial heterogeneous dose-distributions ($S_{H}$=3.36±0.32 μGyBq$^{-1}$h$^{-1}$, $S_{B}$=4.84±0.48 μGyBq$^{-1}$h$^{-1}$, $S_{T}$=6.35±0.47 μGyBq$^{-1}$h$^{-1}$, $S_{B}=218±0.22 μGyBq$^{-1}$h$^{-1}$) are not significantly different from the homogeneous ones, irrespectively of the radionuclide choice. The reduction of SSTR2 expression over time, accounted for $^{177}$Lu-DOTATATE, causes an increase in this $S$-value difference up to +58% at day 11. No significant difference between the heterogeneous and homogeneous in vivo survival is observed, unless the SSTR2 reduction over time is significant and taken into account in the calculations. Within the LQ-model, the best matching in vivo survival