

Article

Head-to-Head Comparison of [68Ga]Ga-PSMA-11 PET Interpreted with Non-Contrast CT Versus Excretory-Phase CT Urography in Biochemical Recurrence of Prostate Cancer

Vicky Betch-Antar ^{1,*}, Juan J. Rosales ¹, Fernando Mínguez ¹, Marta Romera ¹, Luis Fuertes ², Fernando Díez-Caballero ³, Bernardino Miñana-López ³, Rafael Martínez-Monge ², Edgar F. Guillen ¹ and Macarena Rodríguez-Fraile ¹

¹ Department of Nuclear Medicine, Clínica Universidad de Navarra, 31008 Navarra, Spain; mromerac@unav.es (M.R.); mrodriguez@unav.es (M.R.-F.)

² Department of Radiation Oncology, Clínica Universidad de Navarra, 31008 Navarra, Spain

³ Department of Urology, Clínica Universidad de Navarra, 31008 Navarra, Spain

* Correspondence: vbetech@fivo.org; Tel.: +34-961114000 (ext. 5254)

† Current address: Department of Nuclear Medicine, Instituto Valenciano de Oncología, 46009 Valencia, Spain.

‡ The work was performed at Clínica Universidad de Navarra prior to the corresponding author's move to Instituto Valenciano de Oncología.

Simple Summary

[68Ga]Ga-PSMA-11 PET/CT is widely used to evaluate biochemical recurrence after radical prostatectomy. However, physiological urinary tracer excretion may hamper the assessment of the surgical bed and peri-ureteric lymph nodes. This study evaluated whether adding an excretory-phase CT urography acquisition improves interpretation by facilitating ureteral visualization. CT urography increased reader confidence, reduced equivocal surgical-bed findings, and changed peri-ureteric nodal classification in selected patients, supporting its role as a complementary tool in this clinical setting.

Abstract

Background: This study aimed to determine whether incorporating radiologic contrast during the excretory (urographic) phase enhances the detection of recurrence on [68Ga]Ga-PSMA-11 PET/CT in patients with biochemical relapse (BCR) following radical prostatectomy (RP). **Methods:** A single-center retrospective analysis included 43 men with BCR after RP who underwent [68Ga]Ga-PSMA-11 PET/CT. Each patient underwent two comparative assessments. In the first assessment, whole-body PET images acquired at 60 min post-injection were fused with the non-contrast CT from early dynamic pelvic imaging (PET/CTd), and local recurrence and pelvic nodal involvement were evaluated according to PROMISE V2 and E-PSMA frameworks by two blinded readers. In the second assessment, the same PET dataset was fused with the excretory-phase CT urography (CT-U) obtained during the same imaging session at 60 min post-injection, and the same parameters were re-evaluated. Endpoints included surgical-bed classification, peri-ureteric nodal status, reader confidence, ureter visualization/opacification, and interpretation time. Inter- and intra-observer agreement was assessed, and discrepancies were resolved by consensus. **Results:** Surgical-bed positivity decreased from 12/43 (27.9%) on PET/CTd to 5/43 (11.6%) on PET/CT-U, leading to reclassification in seven patients ($p = 0.016$). Reader confidence improved significantly in five cases ($p < 0.005$). Peri-ureteric nodal status was changed in four patients (two positive-to-negative and two negative-to-positive), with overall positivity unchanged (5/43 vs. 5/43; $p = 1.000$). Ureter visualization improved markedly



Academic Editor: Carmelo Caldarella

Received: 29 May 2026

Revised: 1 July 2026

Accepted: 3 July 2026

Published: 6 July 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and

conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

(inadequate: 31 vs. 10 cases), reducing diagnostic uncertainty by 50%. CT-U opacification was $\geq 50\%$ in most cases ($\kappa = 0.814$), enabling reliable delineation of the ureteral course. Inter-reader agreement remained strong (surgical bed κ : 0.944 vs. 0.876; nodes κ : 0.896 both). Interpretation time decreased for both readers (senior: 3.12 vs. 2.10 min (-32.7%); junior: 4.06 vs. 2.42 min (-40.4%)). Conclusions: Adding an excretory-phase CT urography to [^{68}Ga]Ga-PSMA-11 PET/CT improves diagnostic confidence, reduces interpretive uncertainty in the surgical bed, clarifies peri-ureteric nodal findings, enhances ureter visualization, and shortens interpretation time. CT-U is a practical enhancement to low-dose PET/CT protocols for BCR after RP.

Keywords: PET/CT; [^{68}Ga]Ga-PSMA-11; CT urography; prostate cancer; biochemical recurrence

1. Background

Prostate cancer is the most common cancer among men and the third leading cause of cancer-related deaths [1]. With the introduction of prostate-specific antigen (PSA) screening, many patients are diagnosed with localized disease. However, even with early intervention in localized disease, 20–50% of patients will experience biochemical recurrence (BCR) within the first decade after radical prostatectomy (RP) or external beam radiotherapy [2,3].

Positron Emission Tomography targeting Prostate-Specific Membrane Antigen (PSMA PET) has emerged in recent years as an important imaging modality in patients with biochemical recurrence after radical prostatectomy. According to the European Association of Urology (EAU) guidelines, PSMA PET/CT is recommended in patients with PSA recurrence after radical prostatectomy when PSA is >0.2 ng/mL and when the results are expected to influence subsequent management [4] with better accuracy and fewer equivocal results when compared to conventional imaging modalities such as Computed Tomography (CT) and Bone Scan [5–7]. Nonetheless, the technique still presents some challenges mainly due to the physiological elimination of [^{68}Ga]Ga PSMA-11 via renal excretion [8], which can limit disease detection using PET/CT, particularly when sites of recurrence are near the urinary tract or when there is overlap between tumor recurrence and ureteric tracer accumulation [9,10]. Precise diagnosis and identification of the affected anatomical sites are essential for effective treatment planning and metastasis-directed therapies, such as salvage lymph node dissection and radiotherapy [11].

During radical prostatectomy, the prostate is removed, usually with the seminal vesicles, and the urinary tract is reconstructed by dropping the bladder onto the pelvic floor and suturing the bladder neck to the urethra. Postoperative anatomical changes may include bladder descent, bladder diverticula and diverticula at the vesico-urethral anastomosis [12,13]. These alterations can hinder accurate disease visualization and pose diagnostic challenges in this clinical setting, making it difficult to differentiate between excreted radioactivity in the urine and small pelvic nodes or local recurrence situated close to the ureters. Additionally, the CT scan utilized in conventional [^{68}Ga]Ga PSMA-11 PET/CT is usually low-dose, and may not provide sufficient anatomical detail, potentially leading to diagnostic uncertainty regarding whether focal tracer accumulation indicates tumor uptake or ureteric tracer excretion.

Some groups have proposed administering a radiological contrast agent to perform a CT urography protocol (CT-U) only during the urogram phase to facilitate the visualization of the urinary tract, as the preferred imaging technique [14,15]. Integrating CT-U as part of the PET/CT protocol may help address this issue by distinguishing urinary activity from

radiotracer activity. To this day, there are no clear recommendations on the systematic use of contrast-enhanced CT for PSMA PET scans.

This retrospective study aims to evaluate the utility of integrating a CT-U with [68Ga]PSMA-11 PET/CT scans, and to determine whether incorporating a CT-U scan can enhance diagnostic confidence in distinguishing between focal tumor areas and tracer accumulation in the ureteric space and surgical bed after radical prostatectomy, using a head-to-head comparison. Our primary endpoint was to evaluate a possible change in classification of surgical-bed recurrence (positive/negative as per PROMISE criteria [16]) between PET/CT and PET/CT-U. Furthermore, our secondary endpoints included assessing a change in peri-ureteric nodal classification; shifts in five-point E-PSMA reader confidence [17]; and evaluating adequacy of ureter visualization and ureteric opacification on CT-U.

2. Materials and Methods

2.1. Study Design and Population

We retrospectively included consecutive patients with a history of prostate cancer treated with radical prostatectomy who underwent [68Ga]GaPSMA-11 PET/CT for evaluation due to biochemical recurrence between January 2025 and March 2025.

Inclusion criteria were: history of prostate cancer treated with radical prostatectomy, biochemical recurrence after surgery, and availability of both PET/CTd and PET/CT-U acquisitions performed during the same imaging protocol. Patients were excluded if they had contraindications to iodinated contrast administration or if either CT dataset was unavailable. Biochemical recurrence was defined according to EAU guidance as described above.

As part of our standard protocol, patients with a background of radical prostatectomy are studied with an early PET/CT dynamic acquisition (PET/CTd) to improve evaluation of the surgical bed for possible local recurrence. Previous research has shown that early scanning before significant accumulation of urine activity might show better lesion detection in proximity to the urinary bladder and surgical bed [18–20]. Our dynamic protocol involves scanning the pelvic region immediately after the radiotracer injection (from 0 to 8 min) with a low-dose CT without radiological contrast for attenuation correction. Minutes afterwards, a standard 60 min post-injection [68Ga]Ga PSMA-11 PET/CT scan is obtained, supplementing the PET/CT scan with a CT-U “urogram phase” protocol. This protocol is performed to opacify the urinary collecting system so the ureters and bladder are clearly outlined [21–23]. This modification to the standard protocol results in each patient having a pair of CT scans for the same PET imaging, one CT without the use of contrast (derived from the dynamic scan) and a second CT with contrast (derived from the whole-body PET imaging), allowing a head-to-head comparison.

Clinical data such as age, PSA, Gleason Score, type of surgery and previous treatments were extracted from electronic medical records.

The protocol was approved by our institution’s ethics committee (protocol number: 2025.035), and the entire investigation was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and all its subsequent revisions. Institutional informed consent was obtained from all subjects involved in the study.

2.2. Imaging

[68Ga]Ga PSMA PET was performed according to the EANM/SNMMI procedure guidelines [24]. The images were acquired in two tomographs (Siemens Biograph mCT 64 and Siemens Vision 600, Siemens, Knoxville, TN, USA). Patients received an intravenous injection of 160 ± 55 MBq of [68Ga]Ga PSMA-11.

Data acquisition consisted of two parts: the dynamic protocol and the standard whole-body PET/CT. Dynamic PET/CT studies were performed over the pelvic area; a low-dose

attenuation CT (120 kV, 30 mA) was used for the attenuation correction of the dynamic emission PET data and for image fusion.

Renal function was evaluated with a peripheral blood creatinine measurement obtained prior to contrast injection, and patients' histories of allergic reactions to iodinated intravenous contrast were assessed. If no contraindications were present, 50 milliliters of Omnipaque 240 mg/mL (GE Healthcare, Princeton, NJ, USA) was administered through the same intravenous line with a mean of 10 min (range 8–15 min) before whole-body PET/CT scan acquisition. During the uptake period, patients were encouraged to stay hydrated and were asked to void immediately before imaging. Additional measures to enhance ureteric opacification (e.g., furosemide injection) were not used. Attenuation correction was performed using the CT urography (CT-U) data. As explained before, the conventional enhanced arterial, venous and nephrographic phases of CT-U were not acquired.

Whole-body (vertex to mid-thigh) PET/CT scans began 64 ± 10.1 min after injection, with 3 min per bed position for PET imaging and a low-dose CT (Care Dose 4D with a quality reference of 80 mAs at 120 kV). PET data were reconstructed using an iterative algorithm with 3 iterations and 21 subsets (OSEM 3–21) into a 200×200 matrix. For each acquisition, two different reconstructions were performed: a high-quality reconstruction, optimized for lesion detection (PSF + TOF, 2 mm Gaussian filter), and a reconstruction in compliance with EARL Standard 1 for quantification (TOF, 5 mm Gaussian filter). The same protocol was used for all patients and in both imaging devices.

2.3. Image Analysis

The anonymized [^{68}Ga]Ga PSMA PET/CTd and PET/CT-U images were independently reviewed by two nuclear medicine physicians (MRF and VBA), one senior with over 7 years of experience with PSMA PET/CT readings and the other with 3 years of experience.

For the purpose of the study, the examination was focused solely on assessing the pelvis for local recurrence and lymph nodes in the lower abdomen that were close to the ureters. Distant lymph nodes, bone and visceral metastasis were not included in the analysis.

To evaluate the confidence in attributing a PET-positive finding in the surgical bed or ureteric space to either tumor uptake or urinary tracer excretion, a two-step analysis was conducted by both blind readers. In the first step, the whole-body PET dataset acquired approximately 60 min after radiotracer injection was fused with the non-contrast pelvic CT obtained during the early dynamic acquisition (PET/CTd).

Proper fusion between CT and whole-body PET was evaluated, and was manually adjusted when deemed necessary. In this first analysis, the physicians recorded the number of focal abnormalities that could not be definitively identified as urinary activity. PROMISE V2 [25] criteria were utilized, classifying the findings as positive, equivocal or negative, enabling standardized reporting of PSMA expression. Expression categories are defined in relation to mean uptake in the blood pool, liver, and parotid gland.

Lesions were classified according to PROMISE criteria using visual miPSMA expression scoring. Focal uptake not attributable to physiological activity or benign causes was considered suspicious for prostate cancer, with uptake intensity graded relative to the blood pool, liver, and parotid gland. PSMA scores 2–3, corresponding to uptake equal to or higher than liver, were considered typical for prostate cancer lesions. In the surgical bed and peri-ureteric nodal regions, lesions were considered positive when focal uptake occurred in an anatomically plausible site.

Local tumor recurrence and nodal staging on PSMA PET were reported based on the criteria featured in the E-PSMA guidelines.

Then, the diagnostic confidence of this assignment was recorded using the E-PSMA reader confidence expressed through a 5-point scale [17]: 1, benign lesion without abnormal

PSMA uptake; 2, probably benign lesion: faint PSMA uptake; 3, equivocal finding: faint uptake in a site typical for prostate cancer or intense uptake in a site atypical for prostate cancer; 4, probably prostate cancer: intense uptake in typical site of prostate cancer, but without definitive findings on CT; and 5, definitive evidence of prostate cancer: intense uptake in typical site of prostate cancer, with definitive findings on CT. Criteria were applied separately for imaging of the prostate bed and imaging of pelvic lymph nodes in the proximity of the ureters. A positive diagnosis for the surgical bed was attributed when there was a focal PSMA uptake above the blood pool and a correspondence with soft tissue lesion in the CT, or a focal PSMA uptake above the liver when there was no soft tissue lesion present. A positive diagnosis for pelvic lymph nodes was made when an uptake higher than the blood pool was present.

In the second step, the same whole-body PET dataset was reassessed weeks later, this time fused with the excretory-phase CT urography dataset (PET/CT-U). The order of cases within each reading session was not fixed. PET/CTd and PET/CT-U assessments were separated by an 8–10-week interval to reduce recall bias. Readers were blinded to each other's assessments and to follow-up outcomes. No distractor cases were included. The diagnostic confidence for attributing focal areas of tracer accumulation was scored again for each finding. The confidence in attributing a PET-positive finding in the surgical bed or near the ureters due to metastatic disease or ureteric tracer excretion was also evaluated. Increased confidence was defined as a shift from equivocal categories toward more definitive classifications according to the validated E-PSMA reporting framework.

Cases with initial disagreement were subjected to a joint consensus read; agreement was reached in all instances, and the consensus served as the final classification for descriptive analyses.

Proper ureteral visualization was also evaluated by each reader in both PET/CTd and PET/CT-U, noting if the uptake was sufficient and could allow proper visualization and following of the ureters until the bladder portion.

To assess contrast enhancement of the ureters, each reader separately reviewed the CT-U images. The readers assigned an opacification score to each segment based on previously published CT-U analyses. The opacification scores were as follows: 0 for 0% opacification, 1 for <50% opacification, 2 for 50–99% opacification, and 3 for 100% opacification.

The time to evaluate the pelvic area for local recurrence and lymph nodes close to the ureters in both PET/CTd and PET/CT-U were annotated for each reader in order to evaluate if the time to read decreases when using CT-U.

Subsequently, the PET/CT images with CT-U were examined, and the number of equivocal foci corresponding to contrast-enhanced urine was documented.

2.4. Statistics

All continuous variables were tested for normality using the Shapiro–Wilk test. Data are presented as mean $\pm$ SD or $\pm$ median range.

The inter-reader agreement for assessing positive or negative findings for PET/CTd, PET/CT-U, opacification score and ureteral visualization was calculated using the kappa coefficient.

To assess if the detection rate changes between CT and the use of CT-U within each reader, McNemar's test for paired nominal data was used. To assess associations between baseline clinical parameters and CT-U-related reclassification, the Mann–Whitney U test was used. Reader confidence change was analyzed with Wilcoxon signed-rank (paired ordinal) for within-patient shifts.

No formal sample-size calculation was performed because of the retrospective exploratory nature of the study and the inclusion of consecutive eligible patients.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 29 (IBM Corp., Armonk, NY, USA). A p value < 0.05 was regarded as statistically significant.

3. Results

In total, 43 patients were included and 86 [^{68}Ga]Ga PSMA-11 PET/CT studies were reviewed, two per patient. Each patient underwent a non-contrast pelvic CT from the dynamic acquisition and a CT-U acquired at 60 min as part of the standard protocol.

Patients with contraindications to iodinated contrast administration, including severe renal impairment or a history of severe contrast hypersensitivity, were not candidates for the CT-U protocol and were therefore not included in this analysis.

The mean age was 69 ± 7.2 years, with a median PSA of 0.51 ng/mL [IQR: 0.25–1.89; range: 0.00–53.00]. The mean PSA was 3.67 ± 10.49 ng/mL. The most common Gleason Score was 7. Clinicopathological characteristics of patients are summarized in Table 1.

Table 1. Clinicopathological characteristics of patients.

Total (N.)	43
Age [years] (mean, SD)	69.0 ± 7.2
PSA at the time of PET, median [IQR]; range	0.51 [0.25–1.89]; 0.00–53.00
Gleason grade group	
Group 1 (3 + 3)	5 (11.6%)
Group 2 (3 + 4)	7 (16.3%)
Group 3 (4 + 3)	13 (30.2%)
Group 4 (8)	8 (18.6%)
Group 5 (9–10)	10 (23.3%)
Surgical approach	
Laparoscopic	13 (30.2%)
Robot-assisted laparoscopic (RARP)	29 (67.4%)
Open	1 (2.3%)
Type of surgery	
Prostatectomy	26 (60.5%)
Prostatectomy + lymphadenectomy	17 (39.5%)
Type of recurrence	
After prostatectomy	21 (48.8%)
After prostatectomy + radiotherapy	22 (51.2%)

Clinicopathological characteristics of the study cohort ($N = 43$), including demographic data, disease characteristics, surgical approach, type of surgery, and recurrence pattern.

No allergic reactions to iodinated intravenous contrast were reported or noted.

Proper fusion between CTd and whole-body PET was seen in 41 patients (95%), and was manually adjusted in two cases.

3.1. Diagnostic Confidence

3.1.1. Surgical Bed Post-Radical Prostatectomy

In the first read, assessing fused PET/CTd images without radiological contrast, the senior reader identified 12 suspicious focal areas of tracer accumulation in the prostatic bed and the junior reader identified 13. The discrepant case was assessed as negative as per the PROMISE criteria by the senior reader and positive by the junior. Although the uptake was inferior to the liver, it was difficult to visually classify it.

In the second read, assessing fused PET images with the CT-U, the positive findings on the surgical bed decreased for both readers. The senior reader identified four suspicious focal areas of tracer accumulation in the prostatic bed (66.7% decrease in comparison with the first assessment) and the junior reader identified five (54.5% decrease); of these cases four were concordant between both readers.

Overall, after the consensus, for the first analysis (PSMA PET/CTd) 12 patients (27.9%) were reported positive for local recurrence, whereas in PSMA/CT-U only five patients (11.6%) were considered positive. The use of CT-U clarified findings related to diverticula at the vesico-urethral anastomosis after radical prostatectomy in seven patients ($p = 0.016$).

Representative cases are shown in Figures 1–3. Surgical-bed classification consensus results are summarized in Table 2. The paired reclassification matrix for surgical-bed assessment is provided in Supplementary Table S1.

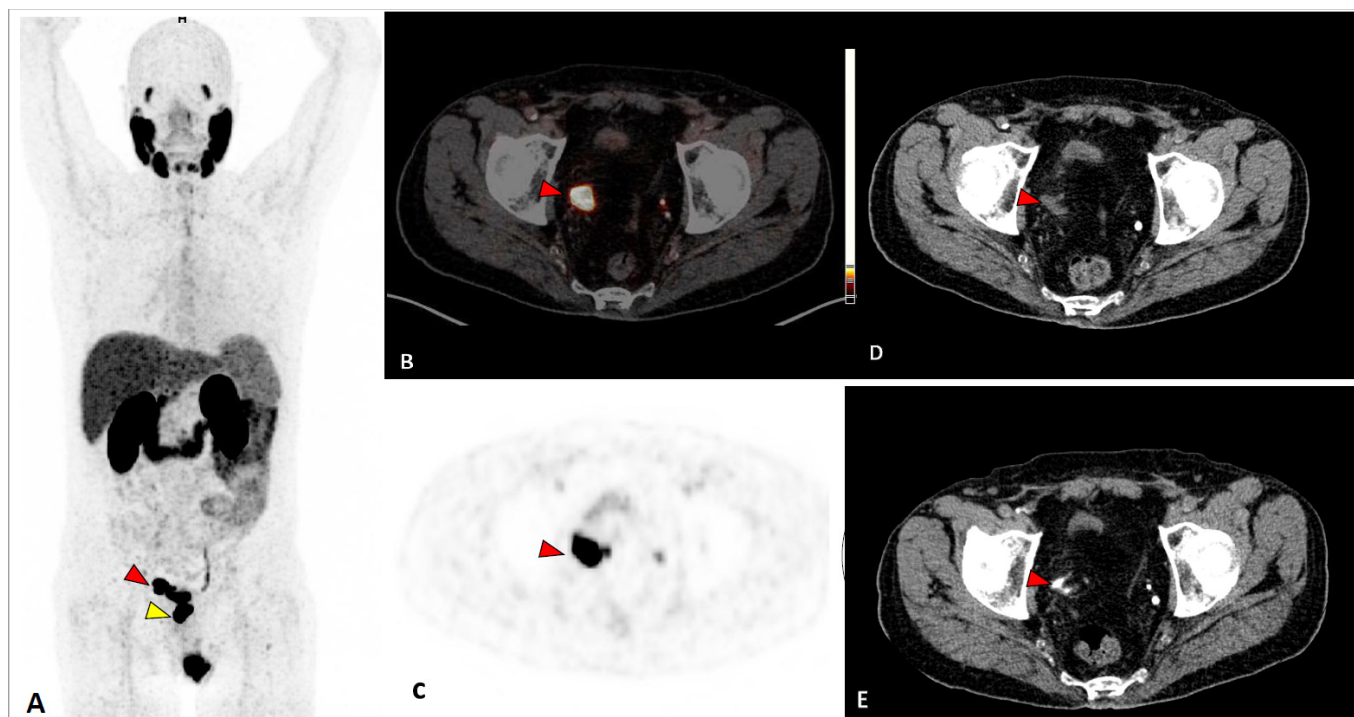


Figure 1. 67-year-old patient with biochemical recurrence after radical prostatectomy (PSA 2.79 ng/mL). PSMA PET MIP image (A) shows irregular high uptake in the right pelvis (red arrow-head), adjacent to the bladder (yellow arrowhead). Axial PET/CT fusion and PET views at 60 min p.i (B,C) showed ill-defined right pelvic PSMA-avid uptake adjacent to the upper right surgical bed with no continuation with the bladder. Axial CT views without the use of contrast shows soft tissue thickening (D). Axial CT with urography protocol contrast (E) shows contrast enhancement of the soft tissue, corresponding to unknown diverticula at the vesico-urethral anastomosis.

Table 2. Surgical-bed classification consensus.

Category	PET/CTd n/N (%)	PET/CT-U n/N (%)	McNemar <i>p</i> -Value
Positive	12/43 (27.9%)	5/43 (11.6%)	$p = 0.016$
Negative	31/43 (72.1%)	38/43 (88.4%)	

Consensus classification of surgical-bed findings using PET/CTd and PET/CT-U protocols, showing proportions of positive and negative cases and comparison between modalities. PET/CTd: PET interpreted with the non-contrast CT from the early dynamic acquisition. PET/CT-U: contrast-enhanced excretory-phase protocol for ureteral opacification PET/CT.

Moreover, the increase or decrease in the five-point scale when using E-PSMA reader confidence was also noted, identifying a significant change in five cases ($p < 0.005$). In two patients the use of CT-U increased the diagnostic confidence from equivocal findings (E-PSMA 3) to definitive evidence of prostate cancer (E-PSMA 5). In three patients there was a change from equivocal findings (E-PSMA 3) to probably benign lesion (E-PSMA 1–2), facilitating differentiation between positive local recurrence and ureteral excretion.

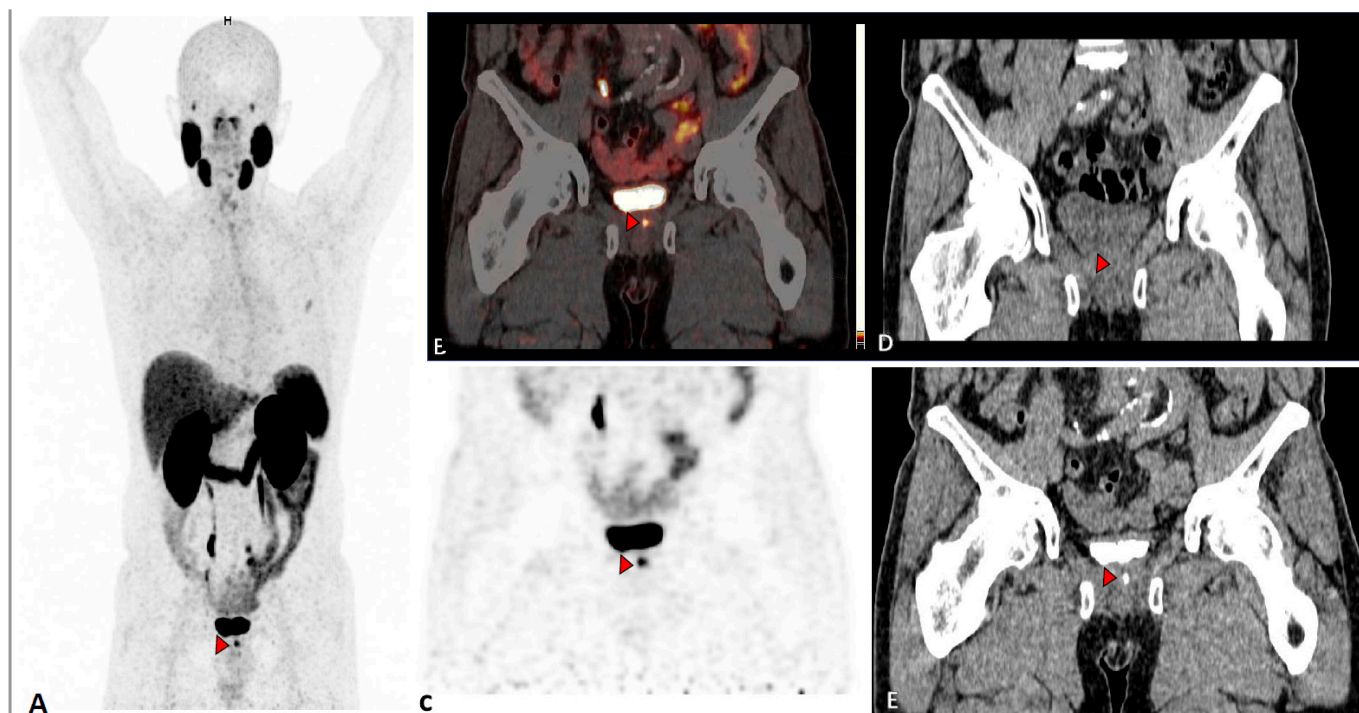


Figure 2. 59-year-old patient with biochemical recurrence (PSA 0.24 ng/mL) following radical prostatectomy. PSMA PET MIP image (A) shows focal uptake in the left side of the pelvis (red arrowhead), inferior to the bladder. Coronal PET/CT fusion and PET views at 60 min p.i (B,C) shows suspicious PSMA-avid foci adjacent to the surgical bed. Coronal CT views without the use of contrast shows no clear soft tissue correlation (D). Coronal CT with urography protocol contrast (E) demonstrates contrast enhancement at the site of uptake (red arrowhead), consistent with urinary excretion of the radiopharmaceutical within a small diverticulum at the vesico-urethral anastomosis, supporting interpretation as urinary excretion rather than local recurrence.



Figure 3. 63-year-old patient with biochemical recurrence (PSA 0.46 ng/mL) after radical prostatectomy. Axial PET/CT fusion (A) shows focal PSMA-avid uptake near the left aspect of the surgical bed (red arrowhead). Axial CT views without the use of contrast shows soft tissue in the surrounding area, making evaluation of the pelvic area difficult (B). Axial CT with urography protocol contrast (C) shows focal contrast enhancement (red arrowhead) corresponding to diverticula at the vesico-urethral anastomosis and physiological urinary excretion of the radiopharmaceutical.

Scheme 2 patients received targeted radiotherapy in a site different to the surgical bed. One patient had SBRT directed to a metastatic bone lesion in the spine and a second one underwent targeted pelvic radiotherapy to the pathological lymph nodes in the retroperitoneum and common iliac artery territory, with both having a biochemical response after the focused treatments. Follow-up was not available for one patient who continued care at another center.

3.1.2. Pelvic Lymph Nodes

In the first read, assessing fused PET/CTd images (without contrast), the senior reader identified six focal areas of tracer accumulation in the pelvic area near the ureters that were suspicious for lymph node infiltration and the junior reader identified five. Of these, one case was non-concordant between readers, due to a faint uptake very close to the ureter, finally classified as negative in the consensus reading.

In the second read, assessing fused PET images with the CT-U, positive findings due to pelvic lymphatic infiltration were stable, the senior reader identified a total of six focal areas of tracer accumulation close to the ureters and the junior reader identified five; of these cases five were concordant between both readers. The case with initial disagreement was subjected to a joint consensus read and an agreement of positivity was reached.

Overall, PSMA PET/CTd was reported positive for pelvic lymph node metastasis in five patients (11%) and also in five (11%) with PET/CT-U. Two of the positive findings in the PET/CTd were subsequently considered negative in the PET/CT-U. Furthermore, two patients that were considered as negative were finally classified as positive. For peri-ureteric nodal classification, four discordant pairs were observed: two positive-to-negative and two negative-to-positive. Exact McNemar's test showed no significant net change between PET/CTd and PET/CT-U classifications, $p = 1.000$.

A representative case is shown in Figure 4. Peri-ureteric nodal classification consensus results are represented in Table 3. The paired reclassification matrix for periureteric nodal assessment is provided in Supplementary Table S2.

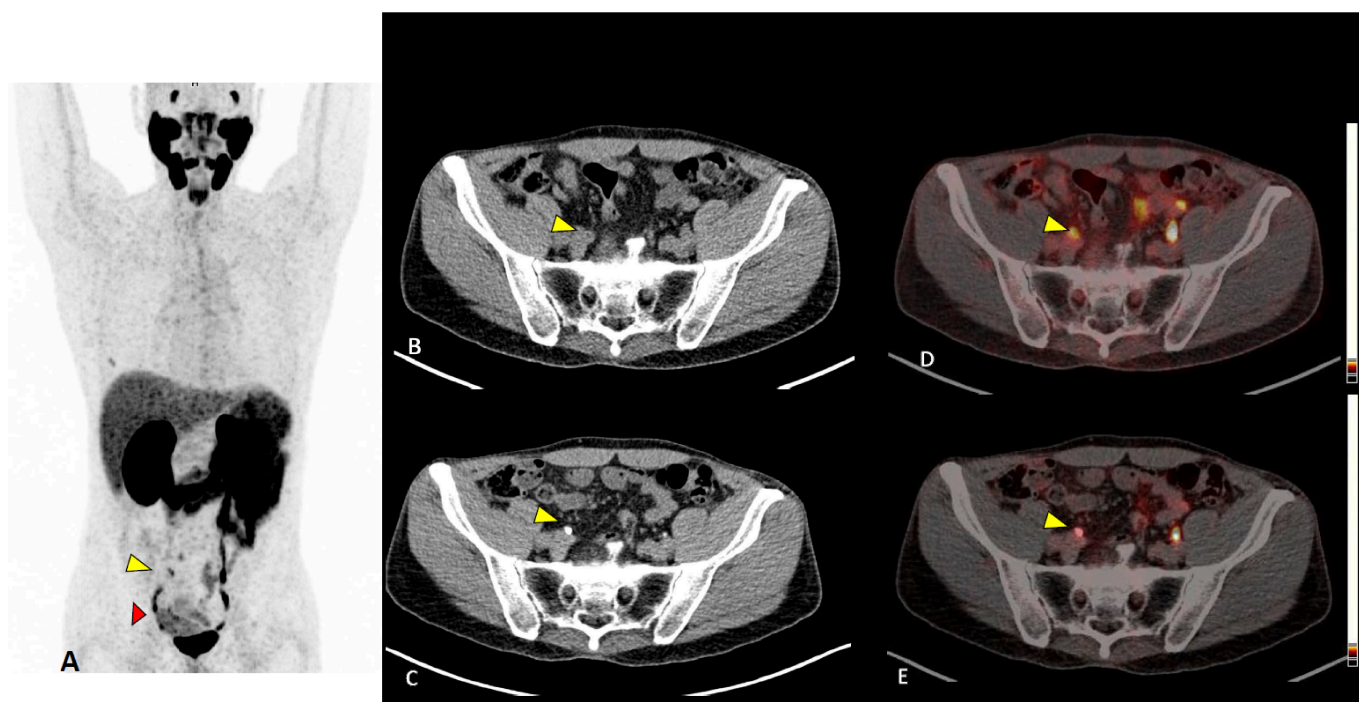


Figure 4. 72-year-old patient with biochemical recurrence (PSA 0.77 ng/mL) following radical prostatectomy. PSMA PET MIP image (A) shows irregular uptake in the proximity of the right ureter (yellow arrowhead). Axial non-enhanced CT (B) and PET/CT at 60 min p.i (D) show discontinuous and tortuous course of the right ureter, making it difficult to distinguish whether it corresponds to a peri-ureteral lymph node or physiological radiotracer urinary elimination. The axial CT and PET/CT with urography protocol (C,E) shows contrast enhancement of the structure, supporting interpretation as ureteral activity rather than nodal disease.

Table 3. Peri-ureteric nodal classification consensus.

Category	PET/CTd n/N (%)	PET/CT-U n/N (%)	McNemar <i>p</i> -Value
Positive	5/43 (11.6%)	5/43 (11.6%)	<i>p</i> = 1.000
Negative	38/43 (88.4%)	38/43 (88.4%)	

Consensus classification of peri-ureteric nodal findings using PET/CTd and PET/CT-U protocols, showing proportions of positive and negative cases and comparison between modalities.

The increase or decrease in the five-point scale when using E-PSMA reader confidence for assessing the pelvic lymph nodes that were close to the ureters was also noted, identifying a significant change in six cases. In one patient the use of CT-U increased the diagnostic confidence from equivocal findings (E-PSMA 3) to definitive evidence of prostate cancer (E-PSMA 5). In another case, it increased the confidence from probably prostate cancer (E-PSMA 4) to definitive evidence of prostate cancer (E-PSMA 5). In four patients there was a change from equivocal findings (E-PSMA 3) to probably benign lesion (E-PSMA 1–2), facilitating differentiation between positive lymph nodes and ureteral excretion.

3.2. Inter-Reader Agreement for Prostate Bed Recurrence Detection

Inter-reader agreement was strong with both CT protocols. Cohen's kappa for inter-reader agreement without the use of contrast was 0.944 ($p < 0.001$), which indicates a strong level of agreement.

Cohen's kappa for inter-reader agreement with the CT-U protocol was slightly lower at 0.876 ($p < 0.001$), which still indicates a strong level of agreement, although it is important to note that the decrease in the kappa can be explained by the decrease in positive cases in the CT-U (5/43) as opposed to the CTd (12/43). When the rate of positive findings is low, even small disagreements in the positive group may have an impact on Cohen's kappa.

3.3. Inter-Reader Agreement for Pelvic Lymph Node Detection

Cohen's kappa for inter-reader agreement for the detection of tumoral lymph nodes in the pelvic area without the use of contrast was 0.896 ($p < 0.001$), which indicates a strong level of agreement. With the CT-U protocol the kappa was the same, 0.896 ($p < 0.001$), which also indicates a strong level of agreement, with no substantial changes. An inter-reader agreement summary is shown in Table 4.

Table 4. Inter-reader agreement (Cohen's κ).

Region	Modality	κ	95% CI
Surgical bed	PET/CTd	0.944	0.835–1.000
Surgical bed	PET/CT-U	0.876	0.638–1.000
Peri-ureteric nodes	PET/CTd	0.896	0.695–1.000
Peri-ureteric nodes	PET/CT-U	0.896	0.695–1.000

Inter-reader agreement measured by Cohen's κ for surgical bed and peri-ureteric nodal assessment according to imaging protocol.

3.4. Opacification Score

Most of the ureters were correctly identified in the low-dose CT despite the small dose of contrast utilized in the protocol (50 mL of contrast of Omnipaque 240 mg/mL). Distribution by category was as follows for the senior reader: score 1 (<50%) in 12 patients, score 2 (50–99%) in 20 patients, and score 3 (100%) in 11 patients. There were no major differences in the evaluation of the junior reader, with slight changes in the distribution: score 1 (<50%) in 10 patients, score 2 (50–99%) in 23 patients, and score 3 (100%) in 10 patients. None of the patients had a 0 opacification score. The majority of the patients had an adequate

opacification score >50%. The inter-reader agreement was strong, with a kappa of 0.814 ($p < 0.001$). Results are shown in Table 5.

Table 5. Ureteral opacification score distribution and inter-reader agreement.

Opacification Score	Senior Reader n (%)	Junior Reader n (%)
Score 0 (0%)	0 (0.0%)	0 (0.0%)
Score 1 (<50%)	12 (27.9%)	10 (23.3%)
Score 2 (50–99%)	20 (46.5%)	23 (53.5%)
Score 3 (100%)	11 (25.6%)	10 (23.3%)

Inter-reader agreement: $\kappa = 0.814$, $p < 0.001$. Distribution of ureteral opacification scores assigned by senior and junior readers, with corresponding inter-reader agreement.

3.5. Ureteral Visualization in PET Images

Inadequate visualization of one or both ureters in the PET/CTd, both in the fusion and maximum intensity projection images, was noted in 31 cases. In most of the cases the uptake was irregular and discontinuous, as opposed to a linear uptake that could allow proper visualization and following of the ureters until the bladder portion. Specifically, the left ureter could not be clearly distinguished in 12 patients, the right ureter in eight patients, and both ureters in 11 patients. Moreover, in 16 cases the lack of visualization generated diagnostic uncertainty, specifically in eight patients for the right ureter and in eight patients for the left ureter. In the remaining 26 patients, the absence of clear ureteral visualization did not result in diagnostic doubt. The inter-reader agreement to determine whether the ureteral course was assessable or not, was moderate with a kappa of 0.598 ($p < 0.001$).

When assessing the PET/CT-U images, the visualization of the ureters improved substantially, due to the combination of radiopharmaceutical and contrast excretion, only noting an inadequate visualization of one or both ureters in 10 patients (23%). Specifically, the left ureter could not be clearly distinguished in five patients and the right ureter in five patients. The diagnostic uncertainty was also lower with eight cases in which the ureters could not be properly followed or the visualization was difficult, a 50% decrease in comparison with the assessment of PET/CTd images (Table 6). The inter-reader agreement improved substantially, with an almost perfect agreement, and a kappa of 0.96 ($p < 0.001$).

Table 6. Ureter visualization and diagnostic uncertainty.

	PET/CTd	PET/CT-U
Inadequate ureter visualization (any side)	31/43 (72.1%)	10/43 (23.3%)
Left ureter not clearly distinguished	12 (27.9%)	5 (11.6%)
Right ureter not clearly distinguished	8 (18.6%)	5 (11.6%)
Both ureters not clearly distinguished	11 (25.6%)	0 (0%)
Diagnostic uncertainty due to ureter visualization	16/43 (37.2%)	8/43 (18.6%)

Assessability agreement: PET/CTd $\kappa = 0.598$ ($p < 0.001$); PET/CT-U $\kappa = 0.960$ ($p < 0.001$). Comparison of ureter visualization and diagnostic uncertainty between PET/CTd and PET/CT-U protocols, including assessability agreement.

3.6. Association Between Baseline Clinical Parameters and CT-U-Related Reclassification

Clinical and pathological parameters, including age, PSA, and Gleason Score, were compared between patients with and without CT-U-related reclassification. No statistically significant associations were observed, suggesting that CT-U-related reclassification was not clearly explained by baseline clinical parameters in this cohort; however, the small sample size may limit the interpretation.

3.7. Comparison of Reading Times

The senior reader had a mean time of 3.12 min (± 1.45 min) when evaluating the prostate bed and pelvic lymph nodes near the ureters in PET/CTd; meanwhile, the junior reader had a slightly extended time with a mean of 4.06 min (± 1.29 min).

When evaluating the PET/CT-U protocol the reading time decreased for both readers, with a mean of 2.1 min (± 1.03 min) and 2.42 (± 1.12 min), indicating reductions of 1.02 min [32.7%] and 1.64 min [40.4%] respectively (Table 7).

Table 7. Reading time by protocol and reader.

Reader	PET/CTd Mean $\pm$ SD (min)	PET/CT-U Mean $\pm$ SD (min)	Δ Time (Absolute; %)
Senior reader	3.12 $\pm$ 1.45	2.10 $\pm$ 1.03	−1.02 min (−32.7%)
Junior reader	4.06 $\pm$ 1.29	2.42 $\pm$ 1.12	−1.64 min (−40.4%)

Mean reading time by reader and imaging protocol, including absolute and percentage differences between protocols.

4. Discussion

This head-to-head retrospective study of patients with biochemical recurrence after radical prostatectomy suggests that the addition of a urography phase contrast-enhanced CT (CT-U) to the standard [^{68}Ga]Ga PSMA-11 PET/CT protocol may reduce equivocal findings in the evaluation of surgical bed and suspicious lymph nodes in the proximity of the ureters. Notably, previous research has shown ureter and bladder activity among the most frequent sources of false positives in PSMA PET [26–28]. In our cohort, surgical-bed positivity decreased from 12/43 (27.9%) on PET/CTd to 5/43 (11.6%) on PET/CT-U, with seven patients reclassified after CT-U visualization of postoperative urinary tract anatomy, including diverticula at the vesico-urethral anastomosis. This distinction may be clinically relevant for salvage treatment planning, as inaccurate localization of recurrence can expose patients to potentially unnecessary toxicity and cost [29].

It further improved the visualization of the ureteral tract, allowing better visualization and following, which consequently facilitated the peri-ureteric nodal classification. Although the overall positivity rate for peri-ureteric nodal involvement remained unchanged (5/43 vs. 5/43), nodal classification changed in four patients: two findings were reclassified from positive to negative and two from negative to positive after CT-U evaluation. This is potentially a clinically relevant effect that could impact radiotherapy planning and may alter nodal target volumes or the decision to pursue metastasis-directed therapy, while avoiding futile treatment of physiologic ureteric activity.

Previous research by Will et al. [14] and Iravani et al. [15] showed a benefit of CT urography in [^{68}Ga]Ga PSMA-11 PET/CT. The small-cohort (10 patients) comparative study of Will et al. was the first to investigate the benefit of a separate CT urography in [^{68}Ga]PSMA-11 PET/CT with low-dose CT and reported a potential benefit when utilizing it. Subsequently Rosar et al. [30] further linked CT-U to discrepant treatment that would have occurred in ~12% without urography and despite including a high number of patients (247), a limitation of the study was a lack of comparative imaging (with and without CT-U), a limitation that in our case has been overcome by using two comparative CT scans for each patient performed on the same equipment on the same day, one without and one with contrast. Therefore, to the best of our knowledge, our study is the first to compare within each patient a CT without the use of radiological contrast and a CT with contrast in the urography phase, allowing a head-to-head comparison.

Our study extends previous observations by pairing CT-U with an early dynamic pelvic PET, using a low contrast volume yet achieving good ureteral opacification on low-

dose CT, and quantifying meaningful reductions in interpretation time—a benefit that, to our knowledge, has been under-reported.

The use of standardized interpretation frameworks (PROMISE and E-PSMA) offers objective rules that stabilize interpretation between centers and physicians. This likely accounts for the high inter-reader agreement we observed on PET/CTd [31]. Nonetheless, borderline classifications persist. Our study applied these outlines and revealed that incorporating the CT-U improved diagnostic certainty. This was reflected by shifts on the E-PSMA five-point scale away from ‘equivocal’ toward definitive categories, a change that could influence therapeutic decisions and planning.

The relevance of accurate nodal classification is further supported by recent evidence showing the role of [68Ga]Ga-PSMA PET/CT in lymph-node assessment in prostate cancer, particularly in patients undergoing surgical management [32].

Our results fit within guideline-endorsed strategies to mitigate urinary activity-related uncertainty; the joint EANM/SNMMI procedure guideline emphasizes hydration, voiding, early pelvic imaging, and forced diuresis to reduce peri-vesical artifacts and facilitate interpretation. Several groups have suggested forced diuresis or delayed imaging to overcome potential pitfalls [33–36]; nonetheless, the topic remains a field of active research. CT-U provides a complementary solution by directly opacifying the collecting systems, clarifying whether the uptake is due to tumoral lesions or urinary activity.

From a CT perspective, the low-dose urogram phase can suffice to depict the ureteral territory and diverticula that could otherwise mimic nodal disease, limiting added radiation and contrast exposure. Our opacification scoring follows validated CT urography descriptors and achieved high inter-reader agreement despite the modest contrast volume [37].

While our study provides valuable insights, it is subject to certain limitations, including the sample size (43 patients), single-center setting, and retrospective design.

Although the paired within-patient design minimized inter-patient variability, residual recall bias cannot be completely excluded because the same PET datasets were reviewed with different CT datasets after an 8–10-week interval. The two CT datasets differed not only by contrast opacification but also by acquisition timing; therefore, potential differences in bladder filling, bowel position, patient motion, and PET/CT co-registration represent methodological considerations of the study design.

The relatively small sample size may have limited the statistical power of some secondary analyses; therefore, the non-significant findings observed for peri-ureteric nodal classification may be attributable to limited power rather than the absence of a clinically relevant effect.

A further limitation is the absence of a systematic independent reference standard. Histopathologic confirmation, MRI correlation, or structured longitudinal follow-up was not available for all reclassified lesions. Therefore, CT-U-based reclassification should be interpreted as a change in imaging assessment rather than definitive diagnostic confirmation. Surgical margin status, PSA doubling time, CT dose metrics and cost analysis were not systematically collected retrospectively and should be evaluated in future prospective studies.

Another limitation, which could also be considered a strength, is the exclusion of tumor sites different from the local recurrence and peri-ureteral lymph nodes. This approach was intentional, as we aimed to evaluate sites close to the ureters that could pose a real diagnostic challenge to evaluate due to its proximity to the ureters, as normally distant lymph nodes and metastatic lesions are simpler to evaluate when using PSMA PET and are usually easier to interpret.

Nonetheless, future research should aim to validate and expand upon these findings through larger cohorts and prospective study designs.

5. Conclusions

Based on our findings, integrating an excretory-phase, contrast-enhanced CT urography (CT-U) improves the interpretation of [⁶⁸Ga]Ga PSMA-11 PET/CT scans. This approach may reduce interpretive uncertainty and misclassification arising from post-prostatectomy anatomical changes and physiologic ureteral radiotracer accumulation. It also improves visualization of the ureteral course, aiding the differentiation of metastatic lymph nodes from ureteral dilatations. In addition, CT-U shortens interpretation time and increases reader diagnostic confidence. This modified CT-U approach is easy to implement and could be considered a useful complementary tool to low-dose [⁶⁸Ga]Ga-PSMA-11 PET/CT protocols in patients with biochemical recurrence, although validation in larger prospective multi-center studies is warranted.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/cancers18132171/s1>, Table S1: Paired reclassification matrix for surgical-bed assessment and Table S2: Paired reclassification matrix for peri-ureteric nodal assessment.

Author Contributions: Conceptualization, V.B.-A. and M.R.-F.; methodology, V.B.-A. and M.R.-F.; formal analysis, V.B.-A. and M.R.-F.; investigation, V.B.-A. and M.R.-F.; data curation, V.B.-A., J.J.R., F.M., M.R., E.F.G. and M.R.-F.; writing—original draft preparation, V.B.-A. and M.R.-F.; writing—review and editing, J.J.R., F.M., L.F., E.F.G., F.D.-C., R.M.-M., B.M.-L. and M.R.-F. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: All procedures performed in the present study followed the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration, as well as its later amendments and other comparable ethical standards. The local institutional ethics committee approved this retrospective study (protocol approval 2025.035).

Informed Consent Statement: Institutional informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author due to privacy.

Conflicts of Interest: The authors declare that they have no competing interests.

References

1. Siegel, R.L.; Miller, K.D.; Wagle, N.S.; Jemal, A. Cancer statistics, 2023. *CA Cancer J. Clin.* **2023**, *73*, 17–48. [[CrossRef](#)] [[PubMed](#)]
2. Eggener, S.E.; Scardino, P.T.; Walsh, P.C.; Han, M.; Partin, A.W.; Trock, B.J.; Feng, Z.; Wood, D.P.; Eastham, J.A.; Yossepowitch, O.; et al. Predicting 15-Year Prostate Cancer Specific Mortality After Radical Prostatectomy. *J. Urol.* **2011**, *185*, 869–875. [[CrossRef](#)] [[PubMed](#)]
3. Zumsteg, Z.S.; Spratt, D.E.; Romesser, P.B.; Pei, X.; Zhang, Z.; Polkinghorn, W.; McBride, S.; Kollmeier, M.; Yamada, Y.; Zelefsky, M.J. The Natural History and Predictors of Outcome Following Biochemical Relapse in the Dose Escalation Era for Prostate Cancer Patients Undergoing Definitive External Beam Radiotherapy. *Eur. Urol.* **2015**, *67*, 1009–1016. [[CrossRef](#)] [[PubMed](#)]
4. Cornford, P.; Bellmunt, J.; Bolla, M.; Briers, E.; De Santis, M.; Gross, T.; Henry, A.M.; Joniau, S.; Lam, T.B.; Mason, M.D.; et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part II: Treatment of Relapsing, Metastatic, and Castration-Resistant Prostate Cancer. *Eur. Urol.* **2017**, *71*, 630–642. [[CrossRef](#)] [[PubMed](#)]
5. Dondi, F.; Albano, D.; Bertagna, F.; Treglia, G. Bone Scintigraphy versus PSMA-Targeted PET/CT or PET/MRI in Prostate Cancer: Lessons Learned from Recent Systematic Reviews and Meta-Analyses. *Cancers* **2022**, *14*, 4470. [[CrossRef](#)] [[PubMed](#)]
6. Chen, B.; Wei, P.; Macapinlac, H.A.; Lu, Y. Comparison of 18F-Fluciclovine PET/CT and 99mTc-MDP bone scan in detection of bone metastasis in prostate cancer. *Nucl. Med. Commun.* **2019**, *40*, 940–946. [[CrossRef](#)] [[PubMed](#)]
7. Pienta, K.J.; Gorin, M.A.; Rowe, S.P.; Carroll, P.R.; Pouliot, F.; Probst, S.; Saperstein, L.; Preston, M.A.; Alva, A.S.; Patnaik, A.; et al. A Phase 2/3 Prospective Multicenter Study of the Diagnostic Accuracy of Prostate Specific Membrane Antigen PET/CT with ¹⁸F-DCFPyL in Prostate Cancer Patients (OSPReY). *J. Urol.* **2021**, *206*, 52–61. [[CrossRef](#)] [[PubMed](#)]

8. Demirci, E.; Sahin, O.E.; Ocak, M.; Akovali, B.; Nematyazar, J.; Kabasakal, L. Normal distribution pattern and physiological variants of 68Ga-PSMA-11 PET/CT imaging. *Nucl. Med. Commun.* **2016**, *37*, 1169–1179. [[CrossRef](#)] [[PubMed](#)]
9. Afshar-Oromieh, A.; Malcher, A.; Eder, M.; Eisenhut, M.; Linhart, H.G.; Hadaschik, B.A.; Holland-Letz, T.; Giesel, F.L.; Kratochwil, C.; Haufe, S.; et al. PET imaging with a [68Ga]gallium-labelled PSMA ligand for the diagnosis of prostate cancer: Biodistribution in humans and first evaluation of tumour lesions. *Eur. J. Nucl. Med. Mol. Imaging* **2013**, *40*, 486–495. [[CrossRef](#)] [[PubMed](#)]
10. Unterrainer, L.M.; Ruchalski, K.; Allen-Auerbach, M.S.; Calais, J.; Benz, M.R. PSMA PET/CT Dual-Time-Point Imaging: Nice to Have or Need to Have? *J. Nucl. Med.* **2024**, *65*, 818–819. [[CrossRef](#)] [[PubMed](#)]
11. Afshar-Oromieh, A.; Holland-Letz, T.; Giesel, F.L.; Kratochwil, C.; Mier, W.; Haufe, S.; Debus, N.; Eder, M.; Eisenhut, M.; Schäfer, M.; et al. Diagnostic performance of 68Ga-PSMA-11 (HBED-CC) PET/CT in patients with recurrent prostate cancer: Evaluation in 1007 patients. *Eur. J. Nucl. Med. Mol. Imaging* **2017**, *44*, 1258–1268. [[CrossRef](#)] [[PubMed](#)]
12. Kadono, Y.; Nohara, T.; Kawaguchi, S.; Iwamoto, H.; Yaegashi, H.; Shigehara, K.; Izumi, K.; Mizokami, A. Impact of Pelvic Anatomical Changes Caused by Radical Prostatectomy. *Cancers* **2022**, *14*, 3050. [[CrossRef](#)] [[PubMed](#)]
13. Allen, S.D.; Thompson, A.; Sohaib, S.A. The normal post-surgical anatomy of the male pelvis following radical prostatectomy as assessed by magnetic resonance imaging. *Eur. Radiol.* **2008**, *18*, 1281–1291. [[CrossRef](#)] [[PubMed](#)]
14. Will, L.; Giesel, F.L.; Freitag, M.T.; Berger, A.K.; Mier, W.; Kopka, K.; Koerber, S.A.; Rathke, H.; Kremer, C.; Kratochwil, C.; et al. Integration of CT urography improves diagnostic confidence of 68Ga-PSMA-11 PET/CT in prostate cancer patients. *Cancer Imaging* **2017**, *17*, 30. [[CrossRef](#)] [[PubMed](#)]
15. Iravani, A.; Hofman, M.S.; Mulcahy, T.; Williams, S.; Murphy, D.; Parameswaran, B.K.; Hicks, R.J. 68Ga PSMA-11 PET with CT urography protocol in the initial staging and biochemical relapse of prostate cancer. *Cancer Imaging* **2017**, *17*, 31. [[CrossRef](#)] [[PubMed](#)]
16. Eiber, M.; Herrmann, K.; Calais, J.; Hadaschik, B.; Giesel, F.L.; Hartenbach, M.; Hope, T.A.; Reiter, R.; Maurer, T.; Weber, W.A.; et al. Prostate Cancer Molecular Imaging Standardized Evaluation (PROMISE): Proposed miTNM Classification for the Interpretation of PSMA-Ligand PET/CT. *J. Nucl. Med.* **2018**, *59*, 469–478. [[CrossRef](#)] [[PubMed](#)]
17. Ceci, F.; Oprea-Lager, D.E.; Emmett, L.; Adam, J.A.; Bomanji, J.; Czernin, J.; Eiber, M.; Haberkorn, U.; Hofman, M.S.; Hope, T.A.; et al. E-PSMA: The EANM standardized reporting guidelines v1.0 for PSMA-PET. *Eur. J. Nucl. Med. Mol. Imaging* **2021**, *48*, 1626–1638. [[CrossRef](#)] [[PubMed](#)]
18. Perveen, G.; Arora, G.; Damle, N.; Prabhu, M.; Arora, S.; Tripathi, M.; Bal, C.; Kumar, P.; Kumar, R.; Singh, P. Role of Early Dynamic Positron Emission Tomography/Computed Tomography with 68Ga-prostate-specific Membrane Antigen-HBED-CC in Patients with Adenocarcinoma Prostate: Initial Results. *Indian J. Nucl. Med.* **2018**, *33*, 112. [[CrossRef](#)] [[PubMed](#)]
19. Uprimny, C.; Kroiss, A.S.; Fritz, J.; Decristoforo, C.; Kendler, D.; von Guggenberg, E.; Nilica, B.; Maffey-Steffan, J.; di Santo, G.; Bektic, J.; et al. Early PET imaging with [68]Ga-PSMA-11 increases the detection rate of local recurrence in prostate cancer patients with biochemical recurrence. *Eur. J. Nucl. Med. Mol. Imaging* **2017**, *44*, 1647–1655. [[CrossRef](#)] [[PubMed](#)]
20. Strauss, D.S.; Sachpekidis, C.; Kopka, K.; Pan, L.; Haberkorn, U.; Dimitrakopoulou-Strauss, A. Pharmacokinetic studies of [68 Ga]Ga-PSMA-11 in patients with biochemical recurrence of prostate cancer: Detection, differences in temporal distribution and kinetic modelling by tissue type. *Eur. J. Nucl. Med. Mol. Imaging* **2021**, *48*, 4472–4482. [[CrossRef](#)] [[PubMed](#)]
21. Nolte-Ernsting, C.; Cowan, N. Understanding multislice CT urography techniques: Many roads lead to Rome. *Eur. Radiol.* **2006**, *16*, 2670–2686. [[CrossRef](#)] [[PubMed](#)]
22. Chow, L.C.; Kwan, S.W.; Olcott, E.W.; Sommer, G. Split-Bolus MDCT Urography with Synchronous Nephrographic and Excretory Phase Enhancement. *Am. J. Roentgenol.* **2007**, *189*, 314–322. [[CrossRef](#)] [[PubMed](#)]
23. Van Der Molen, A.J.; Cowan, N.C.; Mueller-Lisse, U.G.; Nolte-Ernsting, C.C.A.; Takahashi, S.; Cohan, R.H. CT urography: Definition, indications and techniques. A guideline for clinical practice. *Eur. Radiol.* **2008**, *18*, 4–17. [[CrossRef](#)] [[PubMed](#)]
24. Fendler, W.P.; Eiber, M.; Beheshti, M.; Bomanji, J.; Calais, J.; Ceci, F.; Cho, S.Y.; Fanti, S.; Giesel, F.L.; Goffin, K.; et al. PSMA PET/CT: Joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0. *Eur. J. Nucl. Med. Mol. Imaging* **2023**, *50*, 1466–1486. [[CrossRef](#)] [[PubMed](#)]
25. Seifert, R.; Emmett, L.; Rowe, S.P.; Herrmann, K.; Hadaschik, B.; Calais, J.; Giesel, F.L.; Reiter, R.; Maurer, T.; Heck, M.; et al. Second Version of the Prostate Cancer Molecular Imaging Standardized Evaluation Framework Including Response Evaluation for Clinical Trials (PROMISE V2). *Eur. Urol.* **2023**, *83*, 405–412. [[CrossRef](#)] [[PubMed](#)]
26. Hofman, M.S.; Hicks, R.J.; Maurer, T.; Eiber, M. Prostate-specific Membrane Antigen PET: Clinical Utility in Prostate Cancer, Normal Patterns, Pearls, and Pitfalls. *RadioGraphics* **2018**, *38*, 200–217. [[CrossRef](#)] [[PubMed](#)]
27. Mamlins, E.; Novruzov, E.; Watabe, T.; Mori, Y.; Dabir, M.; Mattes-György, K.; Antke, C.; Henke, J.; Boschheidgen, M.; Kirchner, J.; et al. Biphasic contrast-enhanced [18F]PSMA-1007 PET/CT imaging to improve the detection of local relapse of prostate cancer. *EJNMMI Res.* **2025**, *15*, 61. [[CrossRef](#)] [[PubMed](#)]
28. Gelikman, D.G.; Mena, E.; Lindenberg, L.; Azar, W.S.; Rath, N.; Yilmaz, E.C.; Harmon, S.A.; Schuppe, K.C.B.; Hsueh, J.Y.B.; Huth, H.B.; et al. Reducing False-Positives Due to Urinary Stagnation in the Prostatic Urethra on 18F-DCFPyL PSMA PET/CT With MRI. *Clin. Nucl. Med.* **2024**, *49*, 630–636. [[CrossRef](#)] [[PubMed](#)]

29. Jilg, C.A.; Drendel, V.; Rischke, H.C.; Beck, T.; Vach, W.; Schaal, K.; Wetterauer, U.; Schultze-Seemann, W.; Meyer, P.T. Diagnostic Accuracy of Ga-68-HBED-CC-PSMA-Ligand-PET/CT before Salvage Lymph Node Dissection for Recurrent Prostate Cancer. *Theranostics* **2017**, *7*, 1770–1780. [[CrossRef](#)] [[PubMed](#)]
30. Rosar, F.; Hügler, M.J.; Ries, M.; Bartholomä, M.; Maus, S.; Fries, P.; Khreish, F.; Ezziddin, S. Benefit of including CT urography in [68Ga]PSMA-11 PET/CT with low-dose CT: First results from a larger prostate cancer cohort analysis. *Q. J. Nucl. Med. Mol. Imaging* **2022**, *66*, 280–289. [[CrossRef](#)] [[PubMed](#)]
31. Fendler, W.P.; Calais, J.; Allen-Auerbach, M.; Bluemel, C.; Eberhardt, N.; Emmett, L.; Gupta, P.; Hartenbach, M.; Hope, T.A.; Okamoto, S.; et al. ⁶⁸Ga-PSMA-11 PET/CT Interobserver Agreement for Prostate Cancer Assessments: An International Multicenter Prospective Study. *J. Nucl. Med.* **2017**, *58*, 1617–1623. [[CrossRef](#)] [[PubMed](#)]
32. Spena, G.; Moretti, T.B.; Dávila, F.S.; DOS Anjos, G.; Khan, I.; Calace, F.P.; Aveta, A.; Pandolfo, S.D.; Tufano, A.; Izzo, A.; et al. Ga68-PSMA PET for lymph node staging in intermediate and high-risk prostate cancer patients undergoing robotic assisted radical prostatectomy. *Minerva Urol. Nephrol.* **2024**, *76*, 467–473. [[CrossRef](#)] [[PubMed](#)]
33. Derlin, T.; Weiberg, D.; von Klot, C.; Wester, H.-J.; Henkenberens, C.; Ross, T.L.; Christiansen, H.; Merseburger, A.S.; Bengel, F.M. 68Ga-PSMA I&T PET/CT for assessment of prostate cancer: Evaluation of image quality after forced diuresis and delayed imaging. *Eur. Radiol.* **2016**, *26*, 4345–4353. [[CrossRef](#)] [[PubMed](#)]
34. Uprimny, C.; Bayerschmidt, S.; Kroiss, A.S.; Fritz, J.; Nilica, B.; Sviridenka, H.; Decristoforo, C.; von Guggenberg, E.; Horninger, W.; Virgolini, I.J. Early Injection of Furosemide Increases Detection Rate of Local Recurrence in Prostate Cancer Patients with Biochemical Recurrence Referred for ⁶⁸Ga-PSMA-11 PET/CT. *J. Nucl. Med.* **2021**, *62*, 1550–1557. [[CrossRef](#)] [[PubMed](#)]
35. Schmuck, S.; Mamach, M.; Wilke, F.; von Klot, C.A.; Henkenberens, C.; Thackeray, J.T.; Sohns, J.M.; Geworski, L.; Ross, T.L.; Wester, H.-J.; et al. Multiple Time-Point 68Ga-PSMA I&T PET/CT for Characterization of Primary Prostate Cancer. *Clin. Nucl. Med.* **2017**, *42*, e286–e293. [[CrossRef](#)] [[PubMed](#)]
36. Chen, Q.; Dong, L.; Xu, L.; Zhao, H.; Li, L.; Huang, G.; Liu, J.; Chen, R. Comparison of clinical performance between late and standard total-body [68 Ga]Ga-PSMA-11 in biochemical recurrent prostate cancer. *Eur. J. Nucl. Med. Mol. Imaging* **2025**, *52*, 1249–1256. [[CrossRef](#)] [[PubMed](#)]
37. Silverman, S.G.; Leyendecker, J.R.; Amis, E.S. What Is the Current Role of CT Urography and MR Urography in the Evaluation of the Urinary Tract? *Radiology* **2009**, *250*, 309–323. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.