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Positron Emission Tomography Using a GRPR Antagonist ^{68}Ga-RM26 in Healthy Volunteers and Prostate Cancer Patients

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ABSTRACT

This study was designed to study the safety, biodistribution, radiation dosimetry of a gastrin-releasing peptide receptor (GRPR) antagonist positron emission tomography (PET) tracer ^{68}Ga-RM26, to assess its clinical diagnostic value in prostate cancer patients, and to perform a direct comparison between GRPR antagonist ^{68}Ga-RM26 and agonist ^{68}Ga-BBN. **Methods:** Five healthy volunteers were enrolled to validate the safety of ^{68}Ga-RM26 and calculate dosimetry. A total of 28 patients with prostate cancer (17 newly diagnosed and 11 post therapy) were recruited with written informed consent. All the cancer patients underwent PET/CT scans at 15-30 min after intravenous injection of 1.85 MBq (0.05 mCi) per kilogram body weight of ^{68}Ga-RM26. Among them, 22 patients (11 newly diagnosed and 11 post therapy) accepted ^{68}Ga-BBN PET/CT for comparison within 1 week. ^{99m}Tc-MDP (methylene diphosphonate) bone scans were performed within 2 weeks for comparison. GRPR immunohistochemical staining of tumor samples was performed. **Results:** The administration of ^{68}Ga-M26 was well tolerated by all subjects with no adverse symptoms being noticed or reported during the whole procedure and 2 weeks follow up. The total effective dose equivalent (EDE) and effective dose (ED) were 0.0912 ± 0.0140 and 0.0657 ± 0.0124 mSv/MBq, respectively. In the 17 patients with newly diagnosed prostate cancer, ^{68}Ga-RM26 PET/CT showed positive prostate-confined findings in 15 tumors with maximum standard uptake value (SUV_{max}) of 6.49 ± 2.37. In the 11 patients underwent prostatectomy or brachytherapy with/without androgen deprivation therapy (ADT), ^{68}Ga-RM26 PET/CT detected 8 metastatic lymph nodes in three patients with SUVmax of 4.28 ± 1.25, and 21 bone lesions in 8 patients with SUVmax of 3.90 ± 3.07. Compared with ^{68}Ga-RM26 PET/CT, GRPR agonist ^{68}Ga-BBN PET/CT detected less primary lesions and lymph node metastases as well as lower tracer accumulation. There was a significant positive correlation between SUV derived from ^{68}Ga-RM26

PET and the expression level of GRPR ($P < 0.001$). **Conclusion:** This study indicates the safety and significant efficiency of GRPR antagonist ^{68}Ga-RM26. ^{68}Ga-RM26 PET/CT would have remarkable value in detecting both primary prostate cancer and metastasis. ^{68}Ga-RM26 is also expected to be better than GRPR agonist as an imaging marker to evaluate GRPR expression in prostate cancer.

Keywords: GRPR Antagonist; RM26; PET; Dosimetry; Prostate Cancer

INTRODUCTION

Prostate cancer is one of the most highly incident and lethal malignant diseases in men worldwide, with roughly 758,700 new cases diagnosed per year (*1*). Accurate diagnosis and staging of prostate cancer is of utmost importance for effective therapy, especially at early stage (*2*). Currently, the diagnosis of prostate cancer is usually triggered by elevated serum prostate-specific antigen (PSA) level, determined by anatomical imaging such as magnetic resonance imaging (MRI), X-ray computed tomography (CT) or transrectal ultrasound (*3*) and confirmed with prostate biopsy (*4*). These strategies are still considered to be inadequate since PSA level can be elevated in benign conditions and increases with advancing age and a certain portion of prostate cancer lesions might still be missed with these anatomical imaging modalities (*5*).

PET with various imaging probes has been developed to interrogate different pathways of malignant diseases including metabolism, proliferation, and abnormal receptor expression (*6*). PET radiotracers targeting prostate-specific membrane antigen (PSMA) and GRPR have shown promising results for the detection of primary and metastasized prostate cancer in early clinical studies (*7-9*).

GRPR is a member of the G protein-coupled receptor family of bombesin receptors. GRPR is over-expressed in various types of human tumors including prostate cancer, breast cancer, colorectal cancer, pancreatic cancer, small cell lung cancer, head and neck squamous cell tumors, gastric carcinoma and gastrointestinal stromal tumors, neuroblastomas and gliomas (*10-13*). Bombesin is an amphibian homolog of mammalian GRP and its fragmental peptide BBN(7-14) has been extensively used for the development of molecular probes for the imaging of GRPR (*14*). As an agonist, BBN(7-14) showed suboptimal pharmacokinetics *in vivo* and would induce side effects in patients, owing to its physiological activity (*9,15*). Therefore, imaging probes based on

GRPR antagonists have been explored and several GRPR antagonist-based PET tracers have been investigated in the clinic (*13,16,17*). Indeed, the clinical application of several such antagonists including RM2 and NeoBOMB1 showed very promising potential in prostate cancer detection and staging (*16,18*).

RM26, a GRPR antagonist with high affinity, was discovered by peptide backbone modification of bombesin analogues (*19,20*). Preclinical studies confirmed that ^{68}Ga-RM26 displayed high and specific uptake in tumors and high tumor-to-background ratios (*21*). In this study, we aimed to apply GRPR antagonist PET tracer ^{68}Ga-RM26 (^{68}Ga-1,4,7-triazacyclononane-N, N', N''-triacetic acid-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH_2) for first-in-human studies.

MATERIALS AND METHODS

Radiopharmaceutical Preparation

NOTA-RM26 was synthesized according to the previously reported procedure with a PEG3 linker between NOTA and RM26 (*21*). The radiolabeling of NOTA-RM26 and BBN was performed in a sterile hot cell following a procedure reported previously (*10*). The radiochemical purity of the product ^{68}Ga-RM26 and ^{68}Ga-BBN was over 95%.

Subject Enrollment

This clinical study was approved by the Institutional Review Board of Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences and all subjects gave written informed consent. This study was registered at clinicaltrials.gov (NCT03164837).

Five healthy volunteers (M 3, F 2, age range 32–54 y (mean ± SD, 45.2 ± 9.5); weight range 55.0-78.0 kg (mean ± SD, 67.4 ± 9.2)) were enrolled to validate the safety of ^{68}Ga-RM26. A total

of 28 patients (age range, 57-79 y, mean ± SD, 68.9 ± 5.86 y) were recruited, in which 17 patients were newly diagnosed by sextant core needle biopsy without any prior therapy, and 11 patients with histologically confirmed prostate cancer, underwent prostatectomy or radiation therapy or brachytherapy with/without ADT and diagnosed as biochemical recurrence according to the American Urological Association Prostate Guideline and American Society for Therapeutic Radiology and Oncology criteria. The demographics of the patients are listed in Supplemental Tables 1 and 2. All the 28 patients underwent ^{68}Ga-RM26 PET/CT and 22 patients also accepted ^{68}Ga-BBN PET/CT for comparison within 1 week. MRI or enhanced CT, and MDP bone scintigraphy were performed within 2 weeks for comparison. All the 17 primary prostate cancer patients accepted 12-core systematic randomized biopsy and 10 in 17 patients accepted prostatectomy with surgical pathology. Each imaging region corresponding to two needles prostate biopsy points respectively. GRPR immunohistochemical staining of tumor samples against GRPR was performed and correlated with PET. The existence of malignancy in the prostate gland and lymph nodes was confirmed by histologic examination with post-operation sampling or biopsy. The examination was determined by 2 pathologists independently, with a third pathologist to reach consensus if there were any discrepancies.

Examination Procedures

For healthy volunteers, the blood pressure, pulse, respiratory frequency, and temperature were measured, and routine blood and urine tests, liver function, and renal function were examined immediately before and 24 h after the scan. In addition, any possible side effects during ^{68}Ga-RM26 PET/CT scanning and within 1 week after the examination were collected and analyzed.

No specific subject preparation was requested on the day of ^{68}Ga-RM26 PET/CT. For the volunteers, after the whole-body low-dose CT scan, 111-148 MBq (3-4 mCi) of ^{68}Ga-RM26 were injected intravenously, followed by serial whole-body PET acquisitions. The whole body (from the top of skull to the middle of femur) of each volunteer was covered by 6 bed positions. The acquisition duration was 40 s/bed position at 5 and 10 min after injection; and 2 min/bed position at 15, 30, 45, and 60 min after injection.

For the patients, ^{68}Ga-RM26 PET/CT scanning was performed at 15–30 min after tracer administration. For each patient, 1.85 MBq (0.05 mCi) of ^{68}Ga-RM26 per kilogram of body weight were injected intravenously. After a low-dose CT scan, whole-body PET was performed with 2 min per bed position (5–6 bed positions depending on the height of the patient). The emission data were corrected for randoms, dead time, scattering, and attenuation. The conventional reconstruction algorithm was used, and the images were zoomed with a factor of 1.2. The images were transferred to a MMWP workstation (Siemens) for analysis.

Twenty-two patients, including 11 patients with newly diagnosed prostate cancer and 11 patients with recurrent prostate cancer, accepted ^{68}Ga-BBN PET/CT for comparison within 1 week. For each patient, 1.85 MBq (0.05 mCi) of ^{68}Ga-BBN per kilogram of body weight were injected intravenously. The imaging procedure and data analysis were the same as those for ^{68}Ga-RM26 PET/CT. The contrast enhanced CT and multi-parametric MRI (Mp-MRI) were also performed.

Image Data Analysis

A Siemens MMWP workstation was used for postprocessing. Visual analysis was used to determine the general biodistribution and the temporal and inter-subject stability. The volume of interest of normal organs/tissues and concerned lesions were drawn on the serial images. The radioactivity concentration and SUV in the volumes of interest were obtained through the software.

The dosimetry calculation was performed according to the European Association of Nuclear Medicine Dosimetry Guidance (*22*) and calculated using OLINDA/EXM (version 1.1; Vanderbilt University) with the procedure reported in a previous study (*10*). The void time of the bladder was set as 60 min. The absorbed doses were calculated by entering the time-integrated activity coefficient for all source organs into OLINDA/EXM for either a 73.7-kg adult man or a 56.9-kg adult woman.

Regions of interest were drawn manually on the site of lesions using a 3-dimensional ellipsoid isocontour on each image with the assistance of the corresponding CT images by 2 experienced nuclear medical physicians. The results were expressed as SUV_{mean} and SUV_{max}. Prostate MR and enhanced CT imaging were assessed by two experienced radiologists with the updated international prostate MR guideline protocols based on Prostate Imaging Reporting and Data system version 2.

^{99m}Tc-MDP Bone Scintigraphy

Bone scintigraphy images were obtained using a dual-head Siemens single photon emission tomography scanner. Planar images of the whole-body skeleton were acquired in the anterior and posterior views 3 h after intravenous injection of 925 MBq (25 mCi) of ^{99m}Tc-MDP.

Immunohistochemical Staining

Representative tumor and lymph node samples were fixed with 10% neutral buffered formalin and embedded in paraffin. After blocking and washing, 5-mm-thick tissue sections were incubated with mouse antihuman polyclonal antibody against human GRPR (Ab39963; Abcam). Six fields were randomly selected from each section and observed using a light microscope (BX41; Olympus). For semi-quantification of GRPR expression, 5 entire high-power fields (×40) containing clusters of malignant cells were identified randomly per slide and scored for intensity

and percentage of GRPR staining expression. The procedure was repeated by 2 independent experienced examiners.

Tumor section were scored based on the GRPR immunostaining intensity and percentage of positive tumor cells. The immunostaining intensity was graded as 0, none; 1, weak; 2, moderate; and 3, strong. The percentage of positive tumor cells was 0 to 100 %. And the composite score was generated by multiplying the intensity score by the percentage of positive cells.

Statistical Analysis

Statistical analysis was performed with the use of Prism 5.0 software (GraphPad, San Diego, CA). Continuous variables were summarized as means ± standard deviation. The correlation between quantitative parameters was evaluated by Pearson correlation coefficient for data with normal distribution or Spearman correlation coefficient for data with skewed distribution. The student *t* test was used to compare the SUVs of ^{68}Ga-RM26 PET and ^{68}Ga-BBN PET. For the data with normal distribution, paired *t* test (parametric test) was used to compare the mean standard uptake value of ^{68}Ga-RM26 PET and GRPR expression, the max standard uptake value of ^{68}Ga-RM26 PET and Gleason score. All tests were two tailed, with the significance level at 0.05.

RESULTS

Safety and Biodistribution

No adverse events or serious adverse events occurred after ^{68}Ga-RM26 injection for all the healthy volunteers and the patients, and no obvious changes in vital signs or clinical laboratory tests were found before and after the injection of ^{68}Ga-RM26.

As shown in Fig. 1, the whole-body background of ^{68}Ga-RM26 was very low, which facilitated the detection of both primary and metastatic lesions. Due to endogenous GRPR expression (*23*),

the pancreas showed relatively high signal intensity with a SUV_{mean} of 20.34 ± 2.54 at 30 min after tracer injection (Supplemental Table 3). ^{68}Ga-RM26 was mainly cleared through the renal-urinary system so bladder voiding was necessary before PET scan. The spleen and liver showed moderate uptakes with SUVs of 1.28 ± 0.24 and 1.26 ± 0.20 at 30 min p.i., respectively. Uptakes in the skeletal system, brain, lungs, mediastinum, thorax were at background level.

Dosimetry

The estimated absorbed dose of ^{68}Ga-RM26 for each organ derived from PET images of healthy volunteers (n = 5) was shown in Table 1. Due to the high accumulation of radioactivity in the urinary bladder, the urinary bladder wall had the highest absorbed dose of 1.09 ± 0.26 mSv/MBq. The high uptake of ^{68}Ga-RM26 in pancreas resulted in an absorbed dose of 0.225 ± 0.038 mSv/MBq. The total EDE and ED were 0.0912 ± 0.0140 and 0.0657 ± 0.0124 mSv/MBq, respectively.

^{68}Ga-RM26 PET/CT in Patients with Newly Diagnosed Prostate Cancer

For the 17 patients with pathologically diagnosed prostate cancer, by using SUVmax with a cut-off value of 2.0 and at least 1.5 times higher than the surrounding tissues, ^{68}Ga-RM26 PET/CT showed positive findings in 15 patients (88.2%), with SUVmax of 2.71~10.9 (mean ± SD, 6.49 ± 2.37). 11/17 (65%) were with strong localized tracer accumulation in primary prostate-confined lesions with SUVmax higher than 5.0 (Supplemental Fig. 1). No significant positive correlation between SUV_{max} from ^{68}Ga-RM26 PET and Gleason score or PSA level was identified. ^{68}Ga-RM26 PET/CT also detected 19 metastatic lymph nodes in three patients with SUV_{max} of 2.47~9.2 (mean ± SD, 4.98 ± 2.15) and 21 bone metastasis lesions in four patients with SUV_{max} of 1.9~13.7 (mean ± SD 5.91 ± 4.52), respectively. The immunohistochemical staining result showed positive GRPR expression in 21 out of 23 samples (91.7%) including 17 samples from primary tumor

needle biopsy or postoperative samples and 4 postoperative pelvic lymph nodes samples. There was significant positive correlation between ^{68}Ga-RM26 PET SUV and expression level of GRPR ($P < 0.001$) (Fig. 2). Based on the Mp-MRI scanning and Prostate Imaging Reporting and Data System version 2 criteria, 12 out of 17 (70.6%) primary prostate cancer and 6 lymph nodes were detected. No additional lesions were detected by enhanced CT. In comparison to that, ^{68}Ga-RM26 PET/CT detected 15 in 17 (88.2%) primary prostate cancer in a population with an average PSA of 55.7 ± 92.0 ng/ml (Supplemental Table 1) and 9 lymph nodes in the same pelvic scanning area. ^{68}Ga-RM26 PET/CT detected more bone metastatic lesions (n = 2) than bone scintigraphy (Supplemental Table 1).

^{68}Ga-RM26 PET/CT in Patients with Recurrent Prostate Cancer

Eleven patients with pathologically diagnosed prostate cancer underwent prostatectomy or brachytherapy with/without ADT. In these patients, ^{68}Ga-RM26 PET/CT detected 8 metastatic lymph nodes in three patients with an SUVmax of 1.98~5.35 (mean ± SD, 4.28 ± 1.25), and 21 bone lesions in eight patients with an SUVmax of 1.51~9.77 (mean ± SD, 3.90 ± 3.07) (Fig. 3). The immunohistochemical staining revealed positive GRPR expression in 3 samples from pelvic lymph node metastasis in one patients. All the remaining 4 lymph nodes and 23 bone lesions were confirmed by further imaging and/or by response to site-directed therapies.

Comparison between ^{68}Ga-RM26 PET/CT and ^{68}Ga-BBN PET/CT in Prostate Cancer

Among 28 patients recruited, 22 patients underwent both ^{68}Ga-RM26 and ^{68}Ga-BBN PET/CT for a direction comparison (Supplemental Table 1 and 2, Fig. 4). ^{68}Ga-RM26 PET/CT detected 13 primary tumors, 19 lymph nodes lesions, and 31 bone lesions. With the same patient population, 5 primary tumors, 9 lymph nodes and 25 bone lesions were positive on ^{68}Ga-BBN PET/CT. Moreover, SUV_{max} from ^{68}Ga-RM26 PET/CT was significantly higher than that from ^{68}Ga-BBN

PET/CT in both primary lesions 2.71-9.00 (mean ± SD, 5.69 ± 1.90) *vs.* 1.70-4.85 (mean ± SD, 2.71 ± 1.31), $P < 0.01$) and lymph node metastases 2.23-5.90 (mean ± SD, 3.92 ± 1.20 *vs.* 1.30-4.30 (mean ± SD, 2.32 ± 0.95, $P < 0.01$). However, there was no significant difference of SUV_{max} in bone lesions 1.30-9.77 (mean ± SD, 4.27± 2.25) *vs.* 1.37-9.34 (mean ± SD, 4.21 ± 2.31, $P > 0.05$) (Fig. 5). Two primary tumors being positive in ^{68}Ga-RM26 PET but negative in ^{68}Ga-BBN PET were confirmed to have moderate GRPR expression from immunohistochemical staining of the biopsy samples.

DISCUSSION

Although quite a few studies supported the note that GRPR antagonist is better than agonist in lesion detection, there is also report of discrepancy claiming that the agonist peptide ligand is a superior molecular imaging agent for targeting GRPR (*24*). In order to clarify this debate, we performed the first direct comparison of GRPR antagonist (RM26) and agonist (BBN(7-14)) in the clinical setting.

Excretion of ^{68}Ga-RM26 is mainly through the renal-urinary tract, resulting in high radioactivity accumulation and dose exposure in the urinary bladder. With a typical 130 MBq (3.5 mCi) injected activity of ^{68}Ga-RM26, the whole-body effective dose was 8.54 mSv, which was much lower than the dose limit set by the Food and Drug Administration (*25*). All these data confirmed the safety of ^{68}Ga-RM26 for further clinical applications. However, the high exposure to the pancreas and urinary bladder needs to be considered when RM26-based endo-radiotherapy is pursued.

With a large cohort of clinical samples, GRPR expression was found to be positive in around 80% of primary prostate carcinomas (*26*). Herein, ^{68}Ga-RM26 PET/CT showed positive findings

in 15 out of 17 primary lesions (88.2%) in patients with newly diagnosed prostate cancer, and strong localized tracer accumulation was found in 11 lesions (65%) with SUVmax more than 5.0. Moreover, there was a significant positive correlation between SUV from ^{68}Ga-RM26 PET and the expression level of GRPR ($P < 0.001$). However, no significant positive correlation between SUVmax from ^{68}Ga-RM26 PET and Gleason score was identified. In addition, there was no significant positive correlation between PSA-T or PSA-F level and SUVmax from ^{68}Ga-RM26 PET.

In 22 patients that underwent PET/CT using both GRPR antagonist and agonist probes, the antagonist PET identified more primary tumors with significantly higher SUV, suggesting that ^{68}Ga-RM26 antagonist tracer is potentially better than ^{68}Ga-BBN agonist tracer in lesion detection and evaluation of GRPR expression. Moreover, ^{68}Ga-RM26 PET/CT detected more lymph node metastases and bone metastases than ^{68}Ga-BBN PET/CT. RM26 showed high binding affinity for GRPR even after chelator conjugation (*27*), which is very close to that of the agonist BBN (*14*). As the antagonist, RM26 showed much lower internalization rate than BBN determined by *in vitro* cell experiments (*28*). We speculated that the differences in *in vivo* stability and pharmacokinetic profile would be the main reasons for the difference of ^{68}Ga-BBN and ^{68}Ga-RM26 in primary prostate cancer and metastasis detection.

Lesions with high receptor expression may be positively identified by both agonist and antagonist. However, lesions with low or medium receptor expression may not have high enough contrast to be visualized by the agonist. Therefore, this pilot study demonstrates that antagonist tracer ^{68}Ga-RM26 PET/CT is more valuable in prostate cancer diagnosis and staging. Moreover, the same ligand can be used as a therapeutic agent for tumor-targeted radionuclide therapy of prostate cancer after being labeled with alpha- or beta-emitting radioisotopes (*29*). Majority of the

publications so far favored the antagonists over agonists as imaging probes (*30*). However, controversial findings are also available (*24*,*31*). More strict comparison in both preclinical and clinical settings are still needed for further clarification.

The main limitations of this study are the relatively small number of patients investigated and the lack of histologic confirmation of the detected distant lymph node metastases and bone metastases. Furthermore, to avoid the interference from the high background in urinary system, the images were acquired at 15-30 min after tracer injection. Future work may consider imaging at a later time point along with furosemide to increase lesion detectability (*32*). Lastly, direct comparison between ^{68}Ga-RM26 and other prostate cancer targeting PET tracers such as choline and PSMA is missing (*2*). However, in previous studies, Minamimoto *et al*. compared PSMA and GRPR-targeted imaging in prostate cancer and found no significant differences in patients with biochemically recurrent prostate cancer (*33*). By targeting different prostate cancer specific markers, each of these tracers may have advantages and limitations due to the heterogeneity of prostate cancer.

CONCLUSION

This study indicates the safety and efficiency of GRPR antagonist ^{68}Ga-RM26. ^{68}Ga-RM26 PET/CT would have remarkable value in detecting both primary prostate cancer and metastasis. ^{68}Ga-RM26 is also expected to be better than GRPR agonist as an imaging marker to evaluate GRPR expression in prostate cancer and other cancer types.

DISCLOSURE

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Conflicts of interest

None.

Statement of human rights

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.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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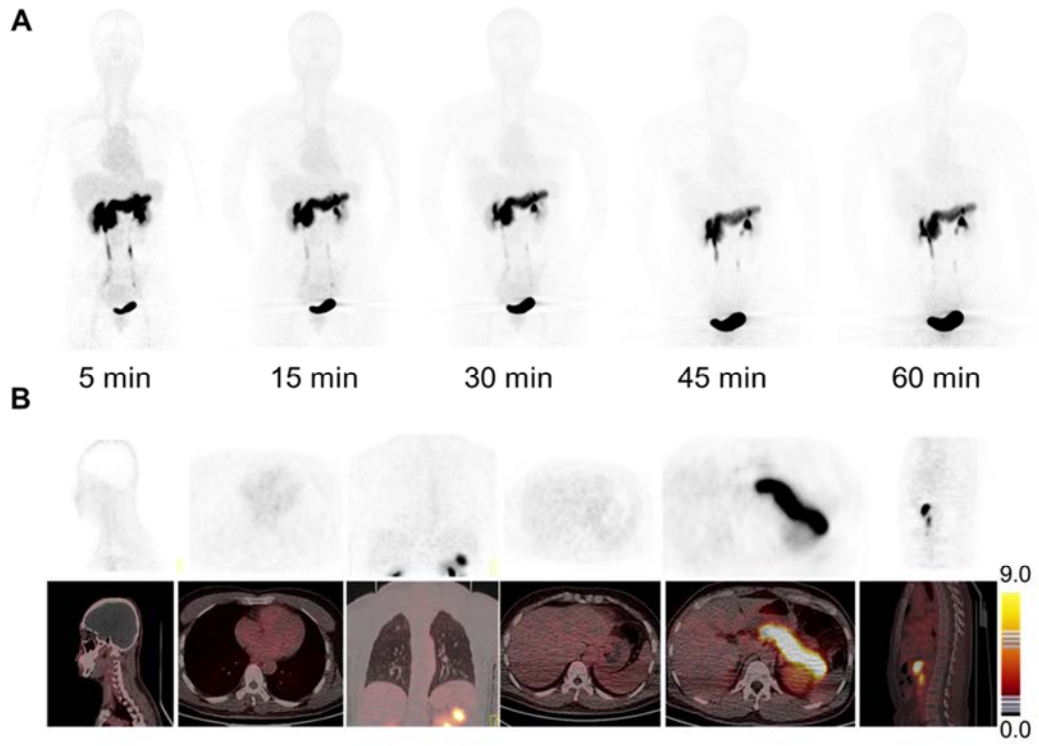

FIGURE 1. (A) Representative torso maximum intensity projection (MIP) images of a 42-y-old female healthy volunteer at 5, 15, 30, 45 and 60 min after intravenous injection of ^{68}Ga-RM26. Main regions with prominent ^{68}Ga-RM26 uptake are pancreas, kidneys, urinary ducts and bladder. (B) PET/CT showed tracer uptake in major organs at 30 min after intravenous administration of 129.5 MBq (3.5 mCi) of ^{68}Ga-RM26 to a 48-y-old male healthy volunteer.

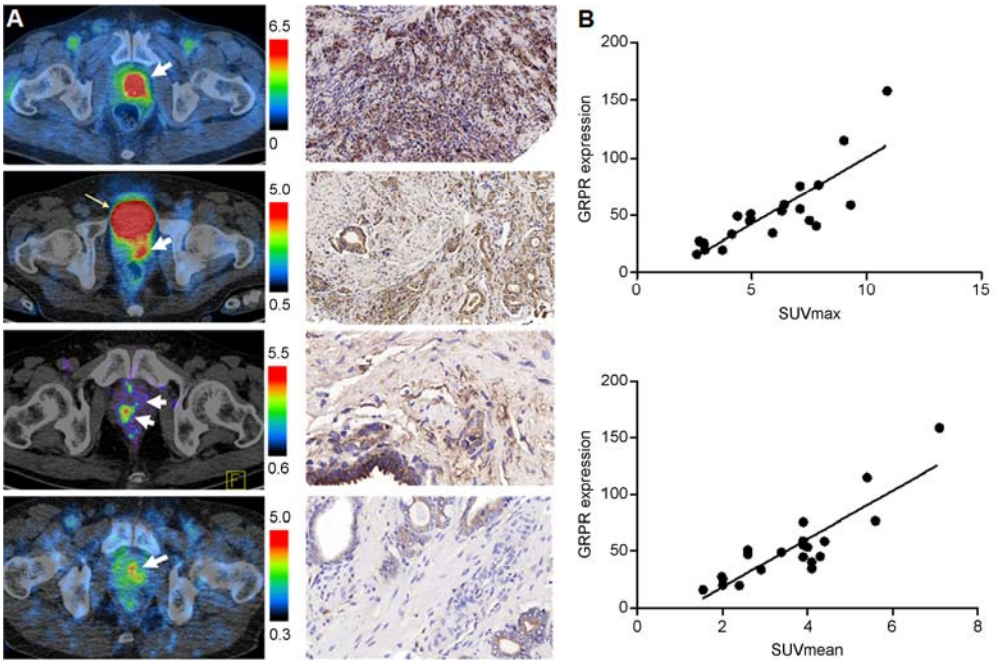

FIGURE 2. (A) Different levels of ^{68}Ga-RM26 accumulation in newly diagnosed prostate cancer and immunohistologic staining against GRPR of the biopsy samples. (B) Correlation of PET quantification and GRPR expression score in primary prostate cancer and metastases.

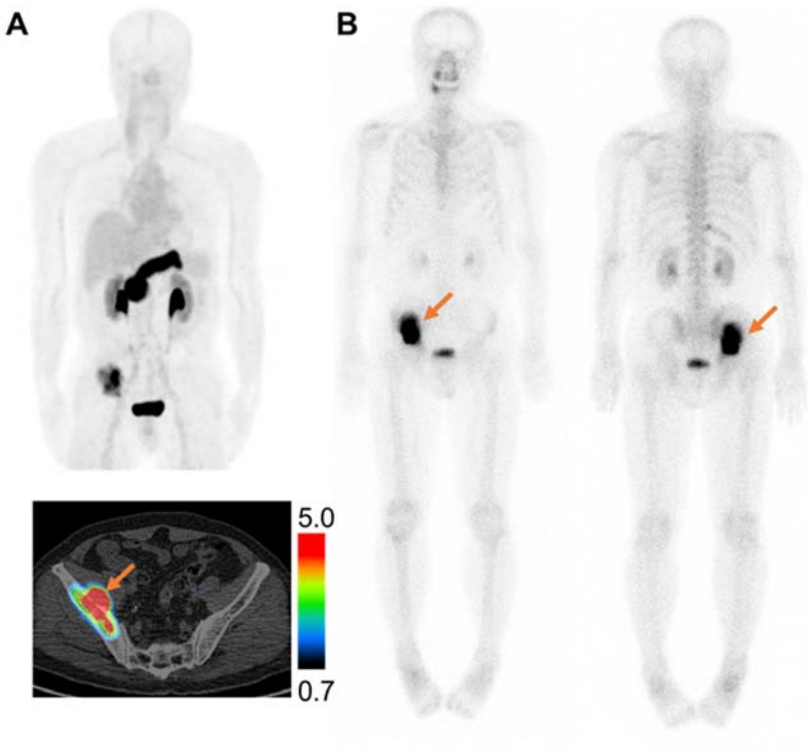

FIGURE 3. ^{68}Ga-RM26 PET/CT (A) and ^{99m}Tc-MDP bone scintigraphy (B) in a 62-year-old man with recurrent prostate cancer, who was diagnosed as prostate cancer 4.5 years ago, and underwent RT and ADT. The current PSA value was 36.0 ng/ml. ^{68}Ga-RM26 PET/CT detected bone metastasis lesion in the right ilium and the surrounding soft tissues.

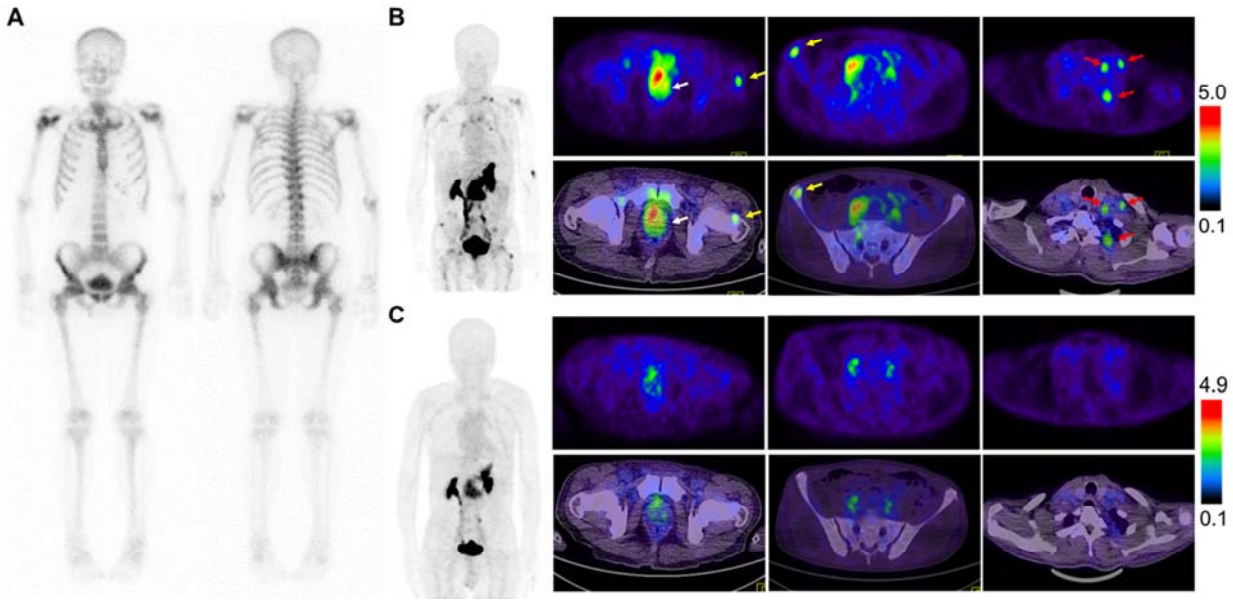

FIGURE 4. Comparison of ^{99m}Tc-MDP bone scintigraphy (A), ^{68}Ga-RM26 PET/CT (B), and ^{68}Ga-BBN PET/CT (C) and in a 73-year-old man diagnosed as prostate cancer (white arrow) with lymph node involvement (red arrow) and bone metastasis (yellow arrow) before prostatectomy. ^{68}Ga-RM26 PET/CT detected the primary tumors, multiple lymph nodes involvement, and bone metastasis lesion, while those lesions did not significantly show up on ^{99m}Tc-MDP bone scintigraphy and extremely mild uptake on ^{68}Ga-BBN PET/CT.

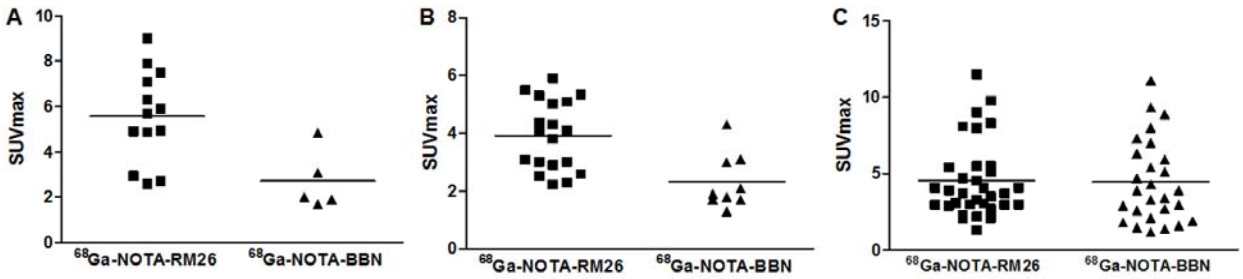

FIGURE 5. Quantitative comparison between ^{68}Ga-RM26 PET/CT and ^{68}Ga-BBN PET/CT in primary tumor (A), lymph node metastases (B), and bone metastases (C) in 22/28 patients who underwent both ^{68}Ga-RM26 and ^{68}Ga-BBN PET/CT.

Table 1. Estimated absorbed dose after intravenous administration of ^{68}Ga-RM26 (mSv/MBq, n = 5, 3 males and 2 females)

Target organ	Mean	SD
Adrenals	7.48E-03	2.71E-03
Brain	1.25E-03	4.08E-04
Breasts	4.56E-03	2.41E-03
Gallbladder Wall	8.00E-03	2.67E-03
LLI Wall	1.74E-02	3.64E-03
Small Intestine	1.04E-02	2.84E-03
Stomach Wall	7.51E-03	2.83E-03
ULI Wall	9.44E-03	3.06E-03
Heart Wall	5.93E-03	2.78E-03
Kidneys	3.60E-02	1.89E-03
Liver	1.59E-02	2.43E-03
Lungs	6.01E-03	1.01E-03
Muscle	7.76E-03	1.19E-03
Ovaries	2.06E-02	
Pancreas	2.25E-01	3.77E-02
Red Marrow	9.15E-03	1.88E-03
Osteogenic Cells	1.04E-02	4.07E-03
Skin	5.16E-03	2.17E-03
Spleen	1.93E-02	1.41E-03
Testes	1.09E-02	6.08E-04
Thymus	5.07E-03	2.60E-03
Thyroid	4.73E-03	2.42E-03
Urinary Bladder Wall	1.09E+00	2.25E-01
Uterus	3.55E-02	
Total Body	9.98E-03	2.51E-03
Effective Dose Equivalent	9.12E-02	1.40E-02
Effective Dose	6.57E-02	1.24E-02