## Absorbed doses to mice for three [<sup>18</sup>F]-tracers calculated from experimental kinetic data and Monte Carlo simulations

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In preclinical microPET imaging, small rodents often have to undergo longitudinal studies involving multiple scans combined with microCT imaging to gather anatomical information. The radiation exposure of the animals needs to be addressed since the impact of the radiation might compromise the validity of the results. The aim of the study was to use experimentally obtained kinetic data of three [18F]-tracers and S-values derived by Monte Carlo simulations to calculate absorbed doses in mice and estimate radiation exposure in longitudinal studies.

The bio-distribution of 6-[18F]fluoro-L-DOPA, 2-[18F]fluoro-LTyrosine and [18F]UCB-H was obtained using organ harvesting (OH) at multiple time points, dynamic microPET imaging (DI) and hybrid imaging (HI), where organs are harvested post scan to improve quantification of microPET. Monte Carlo simulations were carried out using GATE v6.1 and the MOBY phantom to determine S-values of multiple source and target organs. Time activity curves were derived from experimental data and residence times for multiple source organs were calculated and used for absorbed dose calculations.

The average total body absorbed dose for all three [18F]- tracers and all methods was almost identical with 14.19  $\pm$  0.10 mGy/MBq. The critical organs for 6-[18F]fluoro-LDOPA were the kidneys with 23.61  $\pm$  6.34 mGy/MBq for OH and the bladder wall for DI and HM with 660.79  $\pm$  276.57 mGy/MBq and 660.70  $\pm$  276.51 mGy/MBq, respectively. The high derived bladder wall absorbed dose is similar to values provided in literature for bladder wall from [18F]FDG in mice. For 2-[18F]fluoro-L-Tyrosine the highest dose was absorbed by the liver for all three methods with 48.23  $\pm$ 8.32 mGy/MBq derived by OH (DI: 46.26  $\pm$  7.35 mGy/MBq; HM: 49.28  $\pm$  9.97 mGy/MBq). For [18F]UCB-H the critical organs were the liver for OH with 65.14  $\pm$  8.47 mGy/MBq and the bladder wall for DI with 57.63  $\pm$  28.36 mGy/MBq.

The calculated absorbed doses derived from the three experimental methods showed good agreement, and correlations between OH and DI were improved by using HI. When assuming multiple injected activities of 10 MBq plus additional radiation from microCT, an accumulated total body absorbed dose of more than 1 Gy and much higher absorbed doses for single organs can be reached possibly introducing stochastic effects. The lethal absorbed dose for a mouse is considered 6 Gy, however, studies have shown that far lower absorbed doses can alter the physiology and compromise results.