64Cu-PSMA-BCH: A New Radiotracer for Delayed PET Imaging of Prostate Cancer

Teli Liu  
Peking University Cancer Hospital: Beijing Cancer Hospital

Chen Liu  
Peking University Cancer Hospital: Beijing Cancer Hospital

Zhongyi Zhang  
Peking University Cancer Hospital: Beijing Cancer Hospital

Ning Zhang  
Peking University Cancer Hospital: Beijing Cancer Hospital

Xiaoyi Guo  
Peking University Cancer Hospital: Beijing Cancer Hospital

Lei Xia  
Peking University Cancer Hospital: Beijing Cancer Hospital

Jinquan Jiang  
Peking University Cancer Hospital: Beijing Cancer Hospital

Qing Xie  
Peking University Cancer Hospital: Beijing Cancer Hospital

Kun Yan  
Peking University Cancer Hospital: Beijing Cancer Hospital

Steven P. Rowe  
Johns Hopkins Medical Institutions: Johns Hopkins Medicine

Hua Zhu  
Peking University Cancer Hospital: Beijing Cancer Hospital

Zhi Yang ([email protected])  
Peking University Cancer Hospital & Institute  https://orcid.org/0000-0003-2084-5193

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Abstract

Purpose

Develop a $^{64}\text{Cu}$ labeled radiopharmaceutical targeting prostate specific membrane antigen (PSMA) and investigate its application for prostate cancer imaging.

Methods

$^{64}\text{Cu}$-PSMA-BCH was prepared and investigated for stability, PSMA specificity and micro-PET imaging. With the approval of Ethics Committee of Beijing Cancer Hospital (No. 2017KT97), PET/CT imaging in 4 patients with suspected prostate cancer was performed and the radiation dosimetry was estimated. Then, PSMA PET-ultrasound image-guided biopsies were performed on 3 patients and the fine needle aspirates were further performed for autoradiography and immunohistochemistry analysis.

Results

$^{64}\text{Cu}$-PSMA-BCH was prepared with high radiochemical yield and stability. In vivo study showed higher uptake in PSMA (+) 22Rv1 cells than PSMA (-) PC-3 cells (5.59±0.36 and 1.97±0.22 IA%/10$^6$ cells at 1 h). It accumulated in 22Rv1 tumor with increasing radioactivity uptake and T/N ratios from 1 h to 24 h post-injection. In patients with suspected prostate cancer, SUVmax and T/N ratios increased within 24 h post-injection. Compared with image at 1 h post-injection, more tumor lesions were detected at 4 h and 24 h post-injection. The human organ radiation dosimetry showed gallbladder wall was most critical, liver and kidneys were followed, and the whole-body effective dose was 0.0292 mSv/MBq. Two fine needle aspirates obtained by PET-ultrasound guided targeted biopsy showed high radioactive signal by autoradiography, with 100% PSMA expression in cytoplasm and 30% expression in nucleus.

Conclusion

$^{64}\text{Cu}$-PSMA-BCH was PSMA specific and showed high stability in vivo with lower uptake in liver than $^{64}\text{Cu}$-PSMA-617. Biodistribution in mice and PCa patients showed similar profile compared with other PSMA ligands and it was safe with moderate effective dosimetry. The increased tumor uptake and T/N ratios by delayed imaging may facilitate the detection of small lesions and guiding targeted biopsies.

Introduction

Prostate cancer (PCa) is common among men. PSMA PET/CT has shown high sensitivity and specificity in identifying sites of PCa, and some studies have demonstrated that PSMA-based PET/CT and PET/MR can give accurate location of tumor lesions in primary PCa superior to MRI [1, 2], which offers the possibility that PSMA PET images prior to biopsy giving a simpler criteria for targeted biopsy. Our group had tried $^{68}\text{Ga}$-PSMA PET-ultrasound fusion targeted biopsies, which improved the detection rate of PCa and decrease the possibility of repeated biopsy [3]. Unfortunately, limited by the short half-life of $^{68}\text{Ga}$, the
images were obtained at 1 h post injection (p.i.) with high radioactivity in bladder, which lead the low contrast between the PCa and background.

Radiopharmaceuticals labeled with radionuclides having longer half-life can be used in delayed imaging, potentially leading to higher tumor-to-background contrast. Because of the internalization of PSMA radiotracers, the contrast in tumor lesions increases at longer time points after injection, with the radioactivity in non-target organs significantly decreasing at later time points. Among such radionuclides, copper-64 ($^{64}$Cu) was deemed to be a good choice due to its moderate half-life (12.7 h) and high resolution [4].

$^{64}$Cu labelled PSMA-targeting probes, $^{64}$Cu-PSMA-617 [5-9], $^{64}$Cu-DOTA-scFv-anti-PSMA [10] and $^{64}$Cu-CA003 [11] have been reported. $^{64}$Cu-PSMA-617 showed high diagnostic accuracy for primary LN staging [5, 6]. But the preclinical and in-man studies of $^{64}$Cu-PSMA-617 demonstrated high uptake in liver and the in vivo stability showed most of $^{64}$Cu-PSMA-617 has been dissociated within 2 hours [9, 8, 7]. This was possibly due to endogenous proteins involved in copper metabolism transchelating $^{64}$Cu from DOTA [12-14]. As human copper transporter 1 is expressed in most tumors, $^{64}$CuCl$_2$ itself can be used for the diagnosis of PCa [15]. The dissociation of $^{64}$Cu from $^{64}$Cu-PSMA-617 in vivo not only may lead extra radiation exposure of liver but also could affect the detection of some liver metastases. Compared with DOTA, triaza macrocyclic compounds, such as NOTA and its derivatives, have been reported to chelate $^{64}$Cu with higher in vivo stability [16, 17]. In order to obtain high quality images for PCa imaging and give delayed images for improved detection of sites of disease, we prepared a $^{64}$Cu labeled radiotracer, $^{64}$Cu-PSMA-BCH, with a NOTA-conjugated precursor. The in vitro and in vivo studies were performed to evaluate the stability, PSMA specificity, radiation safety and tumor targeting of $^{64}$Cu-PSMA-BCH.

**Materials And Methods**

**General**

$^{64}$CuCl$_2$ was obtained from the department of Nuclear Medicine, Peking University of Cancer Hospital. All chemicals, reagents and solvents were purchased commercially without further purification. Sep-Pak C18-Light cartridges were purchased from Waters. The product was analyzed by reversed-phase high performance liquid chromatography (RP-HPLC; Eclipse Plus C18, 4.5×250 mm, 5μm; Agilent) performed using a linear A-B gradient (15%-60% of B in 15 min) with a flow of 1 mL/min. Solvents were 0.1% aqueous TFA (A) and 0.1% TFA in acetonitrile (B). The HPLC system was equipped with UV and γ detectors. UV absorbance was measured at 220 nm. Micro-PET was performed on Super Argus PET (Sedecal, Spain). PET/CT scans were obtained on a Biograph mCT Flow 64 scanner (Siemens, Erlangen, Germany) with unenhanced low-dose CT. PSMA (+) 22Rv1 and PSMA (-) PC-3 cell lines were obtained from China Cell Line Resource.

**Cell culture and animal models**
Human prostate cancer cell lines 22Rv1 and PC-3 were cultured and the tumor models were established as previously reported [18]. All animal experiments were conducted in accordance with the guidelines approved by Peking University Cancer Hospital Animal Care and Use Committee.

**Radiochemistry and quality control**

$^{64}$CuCl$_2$ was obtained in solution of 0.01 M HCl (3.7 GBq/mL) [4]. 5 µL of PSMA-BCH (2 mM), 200 µL of NaAc (0.1 M) and 50 µL of $^{64}$CuCl$_2$ (187 MBq) were added in a tube and reacted at 95 °C for 10 min. After cooling to room temperature, $^{64}$Cu-PSMA-BCH was purified by C18 Light Cartridge and obtained as shown in supporting information. $^{64}$Cu-PSMA-BCH was diluted with saline for further studies and analyzed by radio-HPLC for radiochemical purity, checked for pH value and sterility tested.

**Partition coefficient**

The partition coefficient of $^{64}$Cu-PSMA-BCH was studied in the PBS (0.1 M, pH 7.4)-octanol system (supporting information) and the value was presented as log $P$±SD, $P$ was calculated as below:

$$P = \frac{\text{average of CPM in octanol}}{\text{average of CPM in PBS}}.$$

**In vitro stability**

The in vitro stability of $^{64}$Cu-PSMA-BCH (3.7 MBq) was tested in solution of saline and 5% HSA at 37 °C till 36 h and analyzed by radio-HPLC (see supporting information).

**Pharmacokinetics in blood**

200 µL of $^{64}$Cu-PSMA-BCH (3.7 MBq) was intravenously injected to BALB/c male mice (n=5). The blood was collected from ophthalmic artery at 1, 2, 5, 10, 15, 30, 45, 60, 90, 120, 180 and 540 min p.i.. Then, the blood was weighted and measured for the radioactivity by $\gamma$-counter. The results were expressed as the percent of injected dose per gram (%ID/g).

**In vitro cell uptake assay**

PSMA (+) 22Rv1 and PSMA (-) PC-3 cell lines were used and the cell uptake study was performed as shown in supporting information. For blocking, 0.5 µg of ZJ-43 ((S)-2-(3-((S)-1-carboxy-3-methylbutyl)ureido), pentanedioic acid), a PSMA inhibitor, was added.

**Biodistribution**

Biodistribution of $^{64}$Cu-PSMA-BCH in normal BALB/c male mice was performed (see supporting information) and results were expressed as the percent of injected dose per gram (ID%/g).

**Micro-PET imaging, biopsy and histology study in tumor model mouse**
18.7 MBq of $^{64}$Cu-PSMA-BCH were injected into mice bearing 22Rv1 and PC-3 vial a tail vein. At 3, 12 and 20 h p.i., the mice were anaesthetized and performed micro-PET imaging on Super Argus PET (Sedecal, Spain) acquired with 80 mm diameter Transaxial FOV, OSEM 3D reconstruction algorithms with attenuation and random corrections. Finally, the images were displayed by MMWKS Super Argus. The milicounts/sec values of ROI (regions of interest) over tumor, kidneys and liver were collected.

After imaging at 20 h p.i., the mouse was anaesthetized with 3% (v/v) and sacrificed. Then puncture in tumor lesions was performed. The samples were immobilized in 10% neutral formaldehyde fixative and then performed radioautography to further investigate the possibility of methodology.

**Radioautography and immunohistochemistry**

The samples were stored on slides with 10% neutral formaldehyde fixative and exposed on a phosphorus plate (Perkin-Elmer, USA) for 12 h. The plate was scanned using a phosphor imaging system (Cyclone, Packard) to obtain the images. The slides were prepared and analyzed for PSMA expression by immunohistochemistry as described previously [7].

**PET/CT imaging and analysis**

With the approval of Ethics Committee of Beijing Cancer Hospital (No. 2017KT97), four patients (age 77.25±5.36, range 68-81, PSA 35.40±31.05 ng/mL, range 8.5-86.15; Gleason score 8.25±0.43, range 8-9) with suspected prostate cancer, who were clinically appropriate for biopsies, were included in this study (Table 1). Three patients without metastasis were performed whole-body PET/CT scans at 1 and 24 h p.i. and pelvic cavity scans at 4h p.i.. One patient with multiple bone and lymph nodes metastases performed whole-body PET/CT scans at 1, 4 and 24 h p.i.. Imaging was performed and all images were read by 2 experienced nuclear medicine specialists, the SUVmean, radioactivity concentration (Bq/mm$^3$) and volume (mm$^3$) of each organ and SUVmax of tumor lesions were obtained as literature as previously reported [18].

**Absorbed dosimetry**

The radioactivity concentration (Bq/mm$^3$) and volume (mm$^3$) were used for calculating ID% of each organ. And the data was used for estimating human organ radiation dosimetry. OLINDA/EXM 2.0 software (Hermes Medical Solution, Sweden) was used with adult male model without special kinetics.

**PET-ultrasound guided targeted biopsy**

After imaging at 24 h p.i., the images were reconstructed and analyzed, then the patients were performed classic ultrasound-guided biopsies with visual fusion of PET images according to PROMISE criteria (version 1.0) as reported [19, 3].

**Results**
**Radiochemistry and quality control**

$^{64}$Cu-PSMA-BCH was prepared with the yield over 95% and the radiochemical purity over 99% analyzed by radio-HPLC. The retention time of $^{64}$Cu-PSMA-BCH and $^{64}$Cu$^{2+}$ were 9.34 min and 3.46 min, respectively. The specific activity of $^{64}$Cu-PSMA-BCH was 14.3±1.91 GBq/μmol. After diluted with saline, the quality control of $^{64}$Cu-PSMA-BCH was performed, and the result was shown in Table 2.

**Partition coefficient and in vitro stability**

The log P value of $^{64}$Cu-PSMA-BCH was calculated as -2.46±0.11, indicating $^{64}$Cu-PSMA-BCH was hydrophilic.

After incubation in saline and 5% HSA at 37 °C for 36 h, the radiochemical purity of $^{64}$Cu-PSMA-BCH was over 95% (Figure 1a), indicating $^{64}$Cu-PSMA-BCH was stable in vitro.

**Cell uptake and binding affinity**

The uptake of $^{64}$Cu-PSMA-BCH in 22Rv1 cells increased with time between 5 min to 120 min, the highest values were 5.71±0.16 %IA/10$^6$ cells at 120 min (Figure 1b). The uptake in 22Rv1 decreased to 3.44±0.13 %IA/10$^6$ (P<0.001) when co-incubated with excess ZJ-43. While the highest uptake in PC-3 was 1.79±0.20 %IA/10$^6$ cells at 60 min and the uptake couldn't be blocked by ZJ-43 (1.86±0.17, P>0.05).

**Pharmacokinetics**

The in vivo metabolism of $^{64}$Cu-PSMA-BCH in blood pool was determined by a two-compartmental model using GraphPad prism 5.0 (Figure 1c). The equation for $^{64}$Cu-PSMA-BCH in BALB/c mice was $C_t = 0.3315+20.60 \times \exp(-3.333t) +9.73 \times \exp(-0.0649t)$, with the half-life of 10.68 min for the distribution phase and the half-life of 0.208 min for the elimination phase, respectively.

**Biodistribution**

In normal BALB/c male mice, kidney showed the highest accumulation of $^{64}$Cu-PSMA-BCH (Figure 1d, Table S1), the values were 29.15 ± 1.85 ID%/g at 0.5 h p.i. and 0.54 ± 0.12 ID%/g at 15 h p.i.. $^{64}$Cu-PSMA-BCH cleared out from blood with the uptake of 0.52 ± 0.26 %ID/g to 0.08 ± 0.01 %ID%/g from 0.5 to 15 h post injection. The uptake in liver decreased form 0.80±0.11 to 0.56±0.07 %ID%/g from 0.5 h to 15 h p.i., which was much lower than that of $^{68}$Ga-PSMA-617 (the uptake in liver was reported as 12.65±0.75 to 9.08±0.57 %ID%/g from 0.5 h to 12 h p.i. in ICR mice and from 24.10±2.34 to 8.13±1.08 %ID%/g from 4 h to 24 h p.i. in BALB/c mice) [7, 5].

**Micro-PET imaging**

Micro-PET imaging was performed on a male BALB/c nude mouse bearing 22Rv1 and PC-3 tumors. 22Rv1 tumor, kidneys, bladder and liver were clearly visualized, while the PC-3 tumors cannot be observed.
The radioactivity accumulation in liver and 22Rv1 tumor was lightly increased within 20 h, while the uptake in kidney was decreased and the kidneys were nearly invisible at 12 h and 20 h p.i.. At 12 h p.i., only 22Rv1 tumor and liver were observed. The ROIs of kidney, liver, 22Rv1 and PC-3 tumors were measured. The 22Rv1/PC-3 tumors and 22Rv1/kidney ratios were increased with time (from 3.92 to 20.30 and from 0.2 to 2.99, respectively) between 3 h and 12 h p.i. (Figure 2b). Compared with reported data of $^{68}$Ga-PSMA-617, the radioactivity of $^{64}$Cu-PSMA-BCH in liver is lower, which was coincidence with the biodistribution result in normal BALB/c mice.

**PET/CT imaging**

Four patients who were suspected of having PCa were included in this study and conducted $^{64}$Cu-PSMA-BCH PET/CT imaging. At 1 h post injection, bladder, kidneys, lacrimal glands, parotid glands, submandibular glands, liver, proximal small bowel and tumor lesion were clearly observed, which was coincidence with other PSMA radioligands (Figure 3a, Table S2). The uptake in liver was increased and the SUVmean was increased from 4.38 to 5.31 between 1 h and 24 h p.i.. Though kidneys, lacrimal glands, parotid glands and submandibular glands were visible at 24 h p.i., the SUVmean values were decreased. The SUVmax of tumor lesions in three PCa patients without metastases were increased between 1 h and 24 h p.i. (Figure 3b), as well as the tumor-to-background contrasts (Figure S2).

In this study, one PCa patient with multiple metastases were included. At 4 h and 24 h p.i., more tumor lesions were observed and the SUVmax values were higher than that at 1 h p.i. (Figure 4).

**Radiation dosimetry estimates**

With the biodistribution data of $^{64}$Cu-PSMA-BCH patients with primary prostate cancer, the human organ radiation dosimetry of $^{64}$Cu-PSMA-BCH was calculated using OLINDA/EXM 2.0 software package. The estimated dosimetry was shown in Table 3. Gallbladder wall was the most critical organ (2.04E+00 mGy/MBq), followed by liver (1.45E-02 mGy/MBq) and kidneys (9.47E-03 mGy/MBq). The effective dose was 0.0292 mSv/MBq, which means the effective dose of a patient was 4.3 mSv when injected with 4 mCi of $^{64}$Cu-PSMA-BCH. The whole-body effective dose of $^{18}$F-FDG that International Commission on Radiological Protection's (ICRP) is 0.019 mSv/MBq, equating to an effective dose for a 70 kg adult man (4.9 mSv). The effective dose of $^{64}$Cu-PSMA-BCH therefore is comparable to $^{18}$F-FDG for a male.

**PET-ultrasound guided targeted biopsy and histology**

After imaging at 4 h p.i., patients with suspected primary prostate cancer underwent PSMA-targeted PET-ultrasound fusion guided biopsies. Figure 5a showed the $^{64}$Cu-PSMA-BCH PET/CT images of one patient (age 80-y, PSA 31.6 ng/mL) at 24 h p.i.. First two targeted scores were kept in 10% neutral formaldehyde fixative and exposed to a screen (Figure 5c). The radioautography images clearly displayed the morphology of corresponding tissues (Figure 5d). The HE (hematoxylin-eosin) and PSMA immunohistochemical staining of targeted biopsies showed Gleason Score of 4+4 with high PSMA expression (100%) in enchylema (Figures 5e and 5f).
Discussion

PCa is widely studied as its high incidence and mortality. PSMA is overexpressed in PCa with high specificity, and has become an important target for the diagnosis and therapy of PCa. Multiple radiotracers targeting PSMA have been developed and PSMA PET/CT showed high sensitivity and specificity for the detection of PCa. In this study, we prepared a tracer, $^{64}$Cu-PSMA-BCH, labeled with copper-64, a radionuclide with longer half-life and allows high resolution imaging. Among the reported $^{64}$Cu labeled PSMA tracers, most of them were chelating with $^{64}$Cu by bifunctional conjugator DOTA. $^{64}$Cu-DOTA complexes was considered to have relative low in vivo stability, especially under acidic condition, which commonly lead to $^{64}$Cu ion transchelation to serum protein.[20] Compared with DOTA, NOTA has higher affinity to copper-64 and the resulting complexes are more stable in vivo with less chance of transchelation by copper metabolism. [16]

Compared with $^{64}$Cu-PSMA-617, a DOTA-conjugated tracer, $^{64}$Cu-PSMA-BCH was more stable in vivo with lower radioactivity accumulation in liver. While the uptake of $^{64}$Cu-PSMA-BCH in kidneys is higher than other organs, which was different from the $^{64}$Cu labeled DOTA-conjugated complexes. Indicating the stability of $^{64}$Cu-PSMA-BCH in vivo.

$^{64}$Cu-PSMA-BCH accumulated in kidneys and excreted through kidneys into urine with high bladder uptake within the first few hours. It can specifically accumulate in PSMA(+) 22Rv1 cells and tumor, which can be blocked by ZJ-43, a potent PSMA inhibitor commonly applied for blocking study [21], while PSMA(-) PC-3 cells or tumor showed low uptake of $^{64}$Cu-PSMA-BCH. In human PET images, $^{64}$Cu-PSMA-BCH showed a biodistribution similar to most other small-molecular ligands for PSMA, with accumulation in kidneys, bladder, submandibular glands, parotid glands and lacrimal glands, which showed the classic property of PSMA targeted tracers and indicated $^{64}$Cu-PSMA-BCH was specific to PSMA.

Because of the internalization of PSMA, $^{64}$Cu-PSMA-BCH increasingly accumulated in PSMA expressing tumors within 24 h. The SUVmax values of tumor lesions from three patients without any therapy increased from 1 h to 24 h p.i.. As the clearance of radiotracer from bladder and other organs, the tumor-to-bladder and tumor-to-background contrast increased.

Though the long half-life of $^{64}$Cu lead to higher effective dose of $^{64}$Cu-PSMA-BCH (0.0292 mSv/MBq) than many $^{68}$Ga and $^{18}$F labeled PSMA radiotracers [18], the long half-life of $^{64}$Cu also allowed lower injected dose. The lower injected dose and higher effective dose of $^{64}$Cu-PSMA-BCH make comparable radiation dose to patients. It also makes $^{64}$Cu-PSMA-BCH based delayed imaging possible.

Some studies showed that delayed PSMA PET/CT imaging can increase the uptake in tumor and may detect more tumor lesions with small volume or low PSMA expression [22-24]. Because of the long half-life of $^{64}$Cu, increased uptake and contrast of $^{64}$Cu-PSMA-BCH, delayed PET/CT imaging were allowed.
$^{64}$Cu-PSMA-BCH-based delayed imaging holds the potential for detecting more small tumor lesions or some occult recurrent metastasis.

Not only for detecting tumors, delayed PSMA PET/CT imaging of $^{64}$Cu-PSMA-BCH may have more application in clinic. Our group had reported a study that performed PSMA PET/CT prior to biopsy and then PSMA PET-ultrasound fusion targeted biopsies, which improved the detection rate and decrease possibility of repeated biopsies [3]. As shown in Figures 4 and 6, the tumor lesion at the right upper lobe of prostate was invisible at 1 h p.i., but it was clearly observed at the pelvic images at 4 h p.i. and images at 24 h p.i. The increased uptake of tumors and contrasts of $^{64}$Cu-PSMA-BCH in delayed images are benefit for offering more accurate sites of PSMA PET images-ultrasound fused targeted biopsies. The preliminary study of $^{64}$Cu-PSMA-BCH PET-ultrasound fused targeted biopsies in this study demonstrated the effectiveness of delayed imaging for locating the puncture sites. With the limited with the number of volunteers, more studies are needed to fully verify the potential of delayed $^{64}$Cu-PSMA-BCH PET imaging for targeted biopsies.

Recently, PSMA radioligand therapy (PRLT) showed inspiring therapeutic results for patients with metastatic castration resistant prostate cancer (mCRPC) [25]. $^{64}$Cu-PSMA-BCH delayed PET/CT imaging provides an approach for multi-temporal monitoring the uptake of radiotracers in tumors, especially for later time point which is beyond $^{68}$Ga and $^{18}$F labeled radiotracers can detect. Thus, to assess the potential benefits for patients from PRLT and then screen the appropriate candidates for PRLT.

**Conclusion**

In this study, $^{64}$Cu-PSMA-BCH was prepared with higher *in vivo* stability than DOTA-conjugated complexes. $^{64}$Cu-PSMA-BCH was PSMA specific and can be used for PSMA PETT/CT imaging of PCa patients. As the longer half-life of $^{64}$Cu and the internalization of radiotracers, delayed imaging with $^{64}$Cu-PSMA-BCH are meaningful in detecting small or insidious lesions, guiding accurate targeted biopsies and screening appropriate mCRPC patients for PRLT. But limited with the number of included volunteers, more studies are needed to further verify the value of the clinical applications of $^{64}$Cu-PSMA-BCH.

**Declarations**

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**Conflicts of Interest:** No other potential conflicts of interest relevant to this article exist.

**Ethical approval:** All animal experiments were conducted in accordance with the guidelines approved by Peking University Cancer Hospital Animal Care and Use Committee. All procedures performed in studies
involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by Ethics Committee of Beijing Cancer Hospital and Institute (No.2017KT97). Informed consent was obtained from all individual participants included in the study.

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### Tables

**Table 1. Characteristics of patients (n=4)**

| No. | Age (y) | Weight (kg) | PSA (ng/mL) | G S | Injected dose (MBq) |
|-----|---------|-------------|-------------|-----|---------------------|
| 1   | 68      | 50          | 8.5         | 5+4 | 119                 |
| 2   | 81      | 75          | 86.15       | 4+4 | 152                 |
| 3   | 80      | 60          | 35.16       | 4+4 | 165                 |
| 4   | 80      | 71          | 11.80       | 4+4 | 160.76              |

**Table 2. Quality control of $^{64}$Cu-PSMA-BCH**

| Parameter                | QC Result                  |
|--------------------------|----------------------------|
| Appearance               | Colorless                  |
| Volume Concentration     | 148 MBq/ mL                |
| pH                       | 6.9-7.2                    |
| Radio-HPLC               | > 99%                      |
| Ethanol                  | < 2%                       |
| Endotoxins               | Pass                       |
| Sterility                | Pass                       |
| Specific Activity        | 29.6-44.4 GBq/µmol         |
Table 3. Estimated human organ absorbed radiation dosimetry of $^{64}$Cu-PSMA-BCH

| Organ                  | Equivalent dose per unit injected dose activity (mGy/MBq) |
|------------------------|----------------------------------------------------------|
| Adrenals               | 1.84E-03                                                 |
| Brain                  | 4.62E-04                                                 |
| Esophagus              | 5.93E-04                                                 |
| Eyes                   | 1.48E-04                                                 |
| Gallbladder Wall       | 2.04E+00                                                 |
| Left colon             | 5.84E-04                                                 |
| Small Intestine        | 5.61E-04                                                 |
| Stomach Wall           | 6.74E-04                                                 |
| Right colon            | 7.09E-04                                                 |
| Rectum                 | 1.39E-04                                                 |
| Heart Wall             | 8.32E-04                                                 |
| Kidneys                | 9.47E-03                                                 |
| Liver                  | 1.45E-02                                                 |
| Lungs                  | 1.68E-03                                                 |
| Pancreas               | 7.16E-04                                                 |
| Prostate               | 1.32E-04                                                 |
| Salivary Glands        | 1.24E-04                                                 |
| Red Marrow             | 4.00E-04                                                 |
| Osteogenic Cells       | 5.20E-03                                                 |
| Spleen                 | 1.40E-03                                                 |
| Testes                 | 6.44E-05                                                 |
| Thymus                 | 3.03E-04                                                 |
| Thyroid                | 2.08E-04                                                 |
| Urinary Bladder Wall   | 9.43E-05                                                 |
| Total Body             | 7.06E-04                                                 |

**Effective dose (mSv/MBq)** 0.0292