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Pretherapeutic ^{68}Ga -PSMA-617 PET may indicate the dosimetry of ^{177}Lu -PSMA-617 and ^{177}Lu -EB-PSMA-617 in main organs and tumor lesions

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Abstract

Aim: Combined ^{68}Ga -PSMA-617 positron emission tomography (PET) imaging and ^{177}Lu -PSMA-617 therapy is a precise targeted theranostic approach for patients with metastatic castration-resistant prostate cancer (mCRPC). The purpose of this study was to determine whether pretherapeutic standard uptake value (SUV) in ^{68}Ga -PSMA-617 PET could indicate the effective dose in the main organs and absorbed dose in tumor lesions.

Methods: Following institutional review board approval and informed consent, 9 patients with mCRPC were recruited and underwent ^{68}Ga -PSMA-617 PET/computed tomography (CT) scans. Five patients received ^{177}Lu -PSMA-617 (1.30–1.42 GBq, 35–38.4 mCi) and then underwent serial whole-body planar imaging and single-photon emission computed tomography/CT (SPECT/CT) imaging of both thoracic and abdominal regions at 0.5, 2, 24, 48, and 72 h time points. The other 4 patients received ^{177}Lu -EB-PSMA-617 (0.80–1.1 GBq, 21.5–30 mCi) and then underwent the same imaging procedures at 2, 24, 72, 120, and 168 h time points. The effective dose in the main organs and the absorbed dose in tumor lesions were calculated. Detailed correlations between the pretherapeutic SUV in ^{68}Ga -PSMA-617 PET and effective dose in the main organs, as well as absorbed dose in the tumor lesions were analyzed.

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Results: SUV of ^{68}Ga -PSMA-617 PET was moderately correlated with effective dose in main organs ($r = 0.610$ for ^{177}Lu -PSMA-617, $r = 0.743$ for ^{177}Lu -EB-PSMA-617, both $P < 0.001$). SUV of tumor lesions in ^{68}Ga -PSMA-617 PET had high correlation with those in ^{177}Lu -PSMA-617 ($r = 0.915$, $P < 0.001$) and moderate correlation with those in ^{177}Lu -EB-PSMA-617 ($r = 0.611$, $P = 0.002$).

Conclusions: Pretherapeutic ^{68}Ga -PSMA-617 PET may indicate the dosimetry of ^{177}Lu -PSMA-617 and ^{177}Lu -EB-PSMA-617. Both the effective dose in main organs and absorbed dose in tumor lesions correlate with SUV of ^{68}Ga -PSMA-617 PET. This relationship may help select appropriate candidates for peptide receptor radionuclide therapy (PRRT). Further investigations of larger cohorts are needed to confirm these initial findings.

Keywords

^{68}Ga ; ^{177}Lu ; prostate-specific membrane antigen (PSMA); metastatic castration-resistant prostate cancer (mCRPC); dosimetry

Prostate cancer (PC) is the most common cancer in men and the second leading cause of cancer-related death in the United States¹. Traditional diagnosis and treatment methods can no longer meet the clinical needs, especially in the management of patients with metastatic castration-resistant prostate cancer (mCRPC). Prostate-specific membrane antigen (PSMA) has attracted wide attention recently. PSMA expression on PC cells is directly correlated with androgen independence, metastasis formation and PC progression^{2,3}. Radionuclide labeled molecules with high affinity for PSMA has become a new theranostic concept in PC management⁴.

^{68}Ga -PSMA-617 PET/CT or PET/MRI in detecting lymph node or bone metastases in PC has shown significantly higher sensitivity, specificity, and accuracy than traditional radiological means⁵⁻⁹. These PSMA-expressing tumor lesions detected by ^{68}Ga -PSMA-617 PET could be subsequently treated by ^{177}Lu -PSMA-617. Several research groups have published favorable results of ^{177}Lu -PSMA-617 dosimetry and treatment¹⁰⁻¹³. According to these studies, the parotid glands, kidneys, and bone marrow were the critical organs with high radiation absorbed doses. More importantly, patients with mCRPC responded well to ^{177}Lu -PSMA-617 treatment, with relieved clinical symptoms, prolonged survival time, and decreased serum PSA levels (>50%) in nearly half of the patients. Targeting PSMA provides a new “image and treat” strategy for precision management of PC patients¹⁴.

Aiming to improve the pharmacokinetics and increase therapeutic efficacy, we previously developed EB-PSMA-617, which was synthesized by conjugating a truncated albumin-binding Evans blue (EB) molecule and 1, 4, 7, 10-tetra-azacyclododecane-1, 4, 7, 10-tetraacetic acid (DOTA) chelator onto PSMA-617. Due to reversible albumin binding, the addition of EB moiety to ^{177}Lu -PSMA-617 improved the pharmacokinetics of the radionuclide therapeutic agent, extended its blood half-life and tumor residence time and exhibited significantly higher uptake in xenograft tumors than PSMA-617¹⁵. These resulted in relatively higher effective dose in main organs and absorbed dose in tumor lesions¹⁶. However, high inter- and inpatient variability was observed. In PRRT for neuroendocrine tumors, a study reported that SUV of tumor lesions in pretherapeutic ^{68}Ga -DOTA-TOC PET

correlated with ^{177}Lu absorbed doses ¹⁷. SUV may serve as an indicator for later-achieved absorbed dose and a predictor for the therapeutic outcome of PRRT ¹⁸. Similarly, the decisions for or against PRRT for mCRPC are presumably influenced and eventually based on pretherapeutic SUV of PET.

In this study, we retrospectively analyzed the patients who underwent pretherapeutic ^{68}Ga -PSMA-617 PET and received low dose of ^{177}Lu -EB-PSMA-617 or ^{177}Lu -PSMA-617 in our institution with the same standardized protocol. We investigated the relationship between pretherapeutic SUV of PET and subsequently effective dose in main organs and absorbed dose in tumor lesions in both ^{177}Lu -EB-PSMA-617 and ^{177}Lu -PSMA-617.

PATIENTS AND METHODS

Patients and radiopharmaceuticals

The patient cohort was from our previous study¹⁶. This study was registered at clinicaltrials.gov (NCT03403595) and was approved by the Institute Review Board of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College. During November 2017 and February 2018, we recruited 9 patients (mean age, 71 years; range, 60–81 years) with mCRPC. Among these patients, 4 were injected with ^{177}Lu -EB-PSMA-617 and the other 5 with ^{177}Lu -PSMA-617. For other details of these patients, inclusion and exclusion criteria, please refer to our previous study ¹⁶.

^{68}Ga -PSMA-617, ^{177}Lu -PSMA-617 and ^{177}Lu -EB-PSMA-617 were labeled according to the procedures reported previously ¹⁶. The radiolabeling yield of ^{177}Lu -EB-PSMA-617 and ^{177}Lu -PSMA-617 was more than 90% and their radiochemical purity was more than 95%.

PET acquisition and quantitative assessment

Intravenous injection of the tracer was performed with an injection activity of 111.1–148.0 MBq. After 45–60 minutes, ^{68}Ga -PSMA-617 PET/CT imaging (Siemens Medical Solutions, Erlangen, Germany) was performed. All PET acquisition was carried out in three-dimensional mode, 2 min per bed, 5–6 bed positions per patient. PET reconstruction used low-dose CT (120 kV, 35 mA, 512×512 matrix, 3-mm layer, 70 cm field of view) for attenuation correction and an ordered-subset expectation maximization iterative algorithm with 2 iterations and 8 subsets, with a 5-mm full width at half maximum postreconstruction Gaussian filter. A Siemens MMWP workstation was used for post-processing. Regions of interests (ROIs) were manually drawn including the main organs (heart, lung, pancreas, liver, spleen, stomach, muscle and salivary glands) and around the target tumor lesions (up to six lesions per patient) on PET slices by referring CT images. The post-processing workstation automatically calculated the volume of interest and SUVs.

SPECT/CT acquisition and quantitative assessment

After ^{68}Ga -PSMA-617 PET acquisition, a single dose of ^{177}Lu -PSMA-617 or ^{177}Lu -EB-PSMA-617 was injected according to our standardized protocol. The time interval between ^{68}Ga -PSMA-617 PET and ^{177}Lu -EB-PSMA-617 (or ^{177}Lu -PSMA-617) therapy was from 1 day to 7 days (2.3 ± 2.2 days). No patients received other treatment during interval time and

^{177}Lu therapy period. Five patients received intravenous administration of ^{177}Lu -PSMA-617 1.30–1.42 GBq (35–38.4 mCi), followed by serial whole-body planar imaging and SPECT/CT of both thoracic and abdominal regions at 0.5, 2, 24, 48, and 72 h postinjection (p.i.). Another 4 patients received intravenous administration of ^{177}Lu -EB-PSMA-617 0.80–1.1 GBq (21.5–30 mCi) with the same imaging acquisition procedures at 2, 24, 72, 120, and 168 h p.i. Images were obtained by the Philips Precedence scanner (Philips Healthcare, Andover, Massachusetts, USA) configured for 2-headed gamma camera, using a medium-energy general-purpose collimator with the energy window centered at 208 keV and a window width of 20%. For whole-body planar imaging, the acquisition matrix was 256×1024 and the scan speed was 15 cm per minute. For SPECT/CT, a procedure of 32 frames was performed, whose exposure time is 40 seconds per frame for each tomographic scan. SPECT reconstruction was performed using an iterative ordered-subset maximum-likelihood expectation maximization algorithm with 3 iterations and 8 subsets in the system's software at the clinical workstation.

Data analysis and statistics

Dosimetry calculation was performed according to the European Association of Nuclear Medicine Dosimetry Guidance¹⁹ and procedure reported previously. In order to calculate the dose concentration factor and voxel-based activity concentration, we utilized two radioactive sources with well-determined ^{177}Lu activity and converted the factors in the volumes of interest to standardized uptake value (SUV). One of them was a cylindrical phantom, homogeneously filled with a solution containing a total of 370 MBq ^{177}Lu activity, with a volume of 6.7 L and an internal diameter of 22 cm, which was used to calculate the SUV of major organs. The other was a cube phantom, homogeneously filled with a solution containing a total of 18.5 MBq ^{177}Lu activity, with a volume of 20 mL, which was used to calculate the SUV of tumor lesions. For each main organ, the corresponding SUVs were used to generate the decay uncorrected time-activity curve. The volumes of individual organ were delineated on the serial CT images of the SPECT/CT slice by slice. SUVs were converted by referring the phantom. The effective doses were derived based on organ weight from the adult male phantom provided by the OLINDA/EXM v1.1 software (Vanderbilt University, Nashville, Tennessee, USA)^{20, 21}. The number of disintegrations for the main organs was obtained by fitting the data using a mono-exponential or a bi-exponential model provided by the software. Since tumor lesions were not included in the software, we assumed them to have a sphere morphology. Per patient, up to 6 lesions in relatively high uptake, large size and spherical shape were measured. The volumes of interests of tumor lesions were manually drawn slice by slice by referring the CT images. The areas under residence times-activity curve (AUC) (MBq-h/MBq/g) of tumor lesions were converted from SUVs and were calculated by the trapezoidal method in the Graphpad Prism software (Version 4.0, GraphPad Software, Inc.). The absorbed dose of tumor lesions was presented as areas under residence times-activity curve. We analyzed a total of 49 representative lesions (25 for ^{177}Lu -PSMA-617 and 24 for ^{177}Lu -EB-PSMA-617). In addition, the main organs (liver, spleen, lung, kidney and salivary glands) and corresponding tumor lesions were manually drawn on the ^{177}Lu whole-body planar imaging. The activities were extracted from the ROIs using the geometric mean of both the anterior and posterior projections of the planar images. The effective doses of main organs were calculated from

the residence time and activity values based on the adult male phantom by OLINDA/EXM v1.1 software. The effective dose of salivary glands and tumor lesions was calculated using the sphere model of the software. Detailed correlations between the pretherapeutic SUV in ^{68}Ga -PSMA-617 PET with effective dose in main organs and with absorbed dose in tumor lesions were assessed using the Spearman rank correlation coefficient. Linear regression analysis was performed using SPSS software (IBM SPSS Statistics for Windows, version 21.0; Armonk, NY). All tests were two sided, and a P -value < 0.05 was considered statistically significant. All quantitative data were expressed as mean $\pm$ standard deviation.

RESULTS

The representative images of patients are shown in Figure 1 and 2. In this study, the SUV_{mean} in ^{68}Ga -PSMA-617 PET, ^{177}Lu -PSMA-617 and ^{177}Lu -EB-PSMA-617 SPECT of the main organs including the heart, lung, pancreas, liver, spleen, stomach, and muscle were measured in each patient. Linear regression analysis (Fig. 3) showed that the SUV_{mean} of main organs in ^{68}Ga -PSMA-617 PET and SUV_{mean} in ^{177}Lu -PSMA-617 SPECT/CT exhibited linear correlation at early time points p.i. ($R^2 = 0.827$ at 0.5 h). However, for ^{177}Lu -EB-PSMA-617, the linear relationship was not seen until late time points ($R^2 = 0.868$ at 24 h).

Effective dose of ^{177}Lu in each main organ per patient was calculated and reported in our previous study¹⁶. SUV_{mean} in ^{68}Ga -PSMA-617 PET and effective dose in the main organs derived from SPECT/CT had a moderately but highly statistically significant correlation with ^{177}Lu -PSMA-617 ($r = 0.610$), and ^{177}Lu -EB-PSMA-617 ($r = 0.743$), both $P < 0.001$ (Fig. 4). SUV_{mean} in ^{68}Ga -PSMA-617 PET showed moderate correlation ($r = 0.694$, $P < 0.001$) with the effective dose derived from the whole-body planar imaging in the ^{177}Lu -PSMA-617 group and no correlation with that in the ^{177}Lu -EB-PSMA-617 group.

For tumor lesions, a total of 49 lesions from 9 patients were included in the analysis (25 lesions for ^{177}Lu -PSMA-617 and 24 lesions for ^{177}Lu -EB-PSMA-617). For the ^{177}Lu -PSMA-617 group, the average SUV_{mean} and SUV_{max} values of tumor lesions in ^{68}Ga -PSMA-617 PET were 9.45 ± 8.33 and 15.75 ± 14.17 , respectively. For the ^{177}Lu -EB-PSMA-617 group, the average SUV_{mean} and SUV_{max} values were 11.21 ± 8.54 and 19.24 ± 14.45 . No significant difference was found in these two groups ($P = 0.36$). The absorbed dose in tumor lesions derived from SPECT/CT was presented by the area under residence time-activity curve (AUCs), which was 0.0356 ± 0.0361 MBq-h/MBq/g for the ^{177}Lu -PSMA-617 group and 0.0766 ± 0.0385 MBq-h/MBq/g for the ^{177}Lu -EB-PSMA-617 group. There were also linear relationships (Fig. 5) between the SUV_{mean} of tumor lesions in ^{68}Ga -PSMA-617 PET and ^{177}Lu -PSMA-617 SPECT at early time points postinjection ($R^2 = 0.837$ at 2 h), and ^{177}Lu -EB-PSMA-617 SPECT at late time points ($R^2 = 0.683$ at 72 h).

SUV of tumor lesions in ^{68}Ga -PSMA-617 PET highly correlated with the corresponding AUC derived from SPECT/CT in the ^{177}Lu -PSMA-617 group ($r = 0.915$ for SUV_{max} and $r = 0.907$ for SUV_{mean} , both $P < 0.001$) (Fig. 6), but moderately correlated with the absorbed dose derived from the planar imaging ($r = 0.592$ for SUV_{max} and $r = 0.585$ for SUV_{mean} , both $P = 0.002$). In the ^{177}Lu -EB-PSMA-617 group, the SUV moderately correlated with

AUC of tumor lesions ($r = 0.611$ for SUV_{max} and $r = 0.594$ for SUV_{mean} , both $P = 0.002$), but had no correlation with the absorbed dose derived from the whole-body planar imaging ($r = 0.449$ for SUV_{max} , $P = 0.062$ and $r = 0.431$ for SUV_{mean} , $P = 0.074$).

Examples of corresponding ^{68}Ga -PSMA-617 PET, ^{177}Lu -PSMA-617 and ^{177}Lu -EB-PSMA-617 SPECT and resulting AUCs of the target tumor lesions are presented in Figure 7 and 8.

DISCUSSION

This retrospective study on 9 patients (5 in the ^{177}Lu -PSMA group, and 4 in the ^{177}Lu -EB-PSMA-617 group) with mCRPC shows that pretherapeutic SUVs of main organs or tumor lesions in ^{68}Ga -PSMA-617 PET may indicate the corresponding effective dose or absorbed dose of ^{177}Lu treatment. Our correlation data confirm the relationship between diagnostic uptake and therapeutic dose within certain range, which may provide a preliminary basis for estimating maximal tolerable dose for radionuclide treatment and therapeutic efficacy.

There are individual variations in the radiation tolerance limits in normal organs. Dosimetry of the radiopharmaceuticals for radionuclide therapy is essential to assess possible toxicity and side effects²². In this study, we found that SUV_{mean} of main organs in pretherapeutic ^{68}Ga -PSMA-617 PET may indicate the dosimetry of ^{177}Lu therapy both in the ^{177}Lu -PSMA and ^{177}Lu -EB-PSMA-617 groups. SUV had a moderate but highly statistically significant correlation with effective dose in main organs. Moreover, SUV_{mean} in ^{68}Ga -PSMA-617 PET and SUV_{mean} in ^{177}Lu -PSMA-617 SPECT were linearly correlated at early time points, while for ^{177}Lu -EB-PSMA-617, at late time points. This was consistent with our previous finding that ^{177}Lu -EB-PSMA-617 ($t_{1/2} = 143.9$ h) has relatively longer circulation time than ^{177}Lu -PSMA-617 ($t_{1/2} = 5.6$ h) due to the albumin binding feature of Evans blue.

The main excretion pathway of radiopharmaceuticals is the kidneys. In several recent studies, the kidneys were regarded as the dose-limiting organs^{23–25}, with the mean limiting administrable activity lying between 30 to 60 GBq, with large inter-individual variation¹⁰. Our previous dosimetry results showed that the highest estimated radiation dose was also in the kidneys, 2.39 ± 0.69 mSv/MBq for ^{177}Lu -EB-PSMA-617, about 6 times higher than that for ^{177}Lu -PSMA (0.39 ± 0.06 mSv/MBq)¹⁶. As the kidneys are the elimination organs of radiopharmaceuticals, PET SUVs of the kidneys are affected by radioactive urine, which could bring measurement error. Thus, it is reasonable that kidneys should be excluded from the correlation study in Figure 4. However, if the kidneys were included in this correlation study, we found the degree of the correlation between SUV_{mean} in ^{68}Ga -PSMA-617 PET and effective dose of main organs seemed slightly higher, with $r = 0.737$ for ^{177}Lu -PSMA-617 and $r = 0.828$ for ^{177}Lu -EB-PSMA-617, both $P < 0.001$ (Fig. 9). For the intestine, from our observation, there are high variations in the tracer uptake of intestine in the same patient, even if this patient underwent ^{68}Ga -PSMA-617 PET/CT examination twice within two days followed by the same procedure. The SUV could not be measured accurately. Because the salivary glands were out of the SPECT/CT field, their effective doses were derived from ^{177}Lu whole-body planar imaging by sphere model of the OLINDA/EXM v1.1

software (1.2500 ± 0.5100 mGy/MBq in ^{177}Lu -PSMA-617 group and 6.4100 ± 1.4000 mGy/MBq in ^{177}Lu -EB-PSMA-617 group).

As a high pretherapeutic PET SUV may serve as a simple surrogate for a high absorbed dose and thus, better clinical response²², several recent studies have found that the median PET SUV_{max} decreased significantly in tumor lesions with higher absorbed dose^{26, 27}. Similar results were also reported for PRRT for neuroendocrine tumors¹⁷. In our analysis, the absorbed dose of tumor lesions was presented by the AUCs. In the ^{177}Lu -PSMA-617 group, a highly significant correlation between pretherapeutic PET SUV and their corresponding AUC derived by SPECT/CT was found ($r = 0.915$ for SUV_{max}, $r = 0.907$ for SUV_{mean}). While in the whole-body planar imaging, only moderate correlation between SUV in ^{68}Ga -PSMA-617 PET and the absorbed dose in tumor lesions could be found in ^{177}Lu -PSMA-617 group ($r = 0.592$ for SUV_{max}, $r = 0.585$ for SUV_{mean}). Recent studies reported only moderate correlation ($r = 0.44$ for SUV_{max}, $r = 0.43$ for SUV_{mean}) using ^{177}Lu -PSMA I&T)²⁸ or no correlation (using ^{177}Lu -PSMA-617)²² could be found. In these two studies, absorbed dose in tumor lesions was obtained from whole-body planar imaging of ^{177}Lu , which may be insufficient to locate the tumor lesions accurately. Another explanation was that the pretherapeutic imaging PET (PSMA-HBED-CC) and subsequent therapy did not share the same peptide^{22, 28}. In our correlation analysis, the ^{177}Lu data with CT attenuation correction was used to correlate the ^{68}Ga PET/CT data so the correlation was stronger.

In the ^{177}Lu -EB-PSMA-617 group, the correlation was moderate ($r = 0.611$ for SUV_{max}, $r = 0.594$ for SUV_{mean}), indicating the difference in the intratumoral residence time with and without EB moiety modification. The representative example of biodistribution in Figure 1 and 2 showed that excessive uptake of ^{177}Lu -EB-PSMA-617 in tumor lesions was still obvious at 168 h time point, while that of ^{177}Lu -PSMA-617 already decreased to nearly background level at 24 h p.i. Furthermore, a relatively strong linear relationship between SUV in ^{68}Ga -PSMA-617 PET and ^{177}Lu -PSMA-617 SPECT was seen at 2 h postinjection ($R^2 = 0.837$), while ^{177}Lu -EB-PSMA-617 at 72 h postinjection ($R^2 = 0.683$), indicating slower tumor uptake and longer tumor residence time in ^{177}Lu -EB-PSMA-617. Meanwhile, the linear relationship suggested the best acquisition time point for these two molecules respectively.

There are several limitations of our study. First, in our limited retrospective patient cohort, only one cycle with imaging dose of administered activity was given. Second, a therapy study with more patients is necessary to assess the relationship between pretherapeutic ^{68}Ga PET imaging and ^{177}Lu therapy for candidate selection. Lastly, these mCRPC patients in our study had a very advanced disease stage and received extensive therapy regimens before, which might bring variations to some extent.

CONCLUSIONS

Our initial findings demonstrate that ^{68}Ga -PSMA-617 PET may indicate effective dose in main organs and absorbed dose in tumor lesions both during the ^{177}Lu -PSMA-617 and ^{177}Lu -EB-PSMA-617 treatment, which may help determine appropriate candidates for

PRRT. Further investigations with increased ^{177}Lu dose and larger series are warranted to confirm and validate these data.

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FIGURE 1.

Representative ^{68}Ga -PSMA PET/CT maximum intensity projection image and SPECT whole-body posterior planar images of an 81-year-old patient in ^{177}Lu -PSMA group. (A) ^{68}Ga -PSMA PET/CT maximum intensity projection image and (B) subsequent SPECT whole-body posterior projection images at different acquisition time points postinjection of ^{177}Lu -PSMA.

FIGURE 2. Representative $^{68}\text{Ga-PSMA}$ PET/CT maximum intensity projection image and SPECT whole-body posterior planar images of a 73-year-old patient in $^{177}\text{Lu-EB-PSMA}$ group. (A) $^{68}\text{Ga-PSMA}$ PET/CT maximum intensity projection image and (B) subsequent SPECT whole-body anterior projection images at different acquisition time points postinjection of $^{177}\text{Lu-EB-PSMA}$.

FIGURE 3.

Linear regression analysis of main organs PET SUV_{mean} and SPECT SUV_{mean}. (A) ¹⁷⁷Lu-PSMA group, $R^2 = 0.827$ at 0.5 h postinjection. (B) ¹⁷⁷Lu-EB-PSMA group, $R^2 = 0.868$ at 24 h postinjection.

FIGURE 4.

Relationship between main organs PET SUV_{mean} and effective dose (mSv/MBq). (A) ¹⁷⁷Lu-PSMA group, $r = 0.610$. (B) ¹⁷⁷Lu-EB-PSMA group, $r = 0.743$. $P < 0.001$ (Spearman rank correlation analysis) for each group.

FIGURE 5.

Linear regression analysis of tumor lesions PET SUV_{mean} and SPECT SUV_{mean}. (A) ¹⁷⁷Lu-PSMA group, $R^2 = 0.837$ at 2 h postinjection. (B) ¹⁷⁷Lu-EB-PSMA group, $R^2 = 0.683$ at 72 h postinjection.

FIGURE 6.

Relationship between tumor lesions PET SUV and absorbed dose. The absorbed dose was presented by the areas under residence time-activity curve (AUC) (MBq-h/MBq/g). (A) ¹⁷⁷Lu-PSMA group, $P < 0.001$ (Spearman rank correlation analysis). (B) ¹⁷⁷Lu-EB-PSMA group, $P = 0.002$ (Spearman rank correlation analysis).

FIGURE 7.

A representative 81-year-old patient in the ^{177}Lu -PSMA group. (A) ^{68}Ga -PSMA PET maximum intensity projection image shows multiple bone metastasis marked with arrows. (B) ^{177}Lu -PSMA SPECT whole-body posterior projection image at 2 h postinjection shows the corresponding tumor lesions. (C) Transverse fused SPECT/CT slices show T11 (red arrow) and L1 (blue arrow) metastasis. (D) The respective time-activity curves are presented.

FIGURE 8.

A representative 73-year-old patient in the ^{177}Lu -EB-PSMA group. (A) ^{68}Ga -PSMA PET maximum intensity projection image shows multiple bone metastasis marked with arrows. (B) ^{177}Lu -EB-PSMA SPECT whole-body posterior projection image at 72 h postinjection shows the corresponding tumor lesions. (C) Transverse fused SPECT/CT slices show T7 (red arrow) and left sacroiliac joint (blue arrow) metastasis. (D) The respective time-activity curves are presented.

FIGURE 9. Relationship between main organs (including the kidneys) PET SUV_{mean} and effective dose (mSv/MBq). (A) ¹⁷⁷Lu-PSMA group, $r=0.737$. (B) ¹⁷⁷Lu-EB-PSMA group, $r = 0.828$. $P<0.001$ (Spearman rank correlation analysis) for each group.