

Original Article

Bladder activity of different PSMA PET radioligands and impact of furosemide

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Abstract: Prostate-specific membrane antigen (PSMA) radioligands used for PET imaging of prostate cancer (PCa) have variable urinary excretion. The prostate bed region is an important site of disease localization where intense bladder activity may obscure lesion detection. We performed a comparative analysis of bladder activity across different PSMA radioligands and investigated the impact of furosemide administration on reducing bladder activity. We analyzed the PSMA PET/CT images of patients with PCa who were imaged with ^{68}Ga -PSMA-11 with/without 20 mg furosemide, ^{18}F -PSMA-1007, ^{18}F -DCFPyL, ^{18}F -rhPSMA-7.3 with/without 20 mg furosemide. We determined and compared bladder volume and bladder activity level using mean and maximum standardized uptake values (SUV_{mean} and SUV_{max}) between PET scans obtained with the different PSMA radioligands using an ANOVA or Kruskal-Wallis test, as appropriate. We also determined the association between the bladder activity level versus bladder volume using Spearman correlation. 210 PSMA PET/CT studies were reviewed, including 50, 20, 20, 28, 42, and 50 completed with ^{18}F -PSMA-1007 without furosemide, ^{18}F -rhPSMA-7.3 without furosemide, ^{18}F -rhPSMA-7.3 with furosemide, ^{68}Ga -PSMA-11 without furosemide, ^{68}Ga -PSMA-11 with furosemide, and ^{18}F -DCFPyL without furosemide, respectively. The median bladder SUV_{mean} (range) without furosemide were: 1.75 (0.4-6.4) [^{18}F -PSMA-1007], 10.00 (1.9-140.0) [^{18}F -rhPSMA-7.3], 15.92 (2.0-106.0) [^{68}Ga -PSMA-11], and 25.7 (7.9-87.6) [^{18}F -DCFPyL], ($P < 0.001$). With 20 mg furosemide co-administered with the radiotracer, there was a significant decline in bladder activity level (median SUV_{mean} of 10.00 (1.9-140.0) to 2.95 (0.8-17.6) for ^{18}F -rhPSMA-7.3 and 15.92 (2.0-106.0) to 10.21 (2.6-281.3) for ^{68}Ga -PSMA-11 and a significant increase in bladder volume, $P < 0.05$. There was a significant negative correlation between bladder SUV_{max} and bladder volume for the entire cohort, $P = 0.008$, $r = -0.181$. There is variation in the bladder radioactivity between the different PSMA radioligands for PCa PET imaging, with ^{18}F -PSMA-1007 demonstrating the lowest, ^{68}Ga -PSMA-11 and ^{18}F -DCFPyL the highest, and ^{18}F -rhPSMA-7.3 intermediate bladder activity level. Administration of 20 mg furosemide produces a significant reduction in bladder activity and an increase in bladder volume. With 20 mg furosemide, bladder activity of ^{18}F -rhPSMA-7.3 approaches that of ^{18}F -PSMA-1007.

Keywords: Bladder activity, furosemide, ^{18}F -PSMA-1007, ^{68}Ga -PSMA-11, ^{18}F -DCFPyL, ^{18}F -rhPSMA-7.3

Introduction

Prostate-specific membrane antigen (PSMA), a trans-membrane glycoprotein with a large extracellular domain, is overexpressed in most prostate cancer cells, making it a suitable target for prostate cancer (PCa) imaging and therapy [1]. Several ligands targeting the PSMA extracellular domain have been developed and complexed with diagnostic radionuclides for positron emission tomography (PET) imaging of PCa. The best-characterized diagnostic PSMA radioligands for PET imaging of PCa include ^{68}Ga -PSMA-11, ^{18}F -DCFPyL, ^{18}F -rhPSMA-7.3, and ^{18}F -PSMA-1007. The diagnostic performance and superiority of ^{68}Ga -PSMA-11, ^{18}F -DCFPyL, and ^{18}F -rhPSMA-7.3 over conventional imaging in PCa initial staging and recurrence detection have been confirmed in several phase III trials [2-8]. PSMA-targeted imaging is currently the diagnostic imaging of choice in PCa management.

All PSMA radioligands are excreted in the urine to a varying extent. The proximity of the prostate gland to the urinary bladder presents a challenge due to the potential of urinary bladder activity from the excreted radiotracer

obscuring the visualization of PCa lesions adjacent to bladder luminal activity. This challenge is particularly important in early PCa recurrence post-prostatectomy, where most PCa recurrence occur as a small lesion in the prostate bed where visualization may be obscured by bladder activity. Detection of local prostate gland/bed recurrence contributes significantly to the overall detection rate of PSMA-targeted PET imaging of PCa at all PSA levels [9, 10]. The closer the lesion is to the urinary bladder with high urine activity, the less likely it is to be detected with PSMA-targeted PET imaging [11].

In phase III trials, PSMA-targeted PET imaging has an excellent lesion detection rate with increasing PSA levels [2, 6, 7]. At PSA below 0.5 ng/mL, detection rates range between 38% and 64% [2, 6, 7], indicating that the approved PSMA radioligands will fail to localize the site of PCa recurrence in 1/3rd to 2/3rd of patients with PSA below 0.5 ng/mL. Therefore, there is a clinical need for strategies to improve PCa lesion detection, especially at low PSA. Also, it is important to understand the differences in biokinetics of the different PSMA radioligands viz-a-viz their urinary excretion rate and explore avenues

to utilize this understanding in interpreting PSMA PET findings and selecting the appropriate PSMA radioligand for a given clinical scenario.

Due to the critical impact of bladder activity level on the visualization of PCa lesions in the prostate bed, several avenues aimed at reducing urinary activity level at the time of PET imaging have been explored, including furosemide administration, early imaging, delayed imaging, dynamic imaging, and dual-timepoint imaging [12-14]. In our centers, we have real-world experience with several PSMA radiotracers and strategies to ameliorate bladder activity in both clinical and research scenarios. In this retrospective study, our aim is to compare bladder activity for these radiotracers and mitigation strategies.

Methods

Patients

This is a retrospective analysis of PSMA PET/CT imaging performed at Emory University in patients who received ^{68}Ga -PSMA-11 with 20 mg intravenous furosemide for PET/CT imaging in the EMPIRE-2 trial (NCT03762759), ^{68}Ga -PSMA-11 without furosemide and ^{18}F -DCFPyL without furosemide as standard of care PET/CT imaging of prostate cancer, and ^{18}F -rhPSMA-7.3 with and without furosemide in a phase II trial (NCT05779943), which is reported separately for an inpatient comparison for ^{18}F -rhPSMA-7.3 alone. The clinical ^{68}Ga -PSMA-11 without furosemide and ^{18}F -DCFPyL without furosemide scans included in this study were randomly selected from cohorts of PCa patients who received standard-of-care PSMA PET imaging until August 2023. This study also retrospectively analyzed ^{18}F -PSMA-1007 PET/CT images of patients with prostate cancer imaged at the Aga Khan University Hospital in Nairobi, Kenya between June and December 2023. Patients were included if they were 18 years and above and had a technically adequate PSMA radioligand PET/CT for initial staging or biochemical recurrence of prostate cancer. Exclusion criteria included PSMA radioligand PET/CT imaging for non-prostate cancers, patients with a urethral catheter or percutaneous nephrostomy tube in place, patients with renal failure defined as estimated glomerular filtration rate (eGFR) of <60 mL/min/m², and patients with prior urinary diversion surgery. The institutional review board of the respective institutions approved this study and granted an informed consent waiver due to the retrospective nature of this work.

PSMA radioligand PET/CT imaging and image analysis

PSMA radioligand PET/CT imaging was performed according to published guidelines/procedure standards [15]. Briefly, no special patient preparation was observed. All patients received intravenous radiotracer administration followed by PET/CT imaging after an approximate 60-minute uptake period. For the diuretic-enhanced

^{68}Ga -PSMA-11 and ^{18}F -rhPSMA-7.3 PET/CT, 20 mg intravenous furosemide was co-administered with the radiotracer. All patients who received furosemide-augmented PSMA PET scans were encouraged to drink at least 500 mL of oral fluid during the uptake period. The patients were encouraged to void during the uptake period but asked to refrain from voiding 15 minutes before the commencement of PET/CT imaging to allow for adequate bladder distention.

Imaging was performed on one of GE Discovery 690 (GE Healthcare, Milwaukee, WI), Siemens Biograph mCT, Siemens Vision 600 (Siemens Medical Solution USA, Inc.), or UMI 550 (United Imaging Healthcare Co., Ltd., Houston, TX) within Emory Healthcare and GE Discovery MI PET/CT system (GE Healthcare, Milwaukee, WI) at Aga Khan University Hospital in Nairobi. Following CT imaging, thigh-to-vertex PET imaging was acquired in 3D mode at 3 minutes per bed position. The PET data was corrected for randoms, scatter, dead time, and attenuation. Image reconstruction was done with the OSEM iterative reconstruction algorithm.

For each PSMA PET/CT study, a volume of interest (VOI) was drawn within the bladder to obtain the mean and maximum standardized uptake values (SUV_{mean} and SUV_{max}) of bladder radioactivity level. Bladder volume was also determined.

Statistical analysis

Descriptive statistics were generated for all patient characteristics. Frequency and percentage were reported for categorical variables. Mean (standard deviation, SD) and median (range or interquartile range, IQR) were reported for numeric variables. We assessed the normality of the data distribution using the Kolmogorov-Smirnov test. The clinical characteristics of patients who received the different PSMA radioligands for PET imaging were compared using an ANOVA or Kruskal-Wallis test, as appropriate. The correlation between bladder SUV_{max} and the bladder volume was compared using Pearson's correlation test or Spearman's correlation test, as appropriate for the entire cohort and separately for each PSMA radioligand group. Similarly, the correlation between SUV_{mean} and the variables was also tested. Variables that did not meet the Gaussian assumption were log-transformed. Bladder volume, SUV_{max} , SUV_{mean} were compared between the ^{18}F -rhPSMA-7.3 with furosemide and ^{18}F -rhPSMA-7.3 without furosemide using a paired t-test. Similarly, ^{68}Ga -PSMA-11 with furosemide and ^{68}Ga -PSMA-11 without furosemide cohorts were compared for the sample variables using an ANOVA or Kruskal-Wallis's test, as appropriate.

Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC), and statistical significance was assessed at the 0.05 level.

Table 1. Comparison of bladder activity and volume across PET imaging acquired with different PSMA radioligands

Covariate	GaPSMA_Furo N=42	GaPSMA_noFuro N=28	PSMA-1007 N=50	DCFPyL N=50	rhPSMA_Furo N=20	rhPSMA_noFuro N=20	P-value
SUV _{max}							<0.001
Median	17.29	41.26	2.60	51.42	4.20	13.35	
Min	4.65	5.23	0.70	15.19	1.70	3.90	
Max	514.65	194.37	11.60	251.81	19.80	165.40	
SUV _{mean}							<0.001
Median	10.21	15.92	1.75	25.70	2.95	10.00	
Min	2.63	2.04	0.40	7.91	0.80	1.90	
Max	281.33	106.00	6.40	87.60	17.60	140.00	
Bladder volume (mL)							<0.001
Median	167.87	95.35	71.50	106.67	296.50	94.75	
Min	72.95	9.70	20.00	9.65	59.90	18.10	
Max	518.62	338.06	236.00	565.68	630.00	717.00	

GaPSMA_Furo: ⁶⁸Ga-PSMA-11 with furosemide; GaPSMA_noFuro: ⁶⁸Ga-PSMA-11 without furosemide; PSMA-1007: ¹⁸F-PSMA-1007 without furosemide; DCFPyL: ¹⁸F-DCFPyL without furosemide; rhPSMA_Furo: ¹⁸F-rhPSMA-7.3 with furosemide; rhPSMA_noFuro: ¹⁸F-rhPSMA-7.3 without furosemide.



Figure 1. MIP images with similar windowing level showing relative bladder activity of different PSMA radioligands on PET imaging acquired with or without furosemide administration.

Results

A total of 210 studies were included in this analysis, including 50, 20, 20, 28, 42, and 50 PSMA PET/CT studies done with ¹⁸F-PSMA-1007 without furosemide, ¹⁸F-rhPSMA-7.3 without furosemide, ¹⁸F-rhPSMA-with furosemide, ⁶⁸Ga-PSMA-11 without furosemide, ⁶⁸Ga-PSMA-11 with furosemide, and ¹⁸F-DCFPyL without furosemide, respectively. There was a significant difference in bladder activity measured by SUV_{mean} and SUV_{max} across the six PSMA PET/CT subgroups considered, P<0.001 (Table 1; Figure 1). ¹⁸F-PSMA-1007 without furosemide demonstrated the lowest SUV_{mean} and SUV_{max} (median SUV_{mean} and median SUV_{max} of 1.75 [range =0.4-6.4] and 2.60 [range =0.7-11.6], respectively), which was closely followed by ¹⁸F-rhPSMA-7.3 with furosemide with median SUV_{mean} (range) and median SUV_{max} (range) of 2.95 (0.8-

17.6) and 4.2 (1.7-19.8), respectively. ¹⁸F-DCFPyL without furosemide and ⁶⁸Ga-PSMA-11 without furosemide had the highest bladder median SUV_{mean} (25.70 [range: 7.9-87.6] and 15.92 [range: 2.0-106.0], respectively) and median SUV_{max} (51.42 [range: 15.2-251.8] and 41.26 [range: 5.2-194.4], respectively). Bladder activity was similar between ¹⁸F-rhPSMA-7.3 without furosemide and ⁶⁸Ga-PSMA-11 with furosemide with intermediate levels of median SUV_{mean} (10.00 [range: 1.9-140.0] and 10.21 [range: 2.6-281.3], respectively) and median SUV_{max} (13.35 [range: 3.9-165.4] and 17.23 [range: 4.7-514.7], respectively). Bladder volume was also significantly different across PSMA PET subgroups, with the highest bladder volume recorded for PSMA PET/CT done with furosemide administration (Table 1). Bladder activity was significantly lower, and bladder volume was significantly higher in ⁶⁸Ga-PSMA-11 with furosemide and ¹⁸F-rhPSMA-7.3

Table 2. Comparison of ⁶⁸Ga-PSMA-11 PET with and without furosemide

Covariate	Statistics	Level	Group		P-value
			⁶⁸ Ga-PSMA-11 with furosemide N=42	⁶⁸ Ga-PSMA-11 without furosemide N=28	
SUV _{max}	N		42	28	<0.001
	Mean		30.82	52.82	
	Median		17.29	41.26	
	Min		4.65	5.23	
	Max		514.65	194.37	
SUV _{mean}	N		42	28	0.035
	Mean		18.16	23.77	
	Median		10.21	15.92	
	Min		2.63	2.04	
	Max		281.33	106	
Bladder Volume (mL)	N		42	28	<0.001
	Mean		183.46	103.29	
	Median		167.87	95.35	
	Min		72.95	9.7	
	Max		518.62	338.06	
	Std Dev		94.21	78.82	

Table 3. Comparison of ¹⁸F-rhPSMA-7.3 with furosemide and without furosemide

Covariate	Statistics	Group		P-value
		¹⁸ F-rhPSMA-7.3 with furosemide N=20	¹⁸ F-rhPSMA-7.3 without furosemide N=20	
SUV _{max}	N	20	20	0.014
	Mean	5.21	26.43	
	Median	4.2	13.35	
	Min	1.7	3.9	
	Max	19.8	165.4	
SUV _{mean}	N	20	20	0.017
	Mean	3.9	20.64	
	Median	2.95	10	
	Min	0.8	1.9	
	Max	17.6	140	
Bladder Volume (mL)	N	20	20	0.003
	Mean	300.22	147.69	
	Median	296.5	94.75	
	Min	59.9	18.1	
	Max	630	717	
	Std Dev	151.3	172.31	

with furosemide compared with ⁶⁸Ga-PSMA-11 without furosemide and ¹⁸F-rhPSMA-7.3 without furosemide (Tables 2 and 3).

Despite their high diagnostic performance for staging and re-staging of PCa, the urinary excretion of most PSMA radioligands presents a challenge, potentially limiting the

Correlation between bladder activity versus bladder volume

Considering all PSMA studies, regardless of the type of PSMA radioligand, there was a significant negative correlation between bladder SUV_{max} and bladder volume and a trend towards significance between bladder SUV_{mean} and bladder volume (Table 4). At all subgroup levels, there was either a significant negative correlation or a trend toward statistical significance between bladder activity (measured by SUV_{max} and SUV_{mean}) and bladder volume for ¹⁸F-PSMA-1007 without furosemide, ¹⁸F-DCFPyL without furosemide, ¹⁸F-rhPSMA-7.3 with furosemide, and ¹⁸F-rhPSMA-7.3 without furosemide. There was no significant association between bladder activity and bladder volume for ⁶⁸Ga-PSMA-11 either with or without furosemide (Table 4).

Discussion

We performed a retrospective analysis of bladder activity on PET imaging obtained with four PSMA radioligands utilized in our clinical and research programs; ⁶⁸Ga-PSMA-11, ¹⁸F-DCFPyL, ¹⁸F-PSMA-1007, and ¹⁸F-rhPSMA-7.3. We also have cohorts imaged with ⁶⁸Ga-PSMA-11 and ¹⁸F-rhPSMA-7.3 who were imaged with and without use of diuretic.

We found that ¹⁸F-PSMA-1007 demonstrated the lowest bladder activity with a median bladder SUV_{mean} of 1.75 [range: 0.4-6.4] compared to 10.00 (1.9-140), 15.92 (2.0-106.0), and 25.7 (7.9-87.6) for ¹⁸F-rhPSMA-7.3, ⁶⁸Ga-PSMA-11, and ¹⁸F-DCFPyL, respectively. Twenty mg furosemide co-administered with the radiotracer led to a 71% and 36% reduction in bladder activity of ¹⁸F-rhPSMA-7.3 and ⁶⁸Ga-PSMA-11 with resultant median SUV_{mean} of 2.95 and 10.21, respectively. As expected, furosemide administration led to increased bladder volume, and the bladder volume, in turn, demonstrated an inverse relationship with bladder activity.

Table 4. Correlation between bladder activity versus bladder volume

Variable	N	Bladder SUV _{mean}		Bladder SUV _{max}	
		<i>r</i>	<i>p-value</i>	<i>r</i>	<i>p-value</i>
All PSMA studies	210				
Bladder volume		-0.135	0.051	-0.181	0.008
⁶⁸ Ga-PSMA-11 with furosemide	42				
Bladder volume (mL)		-0.065	0.682	-0.099	0.531
⁶⁸ Ga-PSMA-11 without furosemide	28				
Bladder volume (mL)		-0.163	0.409	-0.339	0.077
¹⁸ F-PSMA-1007 without furosemide	50				
Bladder volume (mL)		-0.410	0.003	-0.340	0.016
¹⁸ F-DCFPyL without furosemide	50				
Bladder volume (mL)		-0.277	0.052	-0.537	<0.001
¹⁸ F-rhPSMA-7.3 with furosemide	20				
Bladder volume (mL)		-0.550	0.012	-0.536	0.015
¹⁸ F-rhPSMA-7.3 without furosemide	20				
Bladder volume (mL)		-0.561	0.010	-0.603	0.005

r: Spearman Correlation Coefficient.

localization of small lesions with subtle radiotracer avidity in the prostate bed as detection of recurrent disease on PET is adversely influenced by proximity to the bladder [11]. With the availability of multiple PSMA radioligands for routine clinical use, it is important to understand the nuances in their biodistribution and how these may affect lesion detection. Our results are therefore important in that we present data demonstrating the differences in bladder activity levels of different PSMA radioligand and the influence of furosemide administration.

The values we report for ¹⁸F-PSMA-1007 with a median bladder SUV_{mean} of 1.75 (range = 0.4-6.4), was similar to a median SUV_{mean} of 3.08 (IQR = 1.66-4.74) at 60 minutes post-injection without diuresis reported by Rahbar et al. [16]. ¹⁸F-PSMA-1007 has an inherent low rate of urinary excretion among common PSMA radioligands [17]. In the biodistribution study of ¹⁸F-PSMA-1007 by Giesel et al., 1.2% of the administered radiotracer was excreted into the urinary bladder within the first 2 hours post-tracer administration [18]. This is lower than the 2-hour bladder excretory rates of 7.2% for ¹⁸F-rhPSMA-7.3 and 11% for ¹⁸F-DCFPyL and ⁶⁸Ga-PSMA-11, respectively [19-21]. However, ¹⁸F-PSMA-1007 is not FDA-approved and is unavailable for routine clinical use in the United States.

¹⁸F-rhPSMA-7.3 has the next lowest bladder activity with a median SUV_{mean} of 10 (range = 1.9-140) but which may be reduced to a median SUV_{mean} of 2.95 (range = 0.8-17.6) by the use of 20 mg furosemide at the time of radiotracer administration. With this diuretic strategy, the FDA-approved ¹⁸F-rhPSMA-7.3 bladder activity approaches that of ¹⁸F-PSMA-1007. This median SUV_{mean} of the non-diuretic cohort in our study of 10.00 was similar to the median SUV_{mean} of 12.5 (0.7-887) in the LIGHTHOUSE and SPOTLIGHT trial cohorts [22].

⁶⁸Ga-PSMA-11 without diuresis had a median SUV_{mean} of 15.92 and was reduced with furosemide to 10.21 in our series. In the study by Uprimny et al., a group who have done extensive work with forced diuresis with ⁶⁸Ga-PSMA-11, 20 mg intravenous furosemide reduced bladder activity from a median SUV_{mean} of 41.9 to 5.3 [23]. In the study by Uprimny et al., the median SUV_{mean} of ⁶⁸Ga-PSMA-11 without furosemide was higher, and the median SUV_{mean} of ⁶⁸Ga-PSMA-11 with furosemide was lower than in our study. These differences may be due to variance in patient population, including renal function and chronic diuretic use, which were not controlled for in our analysis. Most importantly the lower post-diuretic activity in the study by Uprimny is likely due to more robust forced diuresis utilizing 500 ml IV saline which was also reported in a separate manuscript [24] to result in 40% urinary urgency as compared to our ⁶⁸Ga-PSMA-11 diuretic protocol without IV saline, which was overall well tolerated.

¹⁸F-DCFPyL had the highest median SUV_{mean} of 25.7 on our study. We could not find published data on median SUV_{mean} on this radiotracer, but median SUV_{max} was reported to be 61.7 in the study by Donswijk et al. and 79.32 by Giesel et al. which is similar to the median SUV_{max} in our series of 51.42 [17, 25]. Ferreira and co-workers reported a mean SUV_{peak} of 57.3, which is also not dissimilar to our findings of a mean SUV_{max} of 66.07, as SUV_{peak} would have slightly lower intensity [26]. Yet, the higher the baseline bladder activity, the more difficult it may be to reduce the activity to less interfering levels with a diuretic, as reported by numerous authors [14, 25]. It has been our experience that diuresis is not widely utilized with ¹⁸F-DCFPyL, including in our center, and therefore, we do not have clinical data on its use with furosemide. Because ⁶⁸Ga-PSMA-11 baseline activity is significantly greater than that of ¹⁸F-rhPSMA-7.3, there was only a 36% reduction with the use of furosemide co-administered with ⁶⁸Ga-PSMA-11 versus a 71% reduction with the use of a diuretic workflow with ¹⁸F-rhPSMA-7.3.

We hypothesized that bladder distention may influence bladder activity levels due to the relative dilution of the radiotracer. Considering all 210 included studies, bladder volume showed a negative association with bladder activity, regardless of furosemide use. The negative association between bladder activity and bladder volume was most pronounced for ¹⁸F-rhPSMA-7.3 with/without furosemide and, to a lesser extent, for ¹⁸F-DCFPyL and ¹⁸F-PSMA-1007 (Table 4). We found no significant association between the bladder activity of ⁶⁸Ga-PSMA-11 administered with/without furosemide and bladder volume. The reason for this lack of significant association is

not clear at present. We speculate that this may be related to the less pronounced furosemide-induced bladder activity reduction with ^{68}Ga -PSMA-11 compared to ^{18}F -rhPSMA-7.3. Other factors, including patient-related and radioligand-related factors (such as differences in protein binding and tracer kinetics), may also play a role. A higher bladder volume of dilute urine (less activity) not only reduces the obscuring effect of bladder activity but also allows the urinary bladder to lift away from the prostate bed, allowing better visualization of the prostate bed or intraprostatic lesions. As shown in the study of Freitag et al., lesions closest to the urinary bladder stand the highest risk of being missed on PSMA PET imaging [11]. A full bladder with a lower radioactivity level is also desirable as it mimics the bladder condition during radiotherapy planning, allowing for more accurate PSMA PET and CT simulation image fusion for radiotherapy planning.

Our study has many strengths, including evaluating multiple PSMA radioligands in real world clinical and clinical trial use for PCa staging and restaging. We also investigated the association between bladder volume and bladder activity of these PSMA. Limitations of our study include a relatively heterogenous cohort of clinical and research studies. Three of the radiotracers, ^{18}F -rhPSMA-7.3, ^{18}F -DCFPyL, and ^{68}Ga -PSMA-11 were utilized at multiple hospitals at one university system, while ^{18}F -PSMA-1007 data was from only one hospital at a different university. Differences in tracer biokinetics across patients, which are difficult to eliminate in studies of this design type, may also introduce variability in bladder activity. Diuresis was only utilized with ^{68}Ga -PSMA-11 and rhPSMA-7.3, as diuresis was not necessary with ^{18}F -PSMA-1007 and considered futile with ^{18}F -DCFPyL. Our analysis did not investigate the impact of bladder activity level on lesion detection, as this has been reported elsewhere [27, 28], suggesting a lower bladder activity level improves lesion detection in the prostate bed region in a subset of patients.

Conclusion

There is variation in the bladder activity between the different PSMA radioligands. ^{18}F -PSMA-1007 has the lowest baseline bladder activity level, intermediate for ^{18}F -rhPSMA-7.3, while bladder activity is highest for ^{68}Ga -PSMA-11 and ^{18}F -DCFPyL. Administration of 20 mg furosemide produces a higher reduction in bladder activity for ^{18}F -rhPSMA-7.3 versus ^{68}Ga -PSMA-11. In fact, co-administered with 20 mg furosemide, bladder activity of ^{18}F -rhPSMA-7.3 approaches that of baseline ^{18}F -PSMA-1007. Finally, as an independent factor, there is an inverse relationship between bladder volume and bladder activity for most PSMA radioligands such that bladder activity reduces with increasing bladder volume.

Disclosure of conflict of interest

None.

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