



Clinical performance of [^{18}F]piflufolastat PET/CT on a 194-cm LAFOV PET/CT system in prostate cancer

Pierpaolo Alongi¹ · Agostino Chiaravalloti^{2,3} · Simone Morea⁴ · Daniele Di Biagio⁴

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Abstract

Purpose To assess the clinical performance of [^{18}F]piflufolastat PET/CT acquired on a total-body 194-cm LAFOV PET/CT system in patients with prostate cancer, with particular focus on detection rate, site-specific disease distribution, and the association between PET findings and serum PSA levels.

Methods This retrospective single-centre study included 103 consecutive patients with prostate cancer who underwent clinically indicated [^{18}F]piflufolastat PET/CT on 194-cm LAFOV PET/CT. Indications were primary staging ($n=42$) or suspected recurrence ($n=61$). Only the 8-min acquisition dataset was analyzed. PET findings were assessed on a patient basis and across predefined anatomical sites. In the recurrence subgroup, the association between PSA and PET positivity was evaluated using Mann–Whitney U test, logistic regression with log-transformed PSA, ROC analysis, and Spearman correlation with the number of positive sites.

Results Overall, PET was positive in 91/103 patients (88.3%), negative in 8/103 (7.8%), and indeterminate in 4/103 (3.9%). Positivity was observed in all patients scanned for primary staging (42/42, 100.0%) and in 49/61 patients (80.3%) referred for recurrence. The most frequent positive sites were primary lesion (57.3%), lymph nodes (35.0%), and bone (24.3%). In recurrence, PSA was significantly higher in PET-positive than in non-positive cases (median 2.40 vs. 0.42 ng/mL, $p<0.001$). Log-transformed PSA was significantly associated with PET positivity (OR 7.40, 95% CI 2.18–25.11; $p=0.001$), with an AUC of 0.912 (95% CI 0.828–0.974). PSA also correlated with the number of positive sites ($\rho=0.620$, $p<0.001$).

Conclusion [^{18}F]piflufolastat PET/CT on 194-cm LAFOV PET/CT showed high clinical performance in prostate cancer, with strong PSA-dependent yield in recurrence and effective depiction of site-specific disease distribution.

Keywords Prostate cancer · Piflufolastat · PSMA PET/CT · 194-cm LAFOV PET/CT · Total-body PET/CT · PSA

Introduction

Prostate-specific membrane antigen (PSMA) PET/CT has become an integral imaging modality in prostate cancer, particularly for primary staging and biochemical recurrence, and current procedural guidelines provide standardized recommendations for patient selection, acquisition, and image interpretation [1]. In parallel, long axial field-of-view PET/CT systems have introduced a substantial gain in sensitivity and count statistics. The new total-body PET system with 194-cm axial field of view combines very high sensitivity, approximately 430-ps time-of-flight performance, and sub-3-mm spatial resolution near the center of the field of view, thereby enabling low-dose imaging, shortened acquisitions, delayed scans with preserved image quality, and whole-body dynamic imaging [2, 3]. In prostate cancer, the first research application was generated predominantly with [^{68}Ga]Ga-PSMA-11. Biodistribution

Pierpaolo Alongi and Agostino Chiaravalloti contributed equally to this work.

✉ Agostino Chiaravalloti
agostino.chiaravalloti@uniroma2.it

¹ Department of Biomedicine, Neurosciences and Advanced Diagnostics, University of Palermo, Piazza Marina 61, Palermo 90139, Italy

² Department of Biomedicine and Prevention, University of Rome Tor Vergata, Via Montpellier 1, Rome 00133, Italy

³ IRCCS Neuromed, Via Atinense, 18, Pozzilli, IS 86077, Italy

⁴ Nuclear Medicine Centre, San Pietro Fatebenefratelli Hospital—Express Diagnostics, Via Cassia 600, Rome 00189, Italy

of radiopharmaceuticals using a dynamic study, demonstrated lesion uptake increasing rapidly during the first minutes after injection, whereas urinary bladder activity remained initially low and then rose progressively; pathological lesion uptake exceeded bladder activity at approximately 6–8 min post-injection, and lesion uptake from 35 to 59 min was similar to that at 60 min, supporting both very early pelvic assessment and slightly earlier standard imaging windows [3]. In a subsequent study in biochemical recurrence, total-body [^{68}Ga] Ga-PSMA-11 PET/CT showed a significantly higher overall detection rate than conventional PET/CT (91.0% vs. 74.0%), with the greatest advantage in patients with PSA ≤ 2 ng/mL and Gleason score ≤ 8 , together with better image quality and a clearer benefit from delayed acquisition [4]. Evidence with ^{18}F -labeled PSMA tracers on 194-cm LAFOV PET/CT systems is still limited and has so far been driven mainly by protocol-oriented studies. Total-body dynamic ^{18}F -PSMA-11 imaging showed tumor accumulation as early as 45 s after injection, rapid blood-pool clearance, and favorable tumor-to-background kinetics; Patlak influx constant (Ki) correlated well with 2-tissue-compartment Ki ($r = 0.858$), and an imaging time of 30–35 min was suggested as a reasonable balance between lesion conspicuity and background activity [5]. Consistently, in treatment-naïve prostate cancer, dual-time-point ^{18}F -PSMA-11 PET/CT at 30 and 60 min post-injection yielded identical lesion detection, whereas nonspecific bone uptake was more frequent at 60 min [6]. Beyond platform-specific ^{18}F -PSMA-11 data, a low-dose study with [^{18}F]PSMA-1007 found no significant reduction in lesion detection when acquisitions were shortened from 10 to 5 min, further supporting the feasibility of abbreviated protocols on high-sensitivity systems [7]. Compared with [^{18}F]PSMA-1007, [^{18}F]piflufolastat has been proposed as a tracer with a lower burden of nonspecific or equivocal bone uptake, potentially reducing interpretative uncertainty in the skeleton and the need for additional work-up in selected cases [8]. Combined with the higher sensitivity of a 194-cm LAFOV PET/CT system, this may be advantageous for the detection of low-volume disease [8].

In view of previous consideration, the present study aimed to assess the clinical performance of [^{18}F]piflufolastat PET/CT on a total-body 194-cm LAFOV PET/CT scanner in patients with prostate cancer, focusing on detection rate, site-specific distribution of positive findings, and the relationship between PET positivity and serum PSA in a real clinical scenario.

Materials and methods

Patient selection

This retrospective single-centre study included consecutive patients with prostate cancer who underwent clinically

indicated [^{18}F]piflufolastat PET/CT at the Nuclear Medicine Centre, Fatebenefratelli–Ospedale San Pietro, Rome, Italy, between 13 June 2025 and 6 March 2026. Patients were referred for either primary staging or assessment of suspected recurrence in the setting of rising serum PSA after prior curative-intent treatment. Clinical and imaging data were retrieved from the institutional database after anonymization. Only scans reconstructed from the 8-minute acquisition protocol were included in the present analysis. Patients with incomplete clinical data or non-assessable scans were excluded.

The study was conducted in accordance with the Declaration of Helsinki and approved by the local Ethics Committee. Given the retrospective design of the study and the use of anonymized data, the requirement for written informed consent was waived.

PET/CT acquisition

PET/CT studies were performed on a total-body 194-cm axial field-of-view digital PET/CT scanner (uExplorer, United Imaging Healthcare, Shanghai, China) [2]. Patients were prepared according to current PSMA PET/CT recommendations, including hydration and bladder emptying before scanning [1]. PET data were acquired in list mode and could be reconstructed using different effective acquisition durations, including shorter static reconstructions and dynamic datasets, according to the institutional protocol. For the present study, analysis was restricted to the 8-min dataset because this acquisition duration is routinely used for clinical interpretation and provides robust counting statistics.

PET images were reconstructed using an ordered-subset expectation maximization (OSEM) algorithm (3 iterations, 20 subsets) with both time-of-flight (TOF) and point-spread-function (PSF) modeling. Reconstruction parameters were as follows: 192×192 matrix, 700-mm field of view, 2.886-mm slice thickness, and 3.0-mm FWHM post-reconstruction smoothing filter. Standard corrections included attenuation correction, scatter correction, randoms correction, normalization, alignment matrix correction, and decay correction. The reconstructed PET axial coverage was approximately 184.2 cm.

Low-dose CT was acquired for attenuation correction and anatomical localization. CT images were reconstructed in the axial plane with 2.0-mm slice thickness, 2.0-mm increment, 512×512 matrix, and 500-mm field of view. CT reconstruction was performed in standard mode with adaptive filter, KARL 3D, and B_SOFT_B kernel, with extended field of view enabled.

Image interpretation and scan classification

PET/CT images were reviewed according to the E-PSMA standardized reporting guidelines [9]. Two complementary

E-PSMA-based assessments were used. Visual tracer uptake was graded using the PSMA expression V scale (0–3), whereas lesion interpretation and final scan classification were based on the E-PSMA score (1–5). A V-scale score of 0 indicated uptake below blood pool, score 1 uptake equal to or above blood pool and lower than liver, score 2 uptake equal to or above liver and lower than parotid gland, and score 3 uptake equal to or above parotid gland [9]. For the purposes of the present study, patient-based scan classification was defined as follows. Scans were considered positive when at least one lesion in a typical site for prostate cancer was assigned an E-PSMA score of 4 or 5, corresponding to intense tracer uptake in a typical site without a definite CT substrate (score 4) or with a definite CT correlate (score 5). Scans were considered indeterminate when no positive lesion was present and only equivocal findings were identified, corresponding to E-PSMA score 3, i.e. faint uptake in an atypical site, or faint uptake in a typical site/intense uptake in an atypical site. Scans were considered negative in the absence of suspicious PSMA-avid findings within the predefined anatomical sites included in the analysis. Site-specific analysis was then performed by recording the presence or absence of uptake in the primary lesion, prostate bed, seminal vesicles, lymph nodes, bone, visceral organs, and lungs [9]. The PSMA expression V scale was used for descriptive purposes, whereas final scan classification was based on E-PSMA criteria.

Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR), whereas categorical variables were reported as counts and percentages. Comparisons of serum PSA values between PET-positive and non-positive patients were performed using the Mann–Whitney U test. Because all scans in the primary staging subgroup were PET-positive, inferential analyses exploring the association between PSA and PET findings were restricted to patients referred for suspected recurrence. In this subgroup, the association between serum PSA and PET positivity was further assessed by univariable logistic regression using log-transformed PSA values. Receiver operating characteristic (ROC) analysis was performed to evaluate the discriminatory ability of PSA for PET positivity. The relationship between PSA and disease extent on PET, expressed as the number of positive predefined anatomical sites, was assessed using Spearman's rank correlation coefficient. A two-sided p value < 0.05 was considered statistically significant.

Results

A total of 103 consecutive patients with prostate cancer were included in the study. Of these, 42/103 (40.8%) underwent [^{18}F]piflufolastat PET/CT for primary staging, whereas 61/103 (59.2%) were referred for evaluation of suspected recurrence. Baseline patient characteristics are summarized in Table 1.

Median age was 74 years (IQR 66.5–79) in the overall cohort, 72 years (IQR 65–77) in the primary staging subgroup, and 76 years (IQR 66–80) in the recurrence subgroup. Overall, median body weight was 80.0 kg (IQR 72.0–88.0), median injected activity was 191.0 MBq (IQR 188.0–196.0), median dose-to-weight ratio was 2.40 MBq/kg (IQR 2.19–2.65), and median uptake time was 98 min (IQR 92–107). Serum PSA was available in 102/103 patients (99.0%) and was higher in the staging group than in the recurrence group (8.37 ng/mL [IQR 5.14–14.07] vs. 1.82 ng/mL [IQR 0.61–3.84]). Gleason score was available in 81/103 patients (78.6%), with Gleason ≥ 8 representing the largest category overall (29/81, 35.8%).

Hormonal therapy was recorded in 20/103 patients (19.4%) overall and in 20/61 patients (32.8%) in the recurrence subgroup.

Patient-based PET outcomes are reported in Table 2. Overall, PET was classified as positive in 91/103 patients (88.3%), negative in 8/103 (7.8%), and indeterminate in 4/103 (3.9%). PET positivity was observed in all patients undergoing primary staging (42/42, 100.0%), whereas in the recurrence setting PET was positive in 49/61 patients (80.3%).

With regard to the predefined 8-minute site-specific fields, uptake was recorded in the primary lesion in 59/103 patients (57.3%), in the prostate bed in 6/103 (5.8%), in the seminal vesicles in 11/103 (10.7%), in lymph nodes in 36/103 (35.0%), in bone metastases in 25/103 (24.3%), in visceral metastases in 1/103 (1.0%), and in lung metastases in 3/103 (2.9%). At least one local site (primary lesion, prostate bed, or seminal vesicles) was involved in 67/103 patients (65.0%), whereas at least one metastatic site (lymph nodes, bone, visceral organs, or lung) was recorded in 45/103 patients (43.7%).

In the staging group, disease was predominantly local, with uptake in the primary lesion in 41/42 patients (97.6%), while nodal and bone involvement were observed in 10/42 (23.8%) and 7/42 (16.7%), respectively. In the recurrence group, the most frequent positive sites were lymph nodes (26/61, 42.6%) and bone metastases (18/61, 29.5%), whereas uptake in the prostate bed was observed in 6/61 patients (9.8%). An illustrative case of multifocal disease identified at the initial staging is presented in Fig. 1,

Table 1 Baseline characteristics of the study population

Characteristic	Overall (n=103)	Primary staging (n=42)	Recurrence (n=61)
Age, years	74 (66.5–79)	72 (65–77)	76 (66–80)
Body weight, kg	80.0 (72.0–88.0)	80.0 (70.2–89.0)	79.0 (72.0–86.0)
Injected activity, MBq	191.0 (188.0–196.0)	192.0 (187.5–194.8)	190.0 (188.0–196.0)
Dose-to-weight ratio, MBq/kg	2.40 (2.19–2.65)	2.41 (2.17–2.67)	2.39 (2.20–2.63)
Uptake time, min	98 (92–107)	98 (90–107)	98 (93–107)
Serum PSA, ng/mL*	4.19 (1.29–8.97)	8.37 (5.14–14.07)	1.82 (0.61–3.84)
PSA available, n	102	42	60
Gleason score available, n	81	38	43
Gleason 6	10/81 (12.3%)	6/38 (15.8%)	4/43 (9.3%)
Gleason 7 (3+4)	15/81 (18.5%)	10/38 (26.3%)	5/43 (11.6%)
Gleason 7 (4+3)	27/81 (33.3%)	6/38 (15.8%)	21/43 (48.8%)
Gleason ≥8	29/81 (35.8%)	16/38 (42.1%)	13/43 (30.2%)
Prior prostate surgery†, n (%)	42 (40.8%)	1 (2.4%)	41 (67.2%)
Prior radiotherapy, n (%)	42 (40.8%)	0 (0.0%)	42 (68.9%)
Hormonal therapy, n (%)	20 (19.4%)	0 (0.0%)	20 (32.8%)

Data are median (IQR) unless otherwise indicated

*Latest available PSA value before PET/CT

† Includes prostatectomy/TURP entries as recorded in the dataset

whereas Fig. 2 displays a recurrence of lymph nodes within the recurrence group.

Because all staging scans were positive, subsequent inferential analyses assessing the relationship between PET findings and PSA were restricted to the recurrence subgroup. In this subgroup, PSA was available in 60/61 patients (98.4%).

PSA was significantly higher in PET-positive than in non-positive recurrence cases (negative or indeterminate), with a median PSA of 2.40 ng/mL (IQR 1.09–4.40) versus 0.42 ng/mL (IQR 0.29–0.61) ($p < 0.001$, Mann–Whitney U test). In the recurrence subgroup, the interval between the latest available PSA determination and PET/CT was 15 days (IQR 7.5–32.5; mean 32.9 ± 44.8 days; range 1–235).

Table 2 PET outcomes based on patient-level classification and predefined 8-minute site-specific fields. Positive scans were defined by the presence of at least one lesion scored as E-PSMA 4 or 5; indeterminate scans included only equivocal findings scored as E-PSMA 3

PET outcome	Overall (n=103)	Primary staging (n=42)	Recurrence (n=61)
PET positive	91 (88.3%)	42 (100.0%)	49 (80.3%)
PET negative	8 (7.8%)	0 (0.0%)	8 (13.1%)
PET indeterminate	4 (3.9%)	0 (0.0%)	4 (6.6%)
Primary lesion	59 (57.3%)	41 (97.6%)	18 (29.5%)
Prostate bed	6 (5.8%)	0 (0.0%)	6 (9.8%)
Seminal vesicles	11 (10.7%)	6 (14.3%)	5 (8.2%)
Lymph nodes	36 (35.0%)	10 (23.8%)	26 (42.6%)
Bone metastases	25 (24.3%)	7 (16.7%)	18 (29.5%)
Visceral metastases	1 (1.0%)	0 (0.0%)	1 (1.6%)
Lung metastases	3 (2.9%)	1 (2.4%)	2 (3.3%)
Any local site‡	67 (65.0%)	41 (97.6%)	26 (42.6%)
Any metastatic site§	45 (43.7%)	12 (28.6%)	33 (54.1%)

‡ Primary lesion, prostate bed, or seminal vesicles

§ Lymph nodes, bone, visceral organs, or lung

Among patients with prior treatment history, the interval between the most recent treatment and PET/CT was 16.5 months (IQR 7.8–51.15; mean 39.3 ± 42.1 months; range 1.87–163.73). On univariable logistic regression, log-transformed PSA was significantly associated with PET positivity (OR 7.40, 95% CI 2.18–25.11; $p = 0.001$). ROC analysis showed a strong discriminatory performance of PSA for PET positivity (AUC 0.912, 95% CI 0.828–0.974), and the corresponding ROC curve is shown in Fig. 3. In addition, PSA correlated positively with the number of PET-positive anatomical sites (Spearman $\rho = 0.620$, $p < 0.001$), indicating that higher PSA values were associated not only with a greater likelihood of PET positivity, but also with a wider distribution of disease. Detection rate also increased progressively across PSA categories in the recurrence subgroup, as shown in Fig. 4.

The four indeterminate scans corresponded to isolated equivocal foci with low-level tracer uptake (PSMA expression V=1, E-PSMA score=3): a pulmonary nodule (SUVmax 2.0), a skeletal focus without CT correlate (SUVmax 1.4), a right vesicourethral-space nodule (SUVmax 1.3), and a focus in the anterior arch of the left fourth rib without CT correlate (SUVmax 4.6). In one patient, the pulmonary lesion was subsequently confirmed as metastatic on follow-up PET/CT, although it had been classified as indeterminate at the time of the index scan (Table 3).

Discussion

The present study shows that [^{18}F]piflufolastat PET/CT acquired on a 194-cm LAFOV PET/CT system provides a high positivity rate in routine clinical practice, with

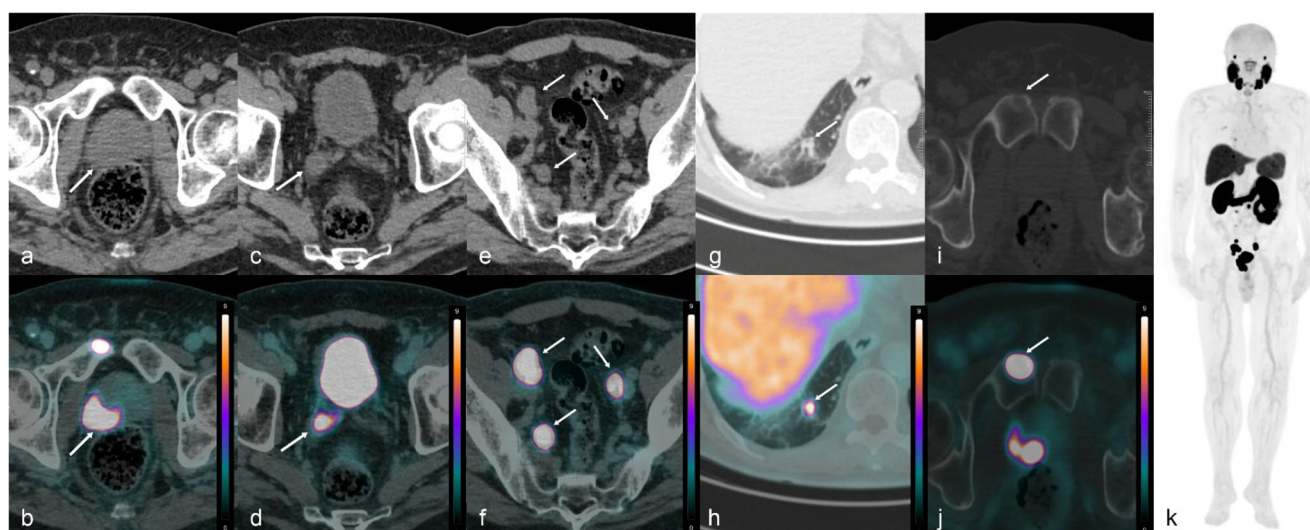


Fig. 1 Representative case of primary staging by [^{18}F]piflufolastat PET/CT on a 194-cm LAFOV PET/CT

A patient referred for primary staging underwent [^{18}F]piflufolastat PET/CT on a 194-cm LAFOV PET/CT system. (a, b) Unenhanced CT and fused PET/CT images of the primary prostatic lesion. (c, d) Unenhanced CT and fused PET/CT images of involvement of the right

seminal vesicle. (e, f) Unenhanced CT and fused PET/CT images of pelvic nodal metastases. (g, h) Unenhanced CT and fused PET/CT images of a pulmonary metastasis. (i, j) Unenhanced CT and fused PET/CT images of a pelvic bone lesion. (k) Maximum intensity projection image demonstrates multifocal PSMA-avid disease

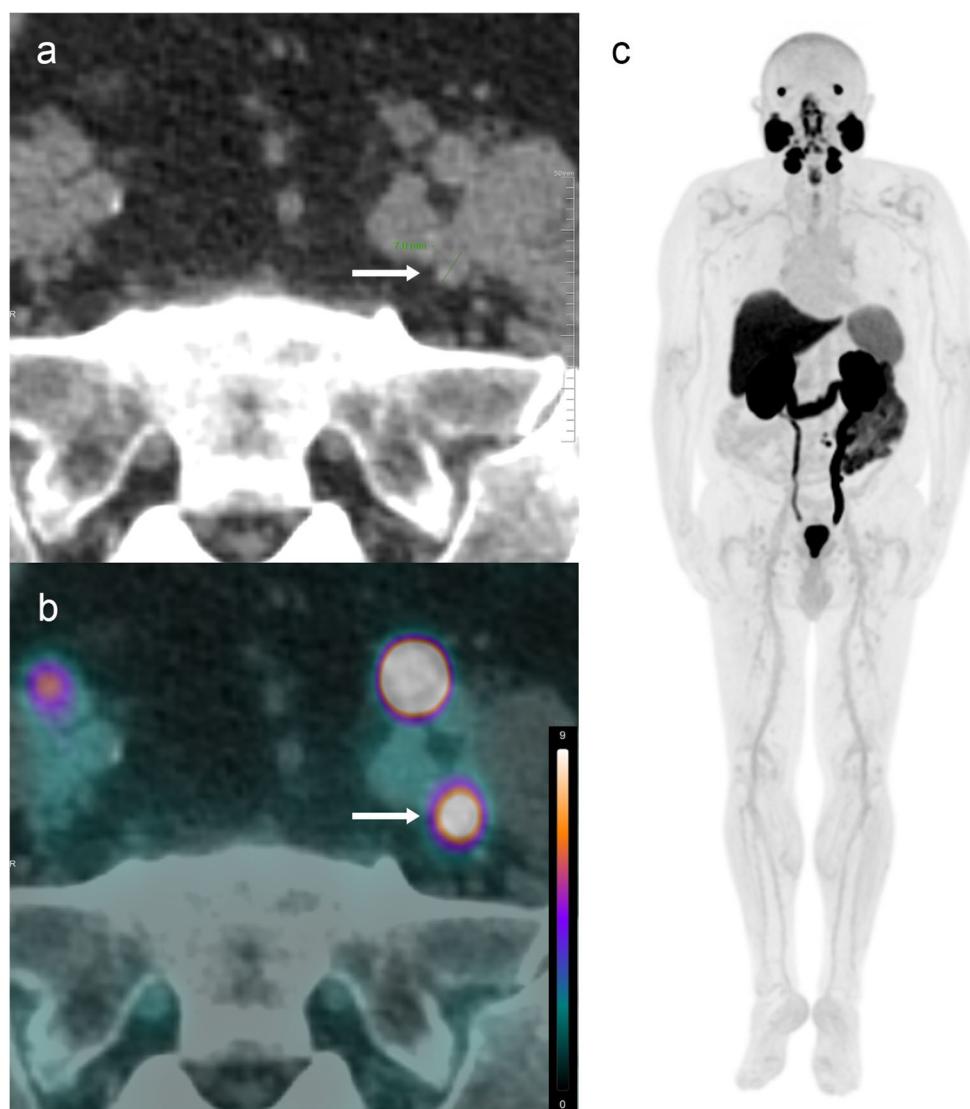
positive findings in 88.3% of the overall cohort, 100.0% of patients imaged for primary staging, and 80.3% of those referred for suspected recurrence. In the recurrence setting, PET positivity was strongly PSA-dependent, and PSA was also associated with disease extent, as reflected by the significant correlation between serum PSA and the number of positive anatomical sites. Overall, our findings support the clinical robustness of [^{18}F]piflufolastat PET/CT on a 194-cm LAFOV PET/CT system while also confirming that, in recurrence, scan yield remains closely related to tumor burden. A first point that deserves emphasis is that the available literature on prostate cancer imaging with uExplorer remains limited and is still dominated by studies using [^{68}Ga]Ga-PSMA-11 and, more recently, [^{18}F]PSMA-11 rather than piflufolastat. From a technical standpoint, the PET system used in this study offers a 194-cm axial field of view, very high sensitivity, and near-isotropic spatial resolution around 3 mm at the centre of the field of view, thereby enabling shortened acquisitions, reduced-count protocols, delayed imaging, and true whole-body dynamic studies. In prostate cancer, early total-body work with [^{68}Ga]Ga-PSMA-11 showed that lesion uptake rises rapidly during the first minutes after injection whereas bladder activity increases later, supporting both very early pelvic assessment and a potentially shorter standard imaging window [3]. In biochemical recurrence, Wang et al. further reported a significantly higher detection rate for total-body than conventional [^{68}Ga]Ga-PSMA-11 PET/CT (91.0% vs. 74.0%), with a particularly evident advantage in patients with PSA ≤ 2 ng/mL [4]. On the ^{18}F side, published data on the same

LAFOV-PET system have remained more protocol-oriented than clinically outcome-driven: dynamic ^{18}F -PSMA-11 imaging suggested favourable tumor-to-background kinetics and a practical acquisition window around 30–35 min [5], while dual-time-point imaging in treatment-naïve disease showed comparable lesion detection at 30 and 60 min with less nonspecific bone uptake at the earlier time point [6]. Leveraging an ^{18}F -PSMA tracer with a “cleaner” skeletal specificity profile together with a 194-cm LAFOV PET system can further reduce misleading bone calls while exploiting the scanner’s higher sensitivity for confident detection of low-volume disease [10, 11]. In this context, the present study extends the clinical evidence base specifically for [^{18}F]piflufolastat on a 194-cm LAFOV PET/CT system.

This distinction matters because [^{18}F]piflufolastat should not simply be collapsed into the broader category of “ ^{18}F -PSMA tracers” when discussing the literature. Although the biological target is shared, the available evidence is tracer-specific in terms of pivotal validation, reported endpoints, interpretive pitfalls, and regulatory approval. In that sense, our data do not merely add another PSMA-on-total-body report; rather, they address a still underdeveloped intersection between [^{18}F]piflufolastat and LAFOV total-body PET/CT. At present, the literature on 194-cm LAFOV PET/CT has largely established the technical rationale of the platform, but dedicated clinical series using [^{18}F]piflufolastat on this scanner remain sparse.

Compared with standard axial field-of-view (SAFOV) PET/CT systems, long-axial-field-of-view (LAFOV) PET/

Fig. 2 Representative case of recurrence detected by [^{18}F]piflufolastat PET/CT on a 194-cm LAFOV PET/CT. At the time of imaging, serum PSA was 0.53 ng/mL. **(a)** Unenhanced CT image of the pelvic lymph node. **(b)** Fused PET/CT image showing focal tracer uptake in the same lesion, consistent with nodal recurrence (SUVmax 23.6). **(c)** Maximum intensity projection image illustrating lesion conspicuity despite the low PSA level



CT provides substantially higher geometric sensitivity and improved count statistics over a much larger axial coverage. In practical terms, this may translate into shorter acquisition times, lower administered activity, improved image quality, and potentially higher lesion detectability, particularly in patients with low-volume disease. In the present setting, these advantages are clinically relevant because they support the feasibility of an 8-min acquisition protocol while maintaining a high positivity rate and meaningful PSA-dependent stratification in the recurrence subgroup.

When our findings are compared with the broader [^{18}F]piflufolastat literature generated on other scanners (mostly SAFOV), they appear clinically credible. In the phase 2/3 OSPREY study, which was designed around diagnostic accuracy rather than simple positivity, [^{18}F]piflufolastat PET/CT showed a median specificity of 97.9% and sensitivity of 40.3% for pelvic nodal disease in high-risk primary staging, while in the cohort with known or suspected

recurrent/metastatic disease the median sensitivity and positive predictive value for extraprostatic lesions were 95.8% and 81.9%, respectively. In CONDOR, a phase III study in biochemical recurrence with negative or equivocal standard imaging, the correct localization rate was 84.8%–87.0%, patient-level detection ranged from 59% to 66%, and intended management changed in 63.9% of evaluable patients [12]. These studies established the clinical validity of [^{18}F]piflufolastat, but their endpoints are not directly interchangeable with the patient-based positivity rate used in our analysis.

A more pragmatic comparison is provided by studies using [^{18}F]piflufolastat on conventional PET/CT systems in recurrence. In the prospective crossover PYTHON trial, [^{18}F]piflufolastat achieved a significantly higher per-patient detection rate than [^{18}F]fluoromethylcholine (58% vs. 40%), with a greater impact on patient management and broadly consistent performance at low PSA values [13]. In

Fig. 3 Receiver operating characteristic (ROC) curve of serum PSA for predicting PET positivity in the recurrence subgroup. ROC analysis based on individual patient-level data in the recurrence subgroup with available PSA values ($n=60$) showed strong discriminatory performance of serum PSA for PET positivity, with an AUC of 0.912 (95% CI 0.828–0.974). The ROC curve includes selected operating points for PSA thresholds of ≥ 0.5 , ≥ 1.0 , ≥ 2.0 , and ≥ 5.0 ng/mL. Each marker represents the sensitivity and false-positive rate ($1 - \text{specificity}$) associated with that threshold. Thus, the point for $\text{PSA} \geq 5.0$ ng/mL indicates a low sensitivity because only a subset of PET-positive patients had PSA values at or above this level, whereas its position on the y-axis reflects 100% specificity in the present cohort

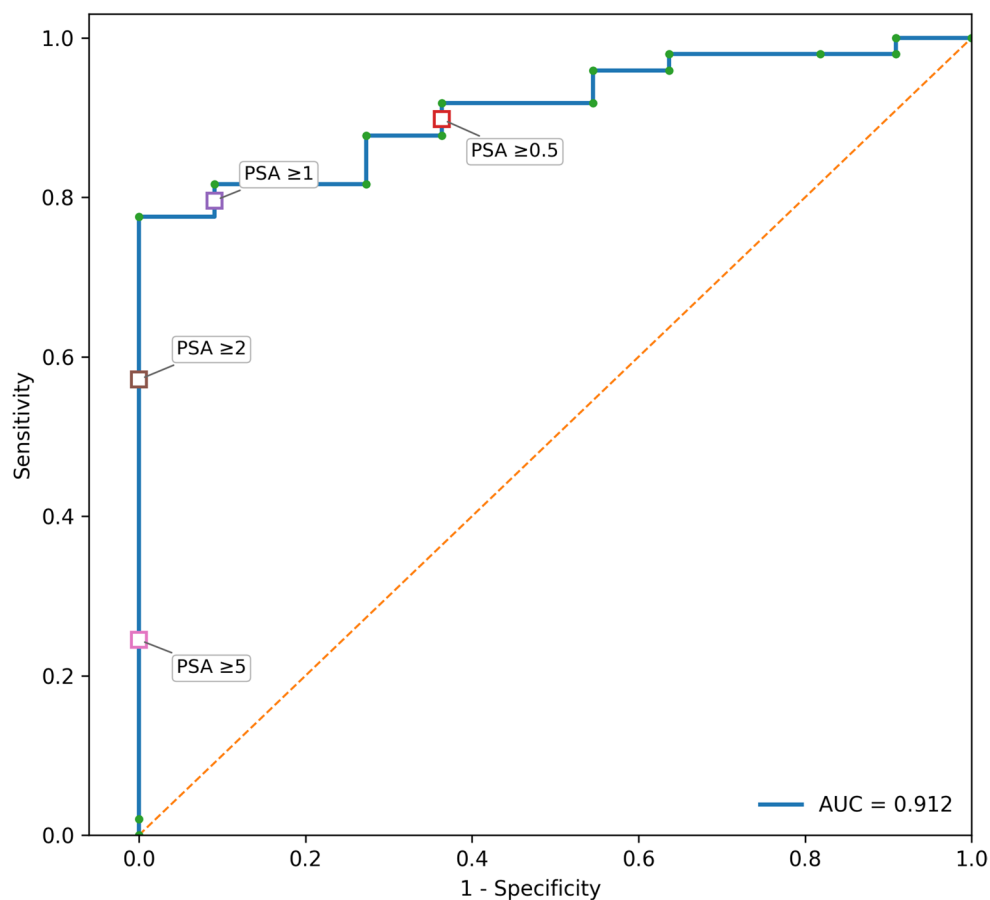


Fig. 4 Detection rate of [^{18}F] piflufolastat PET/CT according to PSA categories in patients referred for suspected recurrence. Bar plot showing the patient-based detection rate across PSA categories in the recurrence subgroup with available PSA data ($n=60$). PET positivity increased progressively with increasing PSA, from 41.7% at $\text{PSA} < 0.5$ ng/mL to 100.0% at $\text{PSA} \geq 2.0$ ng/mL

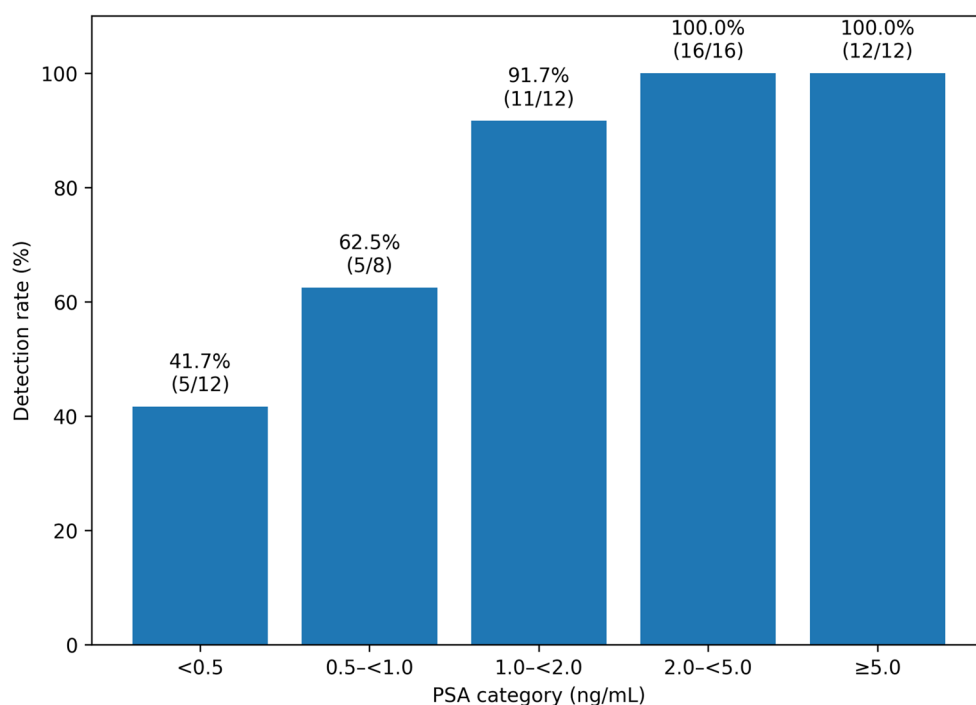


Table 3 Association between serum PSA and PET findings in the recurrence subgroup

Analysis	Result
Patients with available PSA	60/61
PET-positive PSA, ng/mL	2.40 (1.09–4.40)
Non-positive PSA, ng/mL*	0.42 (0.29–0.61)
Mann–Whitney U test	$p < 0.001$
Logistic regression (logPSA)	OR 7.40 (95% CI 2.18–25.11), $p = 0.001$
ROC analysis	AUC 0.912 (95% CI 0.828–0.974)
Correlation between PSA and number of positive sites	Spearman rho = 0.620, $p < 0.001$

Data are median (IQR) unless otherwise indicated

* Non-positive = PET-negative + PET-indeterminate

the prospective single-center experience reported by Metser et al., [^{18}F]piflufolastat PET was positive in 43/47 patients (91.5%) with biochemical failure after primary therapy, including local recurrence in 19.2%, oligometastatic disease in 34.0%, and extensive metastatic disease in 38.3% [14]. In high-risk primary staging, Wondergem et al. evaluated [^{18}F]piflufolastat PET/CT as a first-line modality in 160 patients and found metastatic disease in 56%, with management changes in 17% and the need for additional imaging in only 1% [15]. Taken together, these studies suggest that the performance observed in our cohort is plausible within the broader [^{18}F]piflufolastat literature, although direct numerical comparisons remain limited by differences in population, referral pattern, disease spectrum, and study endpoint.

The PSA dependence observed in our recurrence subgroup is probably the most clinically relevant finding of the study. In our series, higher PSA values were associated not only with a higher likelihood of PET positivity, but also with a broader distribution of disease. This pattern is coherent with the published [^{18}F]piflufolastat literature. In the CONDOR trial, the study enrolled a population with a median PSA of 0.8 ng/mL and still achieved a disease detection rate of 59%–66% despite negative or equivocal conventional imaging [12]. Likewise, the digital-versus-analog system comparison by Maliha et al. suggested that scanner technology may particularly matter in early biochemical failure: in patients with PSA < 0.5 ng/mL, digital piflufolastat PET/CT showed a higher positivity rate than analog PET/CT (69% vs. 37%), whereas at PSA $\geq$ 0.5 ng/mL the two technologies performed similarly [16]. This observation is relevant to the interpretation of our results, because it supports the idea that high-sensitivity systems may offer the greatest practical advantage at lower disease burden, even though our study was not designed as a direct scanner comparison. Another practical point is that our results were obtained on a very high-sensitivity platform using a short 8-minute acquisition protocol. Even without a same-tracer

comparator arm on a conventional scanner, the combination of high positivity, strong PSA association, and site-based disease mapping suggests that [^{18}F]piflufolastat PET on 194-cm LAFOV PET/CT can support an efficient clinical workflow without obvious loss of clinical usefulness. However, our study should not be interpreted as proof of scanner superiority. Because no head-to-head comparison with [^{18}F]piflufolastat on a standard-axial-field PET/CT system was performed, the contribution of scanner geometry cannot be separated from case mix, PSA distribution, or referral bias.

From a practical standpoint, our findings suggest that [^{18}F]piflufolastat PET/CT on a 194-cm LAFOV PET/CT system may support an efficient clinical workflow in prostate cancer imaging, combining abbreviated acquisition time with high positivity rate and clinically meaningful site-based disease mapping. This may be particularly relevant in centres aiming to optimize scanner throughput without an apparent loss of clinical usefulness.

The study has limitations. First, it is retrospective and single-center. Second, the cohort included both primary staging and recurrence, and inferential analyses were necessarily driven by the recurrence subgroup because all staging scans were PET-positive. Third, the outcome measure was patient-based positivity with site distribution rather than histology-based diagnostic accuracy or correct localization rate, which limits direct comparison with pivotal trials such as OSPREY and CONDOR [12, 17]. Fourth, no direct comparator arm was available, either with [^{18}F]piflufolastat on a conventional scanner or with another PSMA tracer on uExplorer. Therefore, our results should be interpreted as evidence of strong clinical performance, not of formal superiority. Histopathological confirmation beyond the primary histopathological diagnosis/Gleason score was not systematically available within the routine clinical workflow and was therefore not included in the present analysis.

In addition, prior hormonal therapy was recorded in 20/61 patients in the recurrence subgroup, although treatment information was not fully available for all cases. Hormonal therapy may have influenced PSA values at the time of imaging and, although the intervals between the latest PSA determination and PET/CT and between the most recent treatment and PET/CT were available, the retrospective design did not allow a treatment-adjusted analysis of PSA kinetics.

Overall, our findings suggest that [^{18}F]piflufolastat 194-cm LAFOV PET/CT is a clinically effective approach for prostate cancer imaging, particularly when interpreted in conjunction with serum PSA. The main value of the present study is not that it demonstrates superiority over all other systems, but that it extends the piflufolastat literature into a platform setting for which dedicated clinical evidence remains limited. In this sense, the study helps bridge

two literatures that have so far remained partly separate: the technically oriented 194-cm LAFOV PET/CT literature and the tracer-specific [^{18}F]piflufolastat/PSMA literature generated predominantly on conventional SAFOV PET/CT systems.

Conclusion

The present study provides initial clinical evidence on the performance of [^{18}F]piflufolastat PET/CT acquired on a 194-cm LAFOV total-body system in patients with prostate cancer. In this real-world cohort, the method showed a high positivity rate, particularly in primary staging, and a strong PSA-dependent yield in the recurrence setting. Higher PSA values were associated with both a greater likelihood of PET positivity and a wider anatomical distribution of disease. These findings support the clinical feasibility of combining [^{18}F]piflufolastat with a high-sensitivity LAFOV PET/CT platform using an abbreviated 8-minute acquisition protocol, although dedicated comparative studies are needed to clarify the incremental contribution of scanner geometry.

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Author Contributions Pierpaolo Alongi and Agostino Chiaravalloti contributed equally to this work.

Conceptualization: Pierpaolo Alongi, Agostino Chiaravalloti.

Methodology: Pierpaolo Alongi, Agostino Chiaravalloti, Simone Morea, Daniele Di Biagio.

Data curation: Simone Morea, Daniele Di Biagio.

Formal analysis: Agostino Chiaravalloti, Pierpaolo Alongi.

Investigation: Simone Morea, Daniele Di Biagio.

Writing—original draft preparation: Agostino Chiaravalloti, Pierpaolo Alongi.

Writing—review and editing: all authors.

Supervision: Pierpaolo Alongi, Agostino Chiaravalloti.

All authors read and approved the final manuscript.

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Data availability The datasets generated and analyzed during the current study are not publicly available due to institutional and privacy restrictions but are available from the corresponding author on reasonable request.

Declarations

Ethics approval The study was conducted in accordance with the Declaration of Helsinki and approved by the local Ethics Committee.

Consent to participate Given the retrospective design of the study and the use of anonymized clinical and imaging data, the requirement for written informed consent was waived by the local Ethics Committee.

Consent for publication Not applicable.

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