Pilot Comparison of $^{68}$Ga-RM2 PET and $^{68}$Ga-PSMA PET in Patients with Biochemically Recurrent Prostate Cancer

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Running Title: Comparison of $^{68}$Ga-RM2 and $^{68}$Ga-PSMA

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ABSTRACT

Objectives: Glu-NH-CO-NH-Lys-(Ahx)-[^68]Ga(HBED-CC)] ([^68]Ga-PSMA) is a positron emission tomography (PET) tracer that can detect prostate cancer relapses and metastases by binding to the extracellular domain of PSMA.[^68]Ga-labeled DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe- Gln-Trp-Ala-Val- Gly-His-Sta-Leu-NH2 ([^68]Ga-RM2) is a synthetic bombesin receptor antagonist that targets gastrin-releasing peptide receptors (GRPr). We present pilot data on the biodistribution of these PET tracers in a small cohort of patients with biochemically recurrent prostate cancer (BCRPC).

Methods: Seven men (mean age ± SD: 74.3±5.9 year-old) with BCRPC had both[^68]Ga-PSMA PET/CT and[^68]Ga-RM2 PET/MRI scans. The maximum standardized uptake value (SUV$_\text{max}$) and mean SUV (SUV$_\text{mean}$) measurements were recorded in normal tissues and areas of uptake outside the expected physiologic biodistribution.

Results: All patients had rising prostate-specific antigen (PSA) (mean±SD: 13.5±11.5) and non-contributory conventional imaging.[^68]Ga-PSMA had the highest physiologic uptake in the salivary glands and small bowel, with hepatobiliary and renal clearance noted, while[^68]Ga-RM2 had the highest physiologic uptake in the pancreas, with renal clearance noted. Uptake values uptake outside the expected physiologic biodistribution were not statistically
different between $^{68}$Ga-PSMA and $^{68}$Ga-RM2; however, $^{68}$Ga-PSMA localized in a lymph node and seminal vesicle in a patient with no abnormal $^{68}$Ga-RM2 uptake. Abdominal periaortic lymph nodes were more easily visualized by $^{68}$Ga-RM2 in two patients due to lack of interference by radioactivity accumulation in the small intestine.

**Conclusions:** $^{68}$Ga-PSMA and $^{68}$Ga-RM2 have distinct biodistribution in this small cohort of patients with BCRPC. The findings here indicate that additional work is needed to understand the expression of PSMA and GRPr in different types of prostate cancer.

**Key words:** prostate cancer; $^{68}$Ga; RM2; PSMA; PET/MRI; PET/CT
INTRODUCTION

Prostate cancer recurrence has been assessed by measurement of prostate-specific antigen (PSA) values and velocity. A detectable or rising PSA level after therapy is considered biochemical recurrence (BCR) or “PSA failure”, even when there are no symptoms or signs of locally recurrent or metastatic disease (1, 2). Imaging is useful to identify the local recurrent or distant lesions when PSA level is rising since it enables the selection of appropriate treatment such as local salvage therapy or systemic therapy (3).

Conventional imaging techniques such as ultrasound, contrast-enhanced computed tomography (CT), or magnetic resonance imaging (MRI) imaging have limited sensitivity and specificity for local recurrence and metastatic lesion (3). $^{11}$C-acetate, $^{11}$C-Choline and $^{18}$F-Choline have been reported to be useful for the diagnosis of recurrent or metastatic prostate cancer (4-8). However, the very short half-life of $^{11}$C limits its use to facilities equipped with cyclotrons. Although choline based PET/CT is widely used outside the US for imaging prostate cancer, there have been numerous studies reporting a low sensitivity and specificity, especially at low prostate specific antigen (PSA) levels (9, 10).

Prostate-specific membrane antigen (PSMA) is significantly overexpressed in prostate cancer cells when compared to other PSMA-expressing tissues such as kidney,
proximal small intestine or salivary glands (11). It therefore provides a promising target for prostate cancer-specific imaging (12). Methods have been recently developed to label PSMA ligands with both $^{68}$Ga and $^{177}$Lu, enabling their use for theranostics (13, 14). Initial experience with PET/CT using Glu-NH-CO-NH-Lys-(Ahx)-[$^{68}$Ga(HBED-CC)] ($^{68}$Ga-PSMA) suggests that this novel tracer can detect prostate cancer relapses and metastases with high contrast by binding to the extracellular domain of PSMA, followed by internalization (15).

$^{68}$Ga-labeled DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH$_2$ ($^{68}$Ga-RM2 or $^{68}$Ga-DOTA-Bombesin, formerly also known as BAY86-7548) is a synthetic bombesin receptor antagonist, which targets gastrin-releasing peptide receptors (GRPr) (16). GRPr proteins are highly overexpressed in several human tumors, including PC (17). GRPr receptor was detected in 63-100 % of human prostate cancer tissue (18, 19). Since $^{68}$Ga-RM2 and $^{68}$Ga-PSMA target different biological processes, understanding how these two tracers behave in patients with biochemically recurrent prostate cancer (BCRPC) is critical for finding the best patient management options for this clinical scenario.
The aim of this study was to compare the biodistribution of $^{68}$Ga-RM2 and $^{68}$Ga-PSMA in patients with BCRPC. In addition, we compared the $^{68}$Ga-PSMA uptake outside the expected physiologic biodistribution with that of $^{68}$Ga-RM2 in the same patients.

MATERIALS AND METHODS

Patient Population

The local Radioactive Drug Research Committee (RDRC), Institutional Review Board (IRB) and the Stanford Cancer Institute Scientific Review Committee approved the protocol. Written informed consent was obtained from all patients before participation in the study. Inclusion criteria were: 1) greater than 18 year-old at the time of radiotracer administration, 2) known diagnosis of prostate cancer, 3) suspected recurrence based on biochemical data (PSA > 2 ng/mL), 4) able to remain still for duration of the imaging procedure (approximately 1 hour). Exclusion criteria were: 1) metallic/conductive or electrically/magnetically active implants without MR safe or MR conditional labeling, 2) standard contraindications for PET and MRI per screening policy of our hospital (e.g., severe claustrophobia, radiation phobia).
Preparation of $^{68}$Ga-PSMA

$^{68}$Ga-PSMA was synthesized as previously reported (20). The precursor, Glu-NH-CO-NH-Lys(Ahx)-HBED-CC (DKFZ-PSMA-11, or PSMA-HBED), was obtained from ABX GmbH (Radeberg, Germany). All other reagents of the highest grade were purchased from commercial suppliers and used as provided (Sigma, EMD Millipore, Hospira, Akorn).

The radiosynthesis was performed on a fully automated synthesis device using sterile single-use cassettes (Modular Lab PharmTracer, Eckert & Ziegler Eurotope GmbH). $^{68}$GaCl₃ was obtained from a $^{68}$Ge/$^{68}$Ga generator (IGG-100; 1,850 MBq); Eckert & Ziegler Isotope Products] by eluting the generator with 6 mL of 0.1 M HCl. The generator eluate was passed through a cation exchange (SCX) cartridge to trap the $^{68}$Ga ions for purification. Purified $^{68}$GaCl₃ was eluted from the SCX cartridge using a concentrated NaCl/HCl solution into a pre-charged reaction vial containing the precursor DKFZ-PSMA-11 (10 µg) in sodium acetate buffer (pH 4.5). The mixture was heated at 85ºC for 180 s. Crude $^{68}$Ga-PSMA was diluted with saline and loaded onto a C18 light cartridge. The loaded cartridge was subsequently washed with saline and eluted with a 50% ethanol solution. The purified product was then diluted with saline and passed through a sterilizing membrane filter (0.2
µm) to afford the final formulated product (~ 10 mL).

The identity and the radiochemical purity of the product (68Ga-PSMA) were evaluated by radio-high-performance liquid chromatography (radio-HPLC) and radio-thin layer chromatography (TLC). Estimated decay-corrected yield (DCY) to start of synthesis (SOS) was 86.5±4.1% with a specific radioactivity of 70±20 GBq/µmol (n=10).

Preparation of 68Ga-RM2

The precursor, DOTA-4-amino-1-carboxymethylpiperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2 (DOTA-RM2), was obtained from ABX GmbH (Radeberg, Germany). A 68Ga-labeling kit including eluent (concentrated NaCl/HCl solution), sodium acetate reaction buffer, ethanol (50% in water) and saline (0.9%, USP) was obtained from Eckert & Ziegler Eurotope GmbH (Berlin, Germany). Phosphate buffer concentrate (1 M Na+, 0.6 M PO₄³⁻) for pH adjustment was obtained from B. Braun (Melsungen, Germany).

Purified 68GaCl₃ was eluted from the SCX cartridge using a concentrated NaCl/HCl solution into a pre-charged reaction vial containing the precursor DOTA-RM2 (40 µg) in sodium acetate buffer (pH 4.5) and ethanol. The mixture was heated at 105°C for 400 s. Crude 68Ga-RM2 was diluted with phosphate buffered saline and loaded onto a C18 light
cartridge. The loaded cartridge was subsequently washed with buffered saline and eluted with a 50% ethanol solution. The purified product was then diluted with phosphate buffered saline and passed through a sterilizing membrane filter (0.2 µm) to afford the final formulated product (~10 mL).

The identity and the radiochemical purity of the product (⁶⁸Ga-RM2) were evaluated by radio-high-performance liquid chromatography (radio-HPLC) and radio-thin layer chromatography (TLC). Estimated decay-corrected yield (DCY) to start of synthesis (SOS) was 86.1±1.2% with a specific radioactivity of 16±1 GBq/µmol (n=7).

**PET/CT Protocol**

No specific patient preparation such as fasting or hydration was requested for ⁶⁸Ga-PSMA PET/CT scans. Whole-body PET/CT images were acquired from vertex to mid-thighs with eight bed positions and 3-minute emission scans/bed at 51-68 minutes (mean±SD: 57.1±5.9) after the i.v. administration of the ⁶⁸Ga-PSMA. The administered activity was 130-144 MBq (mean±SD: 137±4 MBq). The images were reconstructed using an ordered subset expectation maximization (OSEM) algorithm with two iterations and 32 subsets for the GE Discovery 600 (GE Healthcare, Waukesha, WI, USA) scanner (n=6).
patients) and two iterations and 24 subsets for the GE Discovery 690 scanner (n=1 patient).

The CT acquisition was performed for attenuation correction, in helical mode, using 120 kV; 10 mAs; 512×512 matrix; field of view, 867 mm in 22.5 seconds. The mAs value of CT was reduced to 10 mAs, as requested by the local IRB to decrease the radiation exposure. The duration of the PET/CT exam ranged 24-38 minutes (mean±SD: 30.2±4.9).

**PET/MRI Protocol**

No specific patient preparation such as fasting or hydration was required on the day of the scans for $^{68}$Ga-RM2. Imaging (vertex to mid-thighs) started at 42-51 minutes (mean±SD: 48±3 minutes) after injection of 133-152 MBq (mean±SD: 137±7 MBq) of $^{68}$Ga-RM2 using a time-of-flight enabled simultaneous PET/MRI scanner (SIGNA PET/MR, GE Healthcare). The duration of the scan ranged 39-85 minutes (mean±SD: 66±16 minutes), and in addition to the difference in number of beds used related to participants' height also included the time to prep the participants for the scans (positioning the body coils, defining the scan field of view etc). Lastly, patients who did not have prostatectomy received intravenous contrast and additional T1-weighted imaging was done over the prostate bed, contributing to the
duration of the exam. The PET acquisition was performed in 3D mode and 4 minutes/bed position (89 slices/bed) in 5-9 beds. An axial 2-point Dixon 3-dimensional T1-weighted spoiled gradient echo MR sequence (TR/TE1/TE2: 4.1/1.1/2.2 ms; field-of-view (FOV) 50x37.5 cm; matrix 256x128; slice thickness/spacing: 5.2/2.6 mm; 120 images/slab; imaging time 18 sec) was acquired at each table position and used to generate attenuation correction (AC) maps and for anatomic registration of the PET results.

PET images were reconstructed using ordered subset expectation maximization (OSEM) protocol with 2 iterations and 28 subsets. TOF reconstructed images assumed a Gaussian kernel of 400 ps width. The Dixon MRI sequence and the PET acquisition started at the same table position and times, thus ensuring optimal temporal and regional correspondence between MRI and PET data. For AC, the images were segmented into different tissue types with an anatomy-aware algorithm, and were co-registered to a CT atlas in the head region (21).

Additional sequences acquired at each station included: coronal T2-weighted (T2w) single-shot fast spin echo (SSFSE), diffusion weight imaging (DWI) and T1-weighted (T1w) axial 2-point Dixon 3D spoiled gradient echo, as previously described (21).
Image Analysis

Two board certified Nuclear Medicine physicians (AI, RM) with 10 and 8 years experience interpreting PET studies, respectively, reviewed PET images using MIMvista version 6.2 (MIMvista Corp, Cleveland, OH, USA) to select organs throughout the body and evaluated the uptake using the region of interest (ROI) tool within the software. Circular ROIs, whose sizes (diameter 10-30 mm) depended on the structure of interest, were drawn on transaxial $^{68}$Ga-RM2 PET/MRI images and transaxial $^{68}$Ga-PSMA PET/CT images with the reference to anatomical structure confirmed by MRI portion of PET/MRI and CT portion of the PET/CT, respectively. ROI analysis was conducted for the frontal lobe cortex, cerebellar cortex, parotid gland, submandibular gland, thyroid, lung, ascending aorta as blood pool, liver, spleen, pancreas, small intestine, descending colon, kidney, bladder, gluteus maximus muscle, fat tissue of hip, right humerus, right femur, 3rd cervical vertebra, 9th thoracic vertebra, 3rd lumbar vertebra and sacrum. We added ROI measurements for esophagus and stomach for $^{68}$Ga-RM2, as well as lacrimal grand and submandibular salivary gland for $^{68}$Ga-PSMA, in order to take into account specific biodistribution. These
ROIs were carefully positioned over the central portion of each structure depicted on the PET/MRI or PET/CT image. For the aortic blood pool, a circular ROI with a diameter of 10mm was placed centrally within the ascending aorta. An ROI with a diameter of 30mm was placed on right liver lobe.

For the standardized uptake value (SUV) measurements of focal $^{68}$Ga-RM2 uptake outside the expected biodistribution, we reviewed the PET images with reference to the MRI data. Conversely, for the SUV measurements of focal $^{68}$Ga-PSMA uptake outside the expected biodistribution, we reviewed the PET images with reference to the CT data. The PETedge tool of the MIMvista was used for measurements of $^{68}$Ga-RM2 and $^{68}$Ga-PSMA uptake outside the expected biodistribution.

Two board certified radiologists (AML, SSV, 9 and 2 years experience interpreting body MRI studies, respectively) evaluated the MR images for detection of areas of abnormal signal or anatomical structures, blinded to the results of PET or other studies. Visual conspicuity against background on the diffusion weighted images and presence of an anatomically corresponding abnormality on the T1w and T2w images were the criteria for detecting a lesion on MRI.
**Statistical Analysis**

Data regarding time from injection to start of imaging, injected dosages of radiopharmaceuticals, $S_{U V_{\text{mean}}}$ and $S_{U V_{\text{max}}}$ are presented as mean±SD. The Mann-Whitney U test was performed for the evaluation of focal uptake measurements ($S_{U V_{\text{mean}}}$, $S_{U V_{\text{max}}}$ and ratios of $S_{U V_{\text{mean}}}$, $S_{U V_{\text{max}}}$ to normal background [blood pool] [F/N ratio]) outside the expected biodistribution between $^{68}$Ga-RM2 and $^{68}$Ga-PSMA. Pearson correlation coefficient analysis was used to evaluate the $^{68}$Ga-RM2 and $^{68}$Ga-PSMA uptake. All statistical analyses were done with Stata 11 (Stata, College Station, TX). Two-tailed $P$ values <0.05 were considered significant.

**RESULTS**

Seven men (67-83 year-old; mean ± SD: 74.3±5.9) with suspected biochemical recurrence of prostate cancer and PSA values of 13.5±11.5 ng/ml (range 3.5-36.5) were enrolled in this study. Patient characteristics and results are shown in Table 1. Patients had standard of care imaging studies (CT, MRI, $^{18}$F FDG PET/CT, $^{18}$F NaF PET/CT, $^{99m}$Tc MDP
bone scan) prior to enrollment that were non-contributory. $^{68}$Ga-RM2 PET/MRI was performed first, followed by $^{68}$Ga-PSMA PET/CT 13-85 days later (mean±SD: 42.9±25.2). The time from conventional imaging to $^{68}$Ga-RM2 PET/MRI was 10-107 days (mean±SD: 43.3±26.0). The interval from biochemical recurrence to the $^{68}$Ga-RM2 PET/MRI scan was 5-75 months (mean±SD: 30.8±20.4). The interval from most recent PSA measurement to the $^{68}$Ga-RM2 PET/MRI scan ranged 1-30 days (mean±SD: 15.2±12.2).

**Biodistribution and Localization of $^{68}$Ga-PSMA and $^{68}$Ga-RM2**

All patients were on a watch and wait management strategy at the time of enrollment in the protocol. All patients tolerated the procedure without immediate or delayed (up to 7 days) reportable adverse events.

The tissues with the highest uptake for $^{68}$Ga-PSMA were lacrimal, parotid and submandibular glands, and small intestine, while the tissues with the highest $^{68}$Ga-RM2 accumulation were the pancreas and bladder (Fig. 1 and Supplemental Table 1).

$^{68}$Ga-PSMA and $^{68}$Ga-RM2 Uptake Outside the Expected Physiologic Biodistribution
There were 45 areas of high $^{68}$Ga-PSMA uptake that corresponded on the CT images to bone marrow ($n=13$), retroperitoneal lymph nodes ($n=12$), mediastinal lymph nodes ($n=8$), pelvic lymph nodes ($n=9$), seminal vesicle ($n=2$), subclavian lymph node ($n=1$). $^{68}$Ga-RM2 uptake was high all these areas, except for a pelvic lymph node and vas deferens that were negative on the $^{68}$Ga-RM2 study, both in the same patient. The time from $^{68}$Ga-RM2 to $^{68}$Ga-PSMA was 54 days in this case, with PSA changing from 6.8 ng/ml to 9.2 ng/ml in this interval. Conversely, $^{68}$Ga-PSMA uptake and/or clearance in the bowel made small retroperitoneal lymph nodes less conspicuous than on $^{68}$Ga-RM2 in 2 participants.

Measurements of the $^{68}$Ga-PSMA uptake outside the expected physiologic biodistribution were not statistically significant ($\text{SUV}_{\text{max}}$ $P=0.68$, $\text{SUV}_{\text{mean}}$ $P=0.38$) when compared to $^{68}$Ga-RM2 uptake in the same areas (Table 2). The correlation coefficients between the uptake of the two tracers were $r=0.62$ ($P<0.001$) for $\text{SUV}_{\text{max}}$ and $r=0.54$ ($P<0.001$) for $\text{SUV}_{\text{mean}}$.

The ratio of focal uptake to background for $^{68}$Ga-PSMA showed statistically higher values than those of $^{68}$Ga-RM2 ($F/N$ ratio by $\text{SUV}_{\text{max}}$: $5.9 \pm 4.6$, $P<0.003$, $F/N$ ratio by
DISCUSSION

In the present study, we compared the biodistribution of $^{68}$Ga-PSMA and $^{68}$Ga-RM2 in the same patients with BCRPC. $^{68}$Ga-PSMA showed high accumulation in the lacrimal glands, parotid glands, the submandibular glands, small intestine, kidneys and bladder. $^{68}$Ga-RM2 showed high accumulation in the pancreas and bladder. To our knowledge this is the first study directly comparing the biodistribution of these PET tracers in normal tissues and outside the expected physiologic biodistribution in patients with BCRPC. $^{68}$Ga-PSMA has renal and hepato-biliary clearance, while $^{68}$Ga-RM2 has mainly renal clearance with minimal hepato-biliary clearance. This may have implications for detection of abdominal and pelvic lesions, as bowel uptake and/or clearance may mask small lesions. $^{68}$Ga-PSMA and $^{68}$Ga-RM2 had similar localization in lymph nodes, seminal vesicles and bone marrow, but the slower clearance of the latter from major vessels blood pool resulted in less conspicuous uptake in mediastinal and supraclavicular lymph nodes. Conversely, $^{68}$Ga-PSMA uptake and/or clearance in the bowel made small retroperitoneal lymph nodes

SUV$_{\text{mean}}$ $p<0.02$) (Table 3). Representative images are shown in Figs. 2-4 and Supplemental Figs. 1 and 2. Data from clinical follow-up is shown in Table 3.
less conspicuous than on $^{68}$Ga-RM2 in 2 participants. There was only one patient with negative $^{68}$Ga-RM2 and focal uptake in 1 pelvic lymph node and seminal vesicle on $^{68}$Ga-PSMA, but the scans were obtained 54 days apart.

Previous work showed PSMA receptor expression in kidneys and spleen, while GRPR expression in primarily in the pancreas (22). Our results are consistent with the uptake pattern that was previously reported for both $^{68}$Ga-RM2 and $^{68}$Ga-PSMA (15, 23).

$^{68}$Ga-RM2 and $^{68}$Ga-PSMA target different biological processes; therefore, understanding how these two tracers behave in patients with BCRPC is critical for finding the best patient management options for this clinical scenario, as neither is expected to be 100% sensitive or specific. We expect that certain patients will benefit from having both scans done.

The detection rates of $^{68}$Ga-PSMA for recurrent disease were 96.8% when PSA levels were ≥2 ng/ml and 57.9% for PSA of 0.2 to <0.5 ng/mL in a study evaluating 248 patients with BCR after radical prostatectomy. The detection rates increased with higher Gleason scores and were not influenced by antiandrogen therapy (24). Several studies showed superior performance of $^{68}$Ga-PSMA PET/CT when compared $^{18}$F-Choline (25, 26).

Sensitivity of $^{68}$Ga-RM2 performed on a subsector analysis of whole prostatectomy
samples resulted in 88% for the detection of primary prostate cancer and 70% for the
detection of lymph node metastases (27). Early work indicated that GRPr are primarily
expressed in early and androgen-dependent prostate tumors; however, others have
reported high GRPr expression in metastatic disease as well (28). $^{68}$Ga-RM2 targets GRPr
and therefore appears to have potential for detecting prostate cancer lesions that generally
grow slowly and are difficult to detect with conventional imaging in the biochemical
recurrence scenario. Our study showed similar, but not identical patterns of uptake in
suspected lesions for $^{68}$Ga-RM2 and $^{68}$Ga-PSMA. This may be due to heterogeneous
expression of PSMA and GRPr, or to a partial loss of expression of either of these
receptors.

One of the limitations of our study is the small number of patients, but this is
common for pilot studies done under RDRC approval. Another limitation is the lack of
correlation with pathology results for all patients. Given that the protocol was done under
RDRC approval, only basic information on biodistribution and radiopharmaceutical
localization were allowed to be collected. The RDRC mechanism does not allow for
immediate therapeutic, diagnostic or similar purposes or to determine the safety and
effectiveness of a radioactive drug in humans. However, given the encouraging preliminary
results of this pilot study, we plan to evaluate $^{68}$Ga-PSMA and $^{68}$Ga-RM2 further in a larger cohort of patients with BCRPC, including patients with PSA of 0.5 ng/ml and higher. Lastly, due to funding resources, patients were imaged with PET/MRI ($^{68}$Ga-RM2 studies) or PET/CT ($^{68}$Ga-PSMA studies). This may be seen as a bias toward $^{68}$Ga-RM2 given the superior detectors and image quality in the PET/MRI scanner (21).

**CONCLUSION**

The a priori expectation from previous studies was that $^{68}$Ga-PSMA would have performed much better than $^{68}$Ga-RM-2 in such a BCRPC cohort. The findings here indicate that additional work is needed to understand the expression of PSMA and GRPr in different types of prostate cancer. One may therefore imagine personalizing biomarker assessments in the future for patients with prostate cancer. This study also highlights the significant advances in $^{68}$Ga-labeled PET tracers in recent years and the need for consistent regulatory policies to allow easy access to such important radiotracers, including $^{68}$Ga-RM2.
ACKNOWLEDGMENTS

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**Figure 1:** $SUV_{\text{max}}$ of $^{68}$Ga-PSMA and $^{68}$Ga-RM2 in all the analyzed normal tissues.
**Figure 2:** Maximum intensity projection (MIP) images of $^{68}$Ga-RM2 and $^{68}$Ga-PSMA in each of the 7 enrolled patients.
**Figure 3:** 83-year-old man with history of Gleason 5+4 prostate cancer, treated with radiation therapy and androgen blockade, presenting with PSA of 18.7 and non-contributory conventional imaging. MIP images of $^{68}$Ga-RM2 and $^{68}$Ga-PSMA, as well as axial PET show focal uptake corresponding to subcentimeter lymph nodes on MRI and CT, respectively.
Figure 4: 67-year-old man with history of Gleason 3+3 prostate cancer, treated with radiation therapy and androgen blockade, presenting with PSA of 6.7 and non-contributory conventional imaging. $^{68}$Ga-RM2 is negative, while MIP image from $^{68}$Ga-PSMA, as well as axial PET show focal uptake corresponding to a subcentimeter pelvic lymph node and the right seminal vesicle on CT. These were biopsy proven to represent metastatic disease.
<table>
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<th>Patient No</th>
<th>Age</th>
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<th>Gleason score</th>
<th>PSA</th>
<th>Treatment</th>
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<th>$^{68}$Ga-RM2 PET</th>
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<tr>
<td>1</td>
<td>83</td>
<td>II</td>
<td>5+4</td>
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<tr>
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<td>Retroperitoneal LNs, Pelvic LN</td>
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<td>Mediastinal LNs, Retroperitoneal LNs, Pelvic LNs, multiple bone lesions</td>
<td>Mediastinal LNs, Retroperitoneal LNs, Pelvic LNs, multiple bone lesions</td>
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Radiation therapy: RT, Hormone therapy: HT, LN: lymph node
Table 2: $^{68}$Ga-PSMA and $^{68}$Ga-RM2 uptake outside the expected physiologic biodistribution (shown as mean ± SD, range)

<table>
<thead>
<tr>
<th>Index</th>
<th>$^{68}$Ga-PSMA</th>
<th>$^{68}$Ga-RM2</th>
<th>$P$ value</th>
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<tbody>
<tr>
<td>$\text{SUV}_{\text{max}}$</td>
<td>12.4 ± 7.1 (4.1 – 43.6)</td>
<td>13.2 ± 8.0 (2.5 - 33.5)</td>
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<tr>
<td>$\text{SUV}_{\text{mean}}$</td>
<td>7.1 ± 4.0 (2.0 - 14.4)</td>
<td>7.6 ± 3.8 (2.0 - 14.4)</td>
<td>0.38</td>
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<td>Focal uptake ($\text{SUV}_{\text{max}}$/background (F/N) ratio</td>
<td>10.4 ± 9.3 (2.3 - 42.8)</td>
<td>5.9 ± 4.6 (1.2 - 18.8)</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Focal uptake ($\text{SUV}_{\text{mean}}$/background (F/N) ratio</td>
<td>9.2 ± 7.3 (2.4 - 40.4)</td>
<td>5.2 ± 3.5 (1.6 - 12.8)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Patient No</td>
<td>Results of follow-up</td>
<td></td>
<td></td>
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<tr>
<td>1</td>
<td>Started Casodex and Lupron, PSA decreased from 18.7 to 2.53; follow-up MRI showed decreased size and number of retroperitoneal lymph nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Chose no treatment, PSA increased from 8.6 to 10.9</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>Started Casodex and Lupron, PSA decreased from 36.4 to 2.2</td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td>No treatment yet, PSA increased from 6.7 to 12.1; biopsy results: 12 prostate cores negative, right vas deferens showed metastatic adenocarcinoma Gleason 4+3, 15% of the core</td>
<td></td>
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<tr>
<td>5</td>
<td>No treatment yet, PSA increased from 8.53 to 10.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Started Casodex, PSA decreased from 7.36 to 0.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Started Casodex, PSA decreased from 18.2 to 2.5</td>
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</tr>
</tbody>
</table>
Pilot Comparison of $^{68}$Ga-RM2 PET and $^{68}$Ga-PSMA PET in Patients with Biochemically Recurrent Prostate Cancer

Ryogo Minamimoto, Steven Hancock, Bernadette Schneider, Frederick Chin, Mehran Jamali, Andreas Markus Loening, Shreyas Vasanawala, Sanjiv Sam Gambhir and Andrei Iagaru

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