RPS-074 was radiolabeled with Ac-225 in 15 min at 25°C and pH 5-6. Male BALB/C nu/nu mice bearing LNCaP xenograft tumors (4 mice/time point) were injected with 105 kBq [225]Ac-RPS-074 and sacrificed at 4h, 24h, 7d, 14d and 21d post injection (p.i.). For the therapy study, LNCaP bearing mice (7/group) were randomly assigned to one of four groups: 148 kBq, 74 kBq, 37 kBq [225]Ac-RPS-074 or vehicle. Tumor volumes were measured 3x weekly for 75d, and mice were sacrificed when tumor volume exceeded 2000 mm^3. **Results:** [225]Ac-RPS-074 labeling was quantitative. Tumor uptake peaked at 24h p.i. (12.7±1.5 %ID/g) in concert with clearance from the blood, and was sustained beyond 14d p.i. (11.9±1.5 %ID/g). Kidney uptake was highest at 4h p.i. (6.7±0.4 %ID/g) and rapidly decreased such that tumor-to-kidney ratios exceeded 5 by 24h p.i. Activity levels in normal tissues decreased with blood activity. All mice treated with 148 kBq [225]Ac-RPS-074 survived to 75d without loss of body weight and revealed decreasing tumor volumes by 10d p.i. At 30d p.i. 86% (6/7) of tumors were undetectable. At 75d, absence of tumors was confirmed by μPET/CT imaging and dissection. Mice in the 74 kBq group also exhibited decreasing tumor volumes by 10d p.i., but after 42d p.i. tumor re-growth was observed in 86% of mice, and 14% of mice did not survive to the study's endpoint. Although tumor volumes increased following treatment with 37 kBq [225]Ac-RPS-074, survival was significantly prolonged relative to the control (vehicle) group. **Conclusion:** [225]Ac-RPS-074 shows a promising biodistribution profile and a well-defined dose response. A single cycle of 148 kBq [225]Ac-RPS-074 induced a complete response in 86% of mice and a partial response in 14% of mice. With a promising side effect profile and demonstrable efficacy in large tumors (initial volume >800 mm^3), [225]Ac-RPS-074 merits clinical translation for TAT of prostate cancer.

OP-116

Fully Convolutional Neural Network to Assess Skeleton Tumor Burden in Prostate Cancer Using ^{68}Ga-PSMA-11 PET/CT: Preliminary Results

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Aim: Treatment of bone metastases plays an important role for patients with metastatic prostate cancer (mPC). PSMA-based PET imaging is increasingly used to delineate bone tumor burden before therapy. Bone scan Index (BSI) and Bone- PET-Index (BPI) are promising in assessing treatment outcome in patients with mPC. However, the semiautomatic segmentation using conventional methods in skeleton tumor burden assessment can be time-consuming and lengthy. The emerging of deep learning methods have provided great potential to extend the limit of conventional methods. We aimed to assess the feasibility of deep learning network in bone lesion delineation and tumor burden quantification. **Methods and Materials:** A fully convolutional neural network (FCNN) concept was proposed to automatically detect bone lesions and characterize osseous tumor burden from ^{68}Ga-PSMA-11 PET/CT imaging. A pipeline of two FCNNs was employed in a cascaded form. The first part of the cascaded network generates bone mask from CT images as anatomical regions of interest (ROI), while the second part detects and segments bone lesions based on PET imaging restricted to the anatomical regions within the generated bone mask. For proof-of-concept test, 50 ^{68}Ga-PSMA-11 PET/CT from patients with mPC were included. SUV of PET images were calculated and the bone lesions were semi-automatically annotated using an in-house developed software. Forty ^{68}Ga-PSMA-11 PET/CT scans were used as training data set for the FCNN and the remaining 10 scans were used as test dataset for performance assessment. The performance of the developed method was evaluated by considering the overall segmentation result in the form of a slice-wise lesion detection accuracy and Dice score, including the Recall and Precision scores. **Results:** The developed deep learning method has achieved a slice-wise detection accuracy of 91% with a positive predictive value (PPV) of 78%. The average segmentation Dice score was 76%, with a Recall and Precision scores of 86% and 66%, respectively. **Conclusion:** Our results highlight that even in a small size training dataset, deep learning can successfully detect bone lesions in a ^{68}Ga-PSMA-11 PET/CT setting. A higher accuracy for lesion segmentation should be obtained by increasing the number of training dataset and providing physiological lesion contouring to guide the training process. Accurate bone lesions detection and segmentation could be further implemented in the treatment setting.

OP-117

Multimodal anti-PSMA ligands for intra operative tumor detection and targeted photodynamic therapy of PSMA-expressing tumors

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Introduction: Incomplete resection of prostate cancer (PCa) and its metastases may lead to disease recurrence and consequently poor patient outcome. To obtain complete resection of tumor tissue, prostate specific membrane antigen (PSMA) targeting multimodal ligands containing both a radiolabel and a photosensitizer are developed. These ligands may be used for intra-operative tumor detection, accurate tumor delineation, and tumor-targeted photodynamic therapy (tPDT); a selective cancer treatment that induces cell destruction upon exposure to near-infrared (NIR) light. The aim of our study was to develop and evaluate multimodal [^{111}In]In-DOTAGA-IRDye700DX-PSMA targeting agents for intra-operative detection and treatment of PSMA-positive tumor lesions. **Methods:** Different variants of glutamate-urea-lysine based DOTAGA-PSMA-targeting ligands, varying in their linker moieties, were synthesized using solid phase chemistry, coupled to IRDye700DX and labeled with [111]In. PSMA-mediated binding and internalization was determined *in vitro* using PSMA-expressing LNCaP cells. Furthermore,