to those based on the seven-point measurement were calculated for both right and left kidney. To test statistical significance a Wilcoxon matched-pairs signed rank test with a P-value of 0.05 for significance was used. Median, Min and Max of the deviations were also calculated for the AD. For the early measurement points, estimations from the (24-96) for the time of measurement were compared with the measured values. ***Results:*** Bias versus AD(seven) was -0.4%(-1.1-3.8) (Median(Min-Max)) for the right kidney and -0.2%(-1.1-5.4) for the left kidney when the AD(24-96) method was used. The P-values were 0.69 for the right kidneys and 0.84 for the left kidneys and this show no significant difference between the two methods. With errors as small as these and using a fixed limit of the absorbed dose to the kidneys, this would mean that really few patients would be given unoptimized number of treatments. The difference of the estimated activity concentrations for every point was in general small (less than 5%) but could vary up to about 30% for single values. A larger study including more patients and preferably also a later timepoint (maybe 7 days) is highly warranted. ***Conclusion:*** With a difference of less than about 5% for all the measurements the results from this study indicate that the influence of early measurements (earlier than 24 h) is fairly small and can be ignored. ***References:*** None

OP-765

Preliminary results of a Phase II ^{177}Lu and ^{90}Y PRRT study: analysis of OAR dosimetry and dose-response relationship for NET liver metastases

E. Tonini[1], S. Panareo[2], M. Longo[3], L. Longo[4], L. Perrucci[5], E. Fortini[5], G. Di Domenico[4], L. Uccelli[2], C. Cittanti[2], A. Turra[1], M. Giganti[5], M. Bartolomei[2];
[1]Sant'Anna Hospital, Medical Physics Unit, Ferrara, ITALY, [2]Sant'Anna Hospital, Nuclear Medicine Unit, Ferrara, ITALY, [3]Sapienza University of Rome, Ph.D. Program in Morphogenesis & Tissue Engineering, Rome, ITALY, [4]Department of Physics and Earth Sciences, Ferrara University, Ferrara, ITALY, [5]Section of Diagnostic Imaging, Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, ITALY.

Aim/Introduction: Peptide-receptor radionuclide-therapy (PRRT) has become a standard treatment modality for patients affected by neuroendocrine tumors. A phase II study FENET2016 (University Hospital Sant'Anna, Ferrara, Italy) is presented. Treatment protocol relies on either five PRRT cycles with ^{177}Lu-DOTATOC or a sequence of ^{177}Lu followed by ^{90}Y-DOTATOC spaced two months apart. We report about tumors and organ-at-risk (OAR) dosimetry and evaluation of the dose-response relationship for liver metastases. ***Materials and Methods:*** 80 patients underwent PRRT therapy with systemic administration of cumulative activities between 11 and 28 GBq. A validated method based on three-time-point (at 1, 24, 48 hours after administration) SPECT/CT was developed to calculate the absorbed doses (AD) to tumors and OARs. Tumors and kidneys AD were calculated according to MIRD scheme, while L2-L4 lumbar vertebrae imaging method was used to calculate AD to BM. Dosimetric results between first and fifth cycle were compared as well as those obtained with ^{177}Lu and ^{177}Lu\$^{90}$Y modalities. Tumor response was evaluated applying the Response Evaluation Criteria In Solid Tumors (RECIST 1.1) to hepatic lesions. The CTs were performed no earlier than 4 weeks before the treatment and no later than 12 weeks after it. By comparing the lesions in the CT with the areas of high uptake in SPECT\CT, only the superimposable lesions were selected, resulting in 29 lesions in 15 patients. The variations of lesion diameter recorded by CECT and the corresponding absorbed doses were correlated. ***Results:*** The cumulative doses ranged from 13 to 310 Gy for tumors, from 3.5 to 40 Gy for kidneys and from 0.03 to 1.2 Gy for BM. High variability in tumor AD per unit activity was observed with values ranging from 2.5 to 45 mGy/MBq and from 1 to 107 mGy/MBq for ^{177}Lu and ^{177}Lu\$^{90}$Y. The percentage reduction of lesion diameters treated with ^{177}Lu\$^{90}$Y resulted higher than those obtained with ^{177}Lu (mean=29.3%, SD=17.6 for ^{177}Lu\$^{90}$Y; mean=3.4%, SD=19.41 for ^{177}Lu\$^{90}$Y). The dose-response correlation (r=0.92) turned out to be highly significant with a level of sampling significance superior than 99% when considering lesions above 3 cm in diameter treated with ^{177}Lu\$^{90}$Y. No correlation was found below 80 Gy. ***Conclusion:*** The dosimetric protocol routinely established provides reproducible, standardized and patient-tailored dose estimates. The highly significant correlation between the lesion response and the absorbed dose we found for large metastases treated with ^{177}Lu\$^{90}$Y is highly promising for the clinical benefit derived from the implementation of dosimetry in PRRT. ***References:*** None

OP-766

Lesion-wise dosimetry for multiple bone metastases in mCRPC patients undergoing Lu-177-PSMA therapy: comparison of five dosimetric methods

J. Brosch[1], C. Uribe[2], A. Gosewisch[1], L. Kaiser[1], P. Bartenstein[1], A. Todica[1], H. Ilhan[1], A. Rahmim[3], A. Celler[3], S. Ziegler[1], G. Böning[1];
[1]Department of Nuclear Medicine, University Hospital, LMU Munich, Munich, GERMANY, [2]PET Functional Imaging, BC Cancer, Vancouver, BC, CANADA, [3]Department of Radiology, University of British Columbia, Vancouver, BC, CANADA.

Aim/Introduction: Although metastatic, castration-resistant prostate cancer (mCRPC) patients undergoing Lu-177-PSMA-therapy show a large number of bone metastases, tumor dosimetry is typically performed only for a limited number of lesions per patient. To differentiate between responding/non-responding bone lesions, dosimetric calculation for all bone lesions is required. We aimed to investigate the accuracy of 4 computationally-efficient

dosimetric methods against Monte-Carlo (MC) based dosimetry as gold-standard. ***Materials and Methods:*** 10 mCRPC patients, receiving their 1st cycle of Lu-177-PSMA-I&T-therapy (7.4-9GBq), were enrolled. Each patient underwent quantitative Lu-177-SPECT/CT at 24h, 48h and 72h p.i. with 3 bed positions (shoulders-knees). All lesions with volumes >1ml were segmented on the 24h SPECT (kmeans segmentation, PMOD v4.005) and the resulting volumes of interest (VOIs) were copied to the subsequent co-registered SPECTs. For each lesion, the effective half-life was obtained by mono-exponential fitting of activities in these VOIs. To preserve the 3D distribution information within the lesions, the time-integrated activity image was estimated based on the 24h SPECT. Dose estimates per lesion from MC (GATE v8.2) were compared with those from: A) OLINDA v.2.0 using unit-density sphere model, B) OLINDA weighted with CT-based average lesion density, C) ICRP soft tissue Lu-177 voxel-S-values (GATE), and D) voxel-S-values with CT-based voxel density weighting. ***Results:*** In total, 125 lesions (volumes 1.5-420.6ml) were analyzed. On average, method A overestimated doses for all lesions (mean: +10%, range: -12% to +47%), while method B underestimated them (mean: -14%, range: -28% to -2%). Similarly, method C overestimated the lesion doses (mean: +20%, range: -8% to 57%), whereas results from method D were closest to the MC dose estimates showing the smallest range of deviations (mean: -4%, range: -9% to -3%). ***Conclusion:*** Full MC dosimetry is complex and time-consuming, while commonly employed OLINDA is simple and fast. The advantage of MC and voxel-S-value methods is the generation of 3D dose distributions, contrary to OLINDA which assumes spherical tumors and provides only mean doses. Our results show that doses estimated by methods A and C (assuming unit density) reveal a large range of deviations from MC, which is reduced when CT-based density weighting (methods B and D) is applied. To conclude, dosimetric calculation using voxel-S-values with CT-based density weighting represents a simple, yet accurate dosimetric method compared to the gold-standard MC dose estimates. This practical approach would enable determination of dose estimates for all bone lesions in mCRPC patients and visualization of 3D dose maps. ***References:*** None

OP-767

Individualization of ^{177}Lu-PSMA Therapy based on important physiologic parameters using global sensitivity analysis and a physiologically-based pharmacokinetic model

G. Glatting[1,2], P. Kletting[1,2], N. J. Begum[1], M. Eiber[3], A. J. Beer[2], S. A. Pawiro[4], D. Hardiansyah[4];

[1]Medizinische Strahlenphysik, Nuklearmedizin, Universität Ulm, Ulm, GERMANY, [2]Klinik für Nuklearmedizin, Universität Ulm, Ulm, GERMANY, [3]Nuklearmedizin, Klinikum rechts der Isar, Technische Universität München, München, GERMANY, [4]Medical Physics and Biophysics, Physics Department, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, INDONESIA.

Aim/Introduction: Individualized treatment planning is expected to improve outcome of radionuclide therapy. In this study, we identify the most important physiologic parameters for the determination of the individual kidneys and tumor absorbed doses (ADs) in ^{177}Lu-PSMA therapy. Therefore, a global sensitivity analysis (GSA) and a physiologically-based pharmacokinetic (PBPK) model are used. ***Materials and Methods:*** A whole-body PBPK model that has been developed for treatment planning in ^{177}Lu-PSMA therapy was used. As the fixed model parameters have a relatively small effect on the estimation of time-integrated activity coefficients (TIACs) and thus the ADs, the model parameters of interest for the GSA analysis in this study were the parameters that have been estimated from the biokinetic data such as the organ receptor densities Rdens, organ flows f and organ release rates. GSA with the extended Fourier Amplitude Sensitivity Test (eFAST) algorithm was chosen based on its high accuracy for non-linear models and the low number of model evaluations needed. An in-house GSA with eFAST program based on MATLAB software (version R2019b) was developed. The frequency-based sampling method with a log-normal distribution was used to avoid negative values of the sampled parameters. The main effects S_i and total effects S_{Ti} were calculated and analyzed using the GSA program and the PBPK model to identify the importance of each model parameter i for the individualization of the ADs in ^{177}Lu-PSMA therapy. To warrant the convergence of the calculated S_i and S_{Ti}, various numbers of model simulations were performed, i.e. 129, 257, 513, 1025, 2049, 4097 and 8193. ***Results:*** The inter-individual variability of tumor ADs (coefficients of variation CV around 60%) was higher than that in the kidneys (CV around 30%). Based on the GSA with the eFAST algorithm results, the individual calculated tumor ADs were mostly depending on the receptor density RdensTU (S_i and S_Ti values up to 0.72) for the tumor lesions. For the kidneys, receptor density in kidneys RdensK (S_i=0.25, S_{Ti}=0.30) and flows fK (S_i=0.36, S_{Ti}=0.43) were identified as the most important parameters determining the individual kidneys ADs. ***Conclusion:*** We have shown the first implementation of the GSA with the eFAST algorithm to identify the most important parameters that affect the individualization of the calculated ADs in ^{177}Lu-PSMA therapy. These results suggest an accurate measurement of these parameters, i.e. receptor density and blood flow, before ^{177}Lu-PSMA therapy to decrease the inter-individual variability of the ADs in kidneys and tumor. ***References:*** None