ISSN 1669-9106 MEDICINA (Buenos Aires) 0000: 00: 00-00

Original article

COMPARING [18F]-PSMA-1007, [18F]-CHOLINE POSITRON EMISSION TOMOGRAPHY, COMPUTERIZED TOMOGRAPHY AND BONE SCINTIGRAPHY IN PROSTATE CANCER RECURRENCE

MIGUEL ANGEL BERGERO[1], PATRICIO MODINA[1], MARÍA ARCELUZ[2], LILIANA RIOS[2], LUCAS COSTA[3], CARLOS DAVID[1], FERNANDO FACCIO[2]

[1]Departamento Urología, Sanatorio San Gerónimo, [2]Departamento Medicina Nuclear, Sanatorio San Gerónimo, [3]Departamento de Bioestadística, Universidad Nacional del Litoral, Santa Fe, Argentina

Postal address Miguel Angel Bergero, Grupo San Gerónimo, San Jerónimo 3134, 3000 Santa Fe, Argentina
E-mail: angelbergero@hotmail.com
Received: 5-III-2025
Accepted: 22-VII-2025

Abstract

Introduction: Prostate cancer (PC) remains a significant public health concern in developed countries. Following initial treatment, patients may experience biochemical recurrence of prostate cancer (BRPC), defined by an increase in prostate-specific antigen (PSA) levels. [18F]-PSMA positron emission tomography (PET) has shown greater accuracy in detecting clinical prostate cancer recurrence (CPCR), however most evidence comes from retrospective case series with limited prospective studies comparing this novel molecule to conventional diagnostic methods in developed countries.

Materials and methods: A prospective observational, descriptive, analytical study of concordance analysis between imaging methods was conducted on a sample of patients with BRPC following curative or first-line treatment.

Results: Seventy-seven patients with BRPC were analyzed. Imaging studies revealed positive results in 6% of computerized tomographies (CT), 12% of bone scintigraphies (BS), 35% of [18F] choline PET scans, and notably in 84% of [18F] PSMA 1007 PET scans (χ^2 = 22.7, DF = 3; p <0.0001). A significant relationship was observed between the positivity of [18F] PSMA 1007 PET/CT and increasing PSA levels, reaching 100% with PSA ≥ 2 ng/mL.

Discussion: [18F] PSMA 1007 PET demonstrated high efficacy in localizing recurrent PC in BRPC patients compared to CT, BS, and [18F] choline PET, allowing for better restaging of patients with BRPC compared to CT, BS, and [18F] choline PET

Key words: prostate cancer, PET-CT, prostate-specific antigen

Resumen

Comparación entre tomografía por emisión de positrones (PET) con [18F]-PSMA, tomografía computarizada y centellograma óseo en la recurrencia del cáncer de próstata

Introducción: El cáncer de próstata (CP) sigue siendo un importante problema de salud pública en los países desarrollados. Tras el tratamiento inicial, los pacientes pueden experimentar una recurrencia bioquímica del cáncer de próstata (RBCP) La tomografía por emisión de positrones (PET) con [18F]-PSMA ha demostrado una mayor precisión en la detección de la recurrencia del cáncer de próstata; sin embargo, la mayoría de las evidencias provienen de series de casos retrospectivos, y los estudios prospectivos son limitados.

Materiales y métodos: Se realizó un estudio prospectivo, observacional, descriptivo y analítico de análisis de concordancia entre métodos de imagen en una muestra de pacientes con RBCP tras tratamiento curativo o de primera línea.

Resultados: Se analizaron 77 pacientes con RBCP. Los estudios de imagen revelaron resultados positivos en un 6% de las tomografías computarizadas (TC), un 12% de los centellogramas óseos (CO), un 35% de los PET con [18F] colina y, notablemente, en un 84% de los PET con [18F] PSMA 1007 (χ^2 = 22.7; DF = 3; p <0.0001). Se observó una relación significativa entre la positividad del PET con [18F] PSMA 1007 y los niveles crecientes de PSA, alcanzando un 100% en pacientes con PSA ≥ 2 ng/mL.

Discusión: El PET con [18F] PSMA 1007 demostró una alta eficacia en la localización del CP recurrente en pacientes con RBCP, en comparación con la TC, la CO y el PET con [18F] colina, permitiendo una mejor reestadificación de los pacientes con RBCP en comparación con los métodos convencionales.

Palabras clave: cáncer de próstata, PET, antígeno prostático especifico

KEY POINTS
Current knowledge

- [18F] PSMA-1007 PET demonstrates higher sensitivity than CT, BS and [18F]-choline PET for detecting recurrent prostate cancer. Its accuracy improves with increasing PSA levels, aiding in early diagnosis and patient restaging.

Contribution of the article to current knowledge

- This study confirms that [18F] PSMA-1007 PET detects a higher number of lesions than conventional imaging and achieves 100% positivity at PSA ≥ 2 ng/mL, reinforcing its diagnostic superiority in biochemical recurrence.

Prostate cancer (PC) remains a significant public health concern in developed countries[1]. Following initial treatment, patients may experience biochemical recurrence of prostate cancer (BRPC), defined by an increase in prostate-specific antigen (PSA) levels. Optimal diagnosis of PC recurrence remains a critical concern for medical teams owing to the fact that PC has the highest attributable mortality rate among cancers[2,3]. Treatment decisions are taken on the basis of the localization and extent of the disease. Distinguishing between limited metastatic disease and widespread metastatic disease is essential, as the prognosis and subsequent therapeutic strategies differ significantly[4,5].

Guidelines for managing BRPC recommend imaging studies, including CT, BS, and PET with choline for patients with rising PSA levels to detect findings indicative of metastatic lesions. However, an elevated PSA level alone cannot identify the site of recurrence, and conventional imaging techniques demonstrate limited accuracy in this context. Their low sensitivity often leads to numerous negative results complicating the visualization of clinical prostate cancer recurrence (CPCR). Moreover, the sensitivity of these diagnostic methods is further reduced when PSA levels are low[6-8].

To address these limitations, PET using the radiotracer 18F-fluoride ([18F]) associated with prostate-specific membrane antigen (PSMA) has emerged as a valuable tool for evaluating patients with BRPC[9]. PSMA is a type II transmembrane glycoprotein that is overexpressed in PC. A recently developed radiopharmaceutical employs small molecular weight molecules, ligands, or inhibitors of PSMA, which bind to the active site of the extracellular domain of this transmembrane protein, enabling its localization through positron emission tomography[10,11]. [18F]-PSMA PET has shown greater accuracy in detecting CPCR; however, most evidence comes from retrospective case series with limited prospective studies comparing this novel molecule to conventional diagnostic methods in developed countries[12].

The primary objective of this study was to evaluate the concordance of [18F]-PSMA-1007 PET compared to CT, BS, and [18F]-choline PET in diagnosing metastases in patients with BRPC. Secondary objectives included evaluating the effectiveness of [18F]-PSMA-1007 PET in localizing CPCR compared to CT, BS, and [18F]-Choline PET, as well as analyzing the correlation between PSA levels and the CPCR detection rates of CT, BS, [18F]-choline PET, and [18F]-PSMA-1007 PET.

Materials and methods

A prospective observational study with an analytical design and concordance analysis among imaging methods was conducted on a sample of patients with BRPC

following curative or first-line treatment. Imaging studies were performed at the diagnostic unit of *Sanatorio Privado San Gerónimo*, Santa Fe, between July 2019 and December 2021.

To determine the concordance degree between diagnostic methods without a pilot test, the standard error formula for Kappa was applied, using $\alpha = 0.05$ and Kappa ≥ 0.30. Consequently, the total sample size was estimated at 75 patients with BRPC.

This study included patients with BRPC who met the following criteria: serum PSA values > 0.2 ng/mL after radical prostatectomy; serum PSA values > 2 ng/mL above nadir following radiotherapy; or, after first-line hormonal therapy, a 25% increase in PSA nadir with an initial value > 1 ng/mL in the context of testosterone levels < 50 ng/dL. All patients were required to have undergone [18F]-choline PET conducted within one month prior to their inclusion in the study. Additionally, all patients diagnosed with BRPC underwent CT and BS before [18F]-choline PET, in accordance with standardized guidelines for evaluating BRPC (Fig. 1).

Radiotracer

The [18F]-PSMA-1007 marker, produced at the Bacon SAIC Laboratories Cyclotron (Uruguay 136, Villa Martelli, Buenos Aires, Argentina) using the IBA Synthera® synthesizer from Radio Pharma Solutions (Chemin du Cyclotron 3, Louvain-la-Neuve, Belgium), was used. Besides, the synthesis was conducted with the PSMA-1007 kit from ABX Advanced Biochemical Compounds GmbH (H. Glaeser Strasse 10-14, Radeberg, Germany).

Imaging protocol

[18F] - PSMA -1007 PET was performed in accordance with Heidelberg University protocols, as described by Giesel[13]. When not contraindicated, a bolus injection of [18F]-PSMA-1007 was administered intravenously at a dose of 301 MBq (range: 255–347 MBq). Patients were instructed to void to minimize bladder uptake between 93 ± 26 minutes following radioisotope administration. PETimages were then acquired by using a Philips GEMINI GXL 16 hybrid system (Koninklijke Philips N.V., Royal Philips, Amstelplein 2, 1096 BC Amsterdam, Netherlands). It merged PET images with low-dose CT, delivering high-quality morphological information for diagnostic purposes and enabling attenuation correction. Images were subsequently reconstructed in 3D mode, with a 144 x 144 matrix, and an average duration of 10 minutes. A whole-body PET scan was performed from the feet to the cranial vault with the arms raised (to minimize artifacts) after positioning the patient supine on the scanner table.

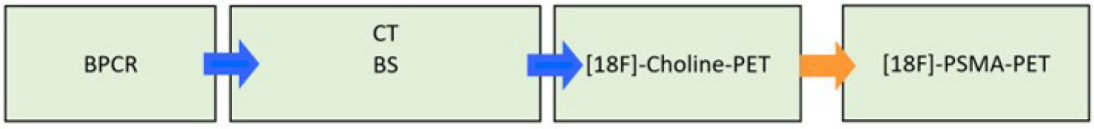
Emission data were corrected for random, scatter, and decay. The ordered-subset expectation-maximization (OSEM) 3D algorithm, using a blob and LOR implementation, was applied for image reconstruction with 3 iterations and 33 subsets. The resulting images were then filtered transaxially using the Gauss method with a full width at half maximum (FWHM) of 5 mm. The PET images were acquired on a Philips GEMINI GXL 16® hybrid system.

Interpretation of [18F]-PSMA-1007 PET results

The results obtained from the imaging study were carefully evaluated and described in detail by three professionals specialized in nuclear medicine and radiology, each with extensive experience in PET. The interpretation of images was carried out by a nuclear medicine physician and a radiologist through visual or qualitative analysis, along with semiquantitative assessment via SUVmax. [18F]-PSMA-1007 PET was considered positive when a focal increase in tracer uptake was observed exceeding the background and not associated with physiological uptake.

The professionals completed a qualitative interpretation report that documented the number of positive lesions (0, 1, 2, 3, 4, 5, 6-10, > 10) and the site of recurrence: local (prostate or prostatic bed), regional lymph nodes, non-regional lymph nodes, and bone or visceral metastases. Regional lymph nodes were defined as those locat-

Figure 1 | Patient inclusion flowchart



BPCR: biochemical prostate cancer recurrence; BS: bone scintigraphy; CT: computerized tomography

ed below the bifurcation of the iliac arteries while other lymph node locations were considered non-regional or metastatic.

The report was compared with the results of [18F]-choline PET and standard imaging studies.

Definition of variables

The analyzed variables included age, PSA trigger (PSA value, ng/mL, prompting the study request), and PSA velocity (PSAV: increase in PSA value, ng/mL/year, over a minimum period of 18 months for calculation). PSAV was calculated using the online application https://psadt.sau-net.org/. PSA doubling time (PSADT: in months, calculated over a minimum period of 12 months) was also determined using the same online application. Other variables included PSA nadir (the lowest PSA value, ng/mL, reached after any treatment for PC), time to recurrence (the number of months from PC treatment until the patient experienced BRPC), Gleason score of PC from biopsy, number of positive prostate biopsies, highest percentage of positive prostate biopsy samples, PC staging (T = tumor confined to the prostate or prostatic bed, N1 = metastasis in a regional lymph node, M1a = metastasis in a non-regional lymph node, M1b = bone metastasis, and M1c = visceral metastasis), CT positivity, BS positivity, [18F]-choline PET positivity, [18F]-PSMA-1007 positivity, and D'Amico risk (ordinal qualitative). D'Amico's risk scale was used for risk scoring with results categorized as low risk (Gleason score ≤ 6 and/or PSA < 10 ng/mL), intermediate risk, and high risk (Gleason score 8-10 and/or PSA > 20 ng/mL). SUV max was assessed and positivity was categorized according to PSA levels (< 0.5 ng/mL, ≥ 0.5 to < 1 ng/mL, ≥ 1 to < 2 ng/mL, and ≥ 2 ng/mL). Additionally, the number of positive lesions was recorded based on the study methods.

Ethical considerations

Patients provided informed consent before enrollment in compliance with the ethical standards and research protocols established by the Ethics Committee of the National University of Litoral.

Study authorization

The protocol is registered with the National Health Research Registry (RENIS) under registration code IS002591.

Data analysis and processing technique

Statistical data analysis was performed using SPSS Statistics v23.0 software (IBM Inc., Armonk, NY, USA). Descriptive statistics for qualitative variables were calculated using absolute and relative frequencies, with 95% confidence intervals applied to the corresponding proportions. Quantitative variables were assessed for normality using the Kolmogorov-Smirnov test and were described using either the mean and standard deviation or the median and interquartile range, as appropriate. Central tendency statistics were accompanied by 95% confidence intervals.

For subgroup analysis, patients were divided into four groups based on their PSA levels: <0.5 ng/mL, ≥0.5 to <1 ng/mL, ≥1 to <2 ng/mL, and ≥2 ng/mL. The Mann-Whitney test (or Kruskal-Wallis for three groups) and the independent samples t-test (or ANOVA for three groups) were used to assess significant differences in the number of positive lesions between PSA groups. Differences in proportions between PSA groups and positive lesion findings were assessed using Pearson's Chi-Square test. The significance level was set at $\alpha = 0.05$.

Concordance between the results obtained with [18F]-PSMA-1007 PET, [18F]-choline PET and standard studies was assessed using Cohen's Kappa index. The degree of concordance was categorized as follows: 0 = poor; 0.01-0.20 = slight; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61-0.80 = substantial; 0.81–1.00 = almost perfect.

Results

A total of 77 BRPC patients were analyzed, and their sample characteristics are shown in Table 1. Imaging studies revealed positivity in 6% of CT, 12% of BS, 35% of [18F]-choline PET, and 84% of [18F]-PSMA-1007 PET, showing a statistically significant difference ($\chi^2 = 22.7$, DF = 3; $p < 0.0001$). Patients presented a median PSA trigger of 3.1 (Q1-Q3: 0.80 to 9.1) ng/mL, median PSAV of 1.70 (Q1-Q3: 0.65 to 6) ng/mL/year, and median PSADT time of 5.95 (Q1-Q3: 3.1 to 12) months.

[18F] PSMA 1007 PET demonstrated an increase in positivity as PSA levels rose. This method showed 50% positivity with PSA < 0.5 ng/mL and 100% positivity with PSA ≥ 2 ng/mL (Table 2). In patients where [18F] PSMA 1007 PET was positive (median: 5, Q1-Q3: 1.5-13) and [18F] choline PET was also positive (median: 2, Q1-Q3: 1-4), [18F] PSMA 1007 PET showed an equal or greater number of lesions ($U = 4.95$, $p = 0.02$) (Fig. 2).

In the analysis of BRPC sites, [18F] PSMA 1007 PET consistently demonstrated superior detection compared to standard methods. For local recurrence (T), [18F] PSMA 1007 PET detected 66 lesions versus 25 with [18F] choline PET, while CT and BS showed no detection. In lymph nodes

Table 1 | Description of the variables analyzed

Variable	Clinical characteristics
Age [year] Media ± ED	68.5 ± 8.0
Family history of prostate cancer %(n)	13 (10)
Time to recurrence [month] Me (Q1 – Q3)	24 (6-60)
Gleason score in prostate biopsy %(n)	
6	8 (6)
7	45 (32)
8	26 (19)
≥ 9	21 (15)
Greater extent of prostate biopsy core involvement [%] Me (Q1 – Q3)	67.5 (45.0-87.5)
Number of prostate biopsy cores involved [%]	5 (4-7)
Me (Q1 – Q3)	
Treatment %(n)	
Radiotheraphy	21 (15)
Prostatectomy with lymphadenctomy	28 (22)
Prostatectomy without lymphadenctomy	28 (22)
1st line of androgen deprivation	23 (18)
Surgical Gleason score %(n)	
6	5 (2)
7	51 (22)
8	23 (10)
≥ 9	21 (9)
PSA before treatment [ng/ml] Me (Q1 – Q3)	10.7 (6.7-18.7)
PSA Trigger [ng/mL] Me (Q1 – Q3)	3.1 (0.8-9.1)
PSA nadir [ng/mL] Me (Q1 – Q3)	0.12 (0.02-0.80)
PSAV [ng/mL/year] Me (Q1 – Q3)	0.65 (1.7-6.0)
PSADT [month] Me (Q1 – Q3)	6 (3-12)

(N), [18F] PSMA 1007 PET identified 38 lesions compared to 10 with [18F] choline PET, with no detection by CT or BS. For distant metastases, [18F] PSMA 1007 PET detected 17 lesions in non-regional lymph nodes (M1a) compared to 3 each for CT and [18F] choline PET. In bone lesions (M1b), [18F] PSMA 1007 PET identified 23 lesions, followed by [18F] choline PET (14 lesions), BS (12 lesions), and CT (4 lesions). Only [18F] PSMA 1007 PET detected visceral metastases (M1c), identifying 4 lesions. Overall, extraprostatic involvement was detected by [18F] PSMA 1007 PET in 49% of cases (n = 38).

Concordance of study methods

When assessing overall concordance between diagnostic methods, 83% of negative CT scans ($\kappa = 0.025$), 82% of negative BS ($\kappa = 0.048$), and 76% of negative [18F] choline PET ($\kappa = 0.18$) were found to be positive with [18F] PSMA 1007 PET, indicating poor concordance. In the heat map diagram illustrating general concordance, a significant discordance between CT, BS, [18F] choline PET, and [18F] PSMA 1007 PET is evident, with the latter demonstrating a substantially higher positivity rate compared to standard diagnostic methods (Fig. 3).

Concordance between diagnostic methods was analyzed according to TNM classification. High discordance was observed between CT, BS, [18F] choline PET, and [18F] PSMA 1007 PET in N1, M1a, and M1c, with [18F] PSMA 1007 PET demonstrating a substantially higher positivity rate compared to standard diagnostic meth-

Table 2 | Analysis of PSA and positivity of conventional imaging methods and [18F] PSMA1007 PET

Variables	Total (n=77)	PSA Trigger <0.5 ng/mL	≥0.5 a <1 ng/mL	≥1 a <2 ng/mL	≥2 ng/mL
PSA Trigger [ng/ml] Median (Q1-Q3)	3.1 (0.80; 9.10)	0.31 (0.26; 0.40)	0.73 (0.57; 0.79)	1.29 (1.08; 1.56)	8.00 (3.91; 18.0)
PSAV* [ng/mL/year] Median (Q1-Q3)	1.70 (0.65; 6.00)	0.22 (0.10; 0.60)	0.8 (0.50; 1.80)	1.00 (1.40; 1.80)	3.5 (1.55; 21.5)
PSADT[ε] [month] Me (Q1-Q3)	5.95 (3.10; 12.00)	10 (7; 15)	4 (3; 7)	8 (4; 16)	5 (3; 11)
Positive CT % (n)	6 (5)	0 (0)	0 (0)	0 (0)	11 (5)
Positive BS % (n)	12 (9)	0 (0)	0 (0)	9 (1)	17 (8)
Positive [18F] choline PET % (n)	35 (27)	0 (0)	9 (1)	20 (2)	52 (24)
Positive [18F] PSMA 1007 PET % (n)	84 (65)	50 (5)	64 (7)	70 (7)	100 (46)

ods (Figs. 3, 4). However, in the assessment of M1b, considerable concordance was observed between BS and [18F] PSMA 1007 PET (Fig. 3). Nonetheless, Figure 4 reveals that [18F] PSMA 007 PET identified 11 more M1b lesions than BS (23 bone lesions compared to 12).

Diagnostic test analysis: [18F] PSMA 1007 PET

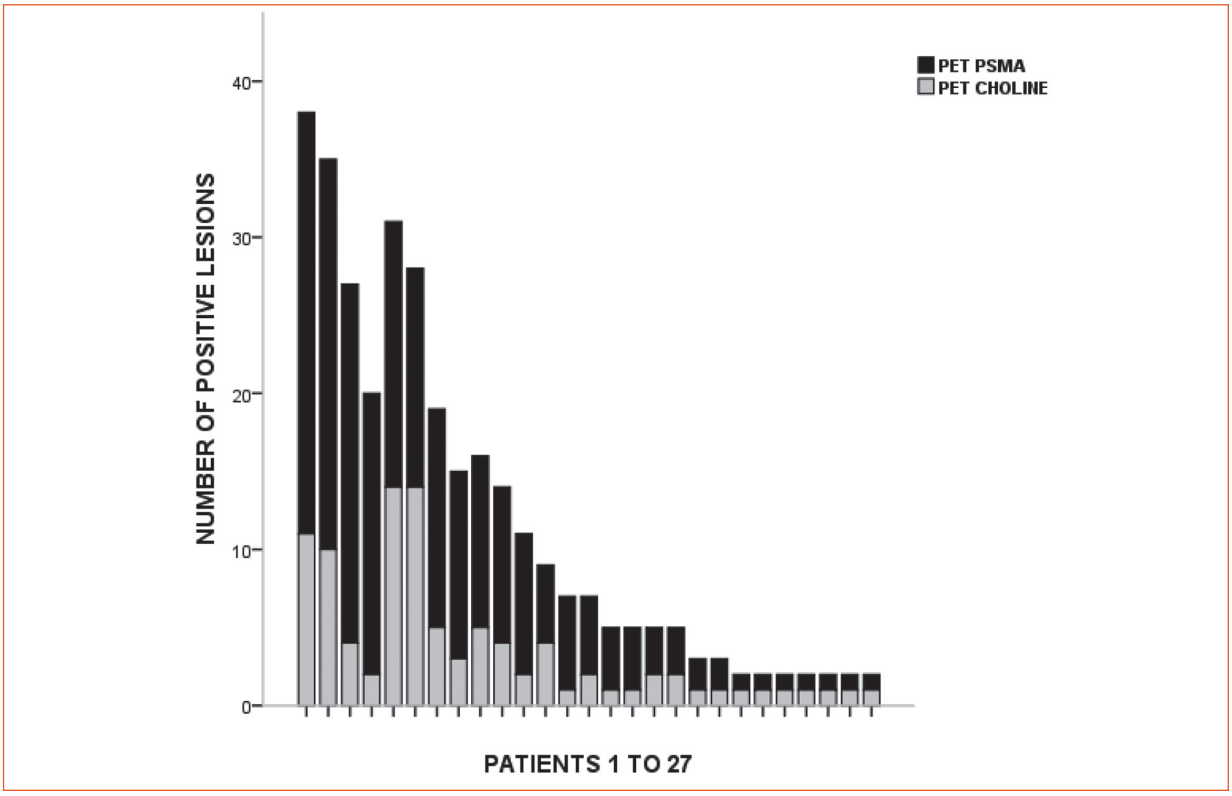
Positive [18F] PSMA 1007 PET scans had a median PSA trigger of 4.3 ng/mL (Q1-Q3: 1.30-12.5), while negative [18F] PSMA 1007 PET scans had a median trigger PSA of 0.61 ng/mL (Q1-Q3: 0.31-0.95). This difference was statistically significant (U = 666.5, p = 0.001). Positive [18F] choline PET scans had a median PSA trigger of 14.35 ng/mL (Q1-Q3: 4.56-37.3), while negative [18F] choline PET scans had a median PSA trigger of 1.38 ng/mL (Q1-Q3: 0.60-3.63). This difference was statistically significant (U = 1069.5, p = 0.001).

Discussion

There is growing scientific evidence showing that PSMA PET outperforms conventional methods in assessing patients with BRPC due to its high diagnostic accuracy. However, there is limited comparative data between PSMA PET and choline PET, and no existing evidence comparing [18F] PSMA-1007 PET with [18F] choline PET.

Alonso et al. conducted a prospective study to evaluate the detection rate of [68Ga] PSMA-11 PET compared to standard diagnostic methods in men with PC and BRPC, aiming to demonstrate the added value of PSMA PET[14]. The study, which included 36 patients with BRPC, reported a detection rate of 75% for [68Ga] PSMA-11 PET, compared to 53% for [11C] choline PET. For patients with PSA values ≥ 2 ng/mL, the detection rate was 73% for [11C] choline PET and 95% for [68Ga] PSMA-11 PET. For those with PSA values ≤ 1 ng/mL, the detection rate was 22% for [11C] Choline PET and 33% for [68Ga] PSMA-11 PET. Additionally, the number of lesions detected per patient was higher for [11C] choline PET in those with PSA ≥ 3.3 ng/mL, while for [68Ga] PSMA-11 PET, the number of lesions detected was independent of PSA values at the same cutoff. Pelvic

Figure 2 | Number of positive lesions in both [18F] PSMA 1007 PET and [18F] choline PET



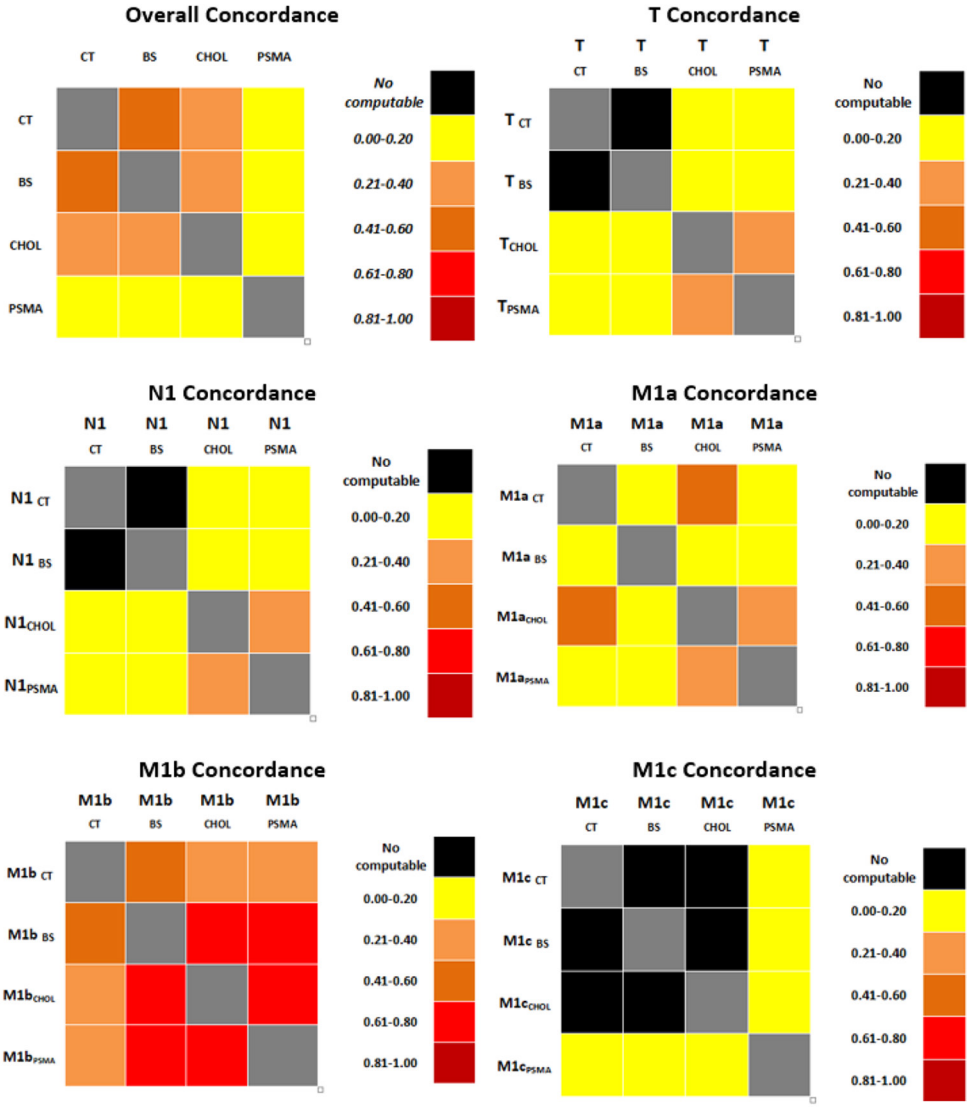
metastases were identified in 69% of patients with [68Ga] PSMA-11, 50% with [11C] choline, and 58% with MRI.

Cantiello et al. conducted an observational study of 43 BRPC patients who underwent laparoscopic radical prostatectomy and subsequently had both [64Cu] PSMA-617 PET and [18F] choline PET for restaging[15]. This study revealed a positivity rate of 74.5% for [64Cu] PSMA-617 PET compared to 44% for [18F] choline PET. [64Cu] PSMA-617 PET consistently outperformed [18F] choline PET across all PSA values, with detection rates of 57% vs 14% for PSA values between 0.2 to 0.5 ng/mL, and 60% vs. 30% for PSA values between 0.5 to 1 ng/mL.

Schwenck et al. analyzed 103 BRPC patients who underwent whole-body PET using both [68Ga] PSMA-11 and [11C] choline, evaluating suspicious lesions both visually and semi-quantitatively[16]. Metastases in lymph nodes were detected in 67 of the 103 patients studied. Among those with positive lymph nodes, 39% had lesions detected only with [68Ga] PSMA-11, while 6% had uptake only with [11C] Choline. The mean uptake in positive lymph nodes was significantly higher for [68Ga] PSMA-11, with a SUVmax of 13.3 ± 0.7, compared to [11C] choline, which had a SUVmax of 4.8 ± 0.2. Consequently, the lymph node detection rate was significantly higher with [68Ga] PSMA-11 PET (94%) compared to [11C] choline PET (71%) ($p < 0.001$). Regarding bone lesions, [68Ga] PSMA-11 PET also showed significantly higher uptake, with an SUVmax of 13.7 ± 0.6, compared to [11C] Choline PET, which had an SUVmax of 4.8 ± 0.2. Among the detected bone lesions, 62% showed uptake in both [68Ga] PSMA-11 and [11C] choline, while 36% were visible only with [68Ga] PSMA-11. This resulted in a significantly higher detection rate for [68Ga] PSMA-11 PET (98%) compared to [11C] Choline PET (64%).

Morigi et al. prospectively analyzed the diagnostic performance of [68Ga] PSMA-11 and [18F] choline PET in 38 patients with BRPC after curative treatment for PC[17]. The study demonstrated a detection rate of 33% for [18F] choline PET, compared to 66% for [68Ga] PSMA-11.

Figure 3 | Heat map diagram of general agreement levels (Kappa index) between diagnostic study methods with the clinical recurrence site using the TNM classification



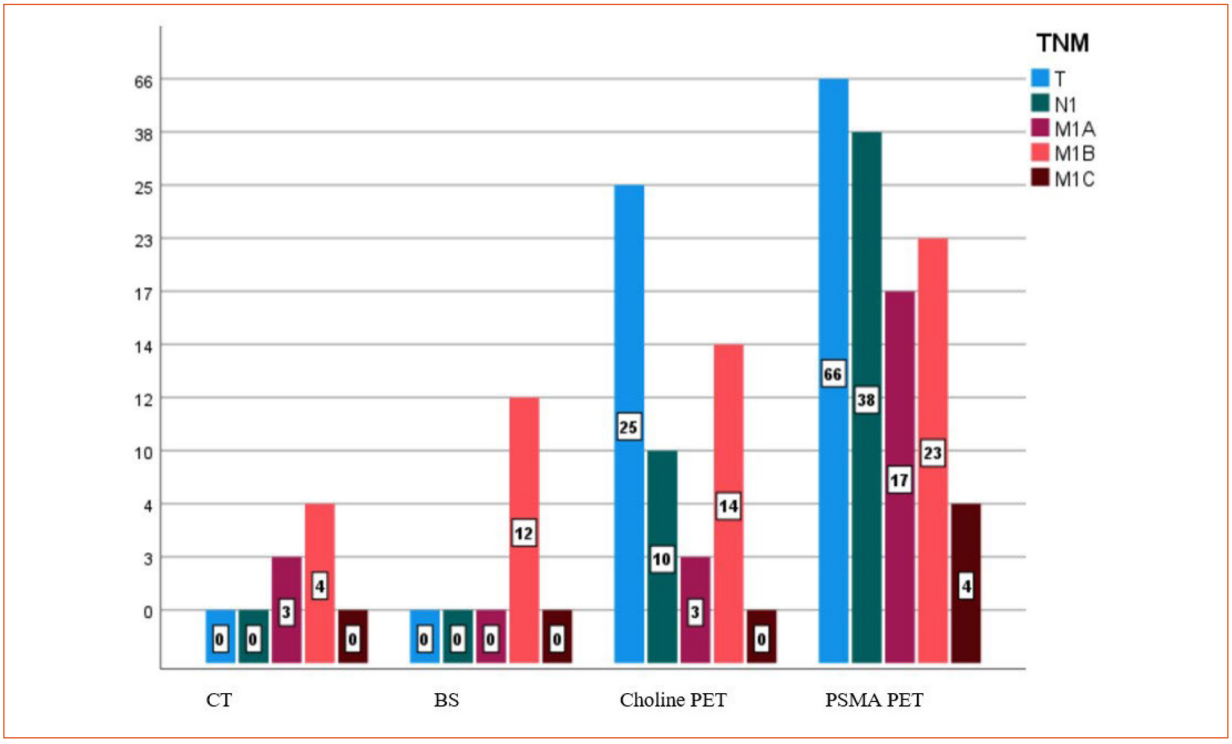
BS: bone scintigraphy; CT: computerized tomography; CHOL: Choline PET; PSMA: PSMA PET

Additionally, for PSA values below 0.5 ng/mL, the detection rate was 50% for [68Ga] PSMA-11 compared to 12.5% for [18F] choline. For PSA values between 0.5 and 2.0 ng/mL, the detection rate was 69% for [68Ga] PSMA-11 versus 31% for [18F] choline. For PSA values greater than 2.0 ng/mL, the detection rate was 86% for [68Ga] PSMA-11 compared to 57% for [18F] choline.

Afshar-Oromieh et al. also evaluated the diagnostic performance of [68Ga] PSMA-11 versus [18F] choline PET in 38 patients with BRPC[18]. This study detected a total of 78 PC-specific lesions in 32 patients using [68Ga] PSMA-11, compared to 56 lesions in 26 patients using [18F] choline. The detection rate of [68Ga] PSMA-11 was statistically significant ($p = 0.04$). All lesions detected by [18F] choline were also visible on [68Ga] PSMA-11. In [68Ga] PSMA-11 PET, SUVmax was significantly higher (>10%) in 62 of 78 lesions (79%), and the tumor-to-background ratio was greater (>10%) in 74 of 78 lesions (94.9%) compared to [18F] choline.

In a meta-analysis that incorporated the five previously analyzed studies, Treglia et al. compared the detection rates between PSMA PET and Choline PET in BRPC patients[19]. The meta-

Figure 4 | Lesions detection number from standard diagnostic methods and [18F] PSMA 1007 PET based on CPCR site according to TNM classification



PSMA: prostate-specific membrane antigen; CPCR: clinical prostate cancer recurrence; BS: bone scintigraphy; CT: computerized tomography

analysis reported a detection rate of 56% (95% CI: 37-75%) for Choline PET and 78% (95% CI: 70-84%) for PSMA PET. A significant difference in detection rates was observed only in patients with PSA ≤ 1 ng/mL, where choline PET had a detection rate of 27% (95% CI: 17-39%) compared to 54% (95% CI: 43-65%) for PSMA PET. The superiority of PSMA PET was less pronounced in patients with PSA > 1 ng/mL.

Recently, Oprea Lager et al. evaluated a total of 201 BRPC patients after radical prostatectomy (73%, median PSA of 0.46 ng/mL) or radiotherapy (27%, median PSA of 4.23 ng/mL), who underwent both [18F] DCFPyL PET and [18F] choline PET across 22 European centers in the PYTHON study[20]. The analysis revealed that the detection rate per patient was significantly higher for [18F] DCFPyL compared to [18F] choline, with a total of 58% positive versus 40% positive. The detection rate increased with higher PSA values for both tracers, with values ≤ 0.5 ng/mL at 35% vs. 30%, values from 0.5 to ≤ 1.0 ng/mL at 55% vs. 32%, values from 1.01 to < 2 ng/mL at 68% vs. 32%, and values > 2 ng/mL at 88% vs. 68% for [18F] DCFPyL and [18F] choline, respectively. In the subanalysis, [18F] DCFPyL demonstrated a significantly higher detection rate for local recurrences (21% vs. 11%), bone metastases (17% vs. 9%), and visceral metastases (9% vs. 2%). There was a trend toward higher detection of pelvic lymph nodes (29% vs. 25%, p = 0.16), although this difference was not statistically significant. No differences were observed in the detection rates between regional and non-regional lymph nodes (8% vs. 14%, p = 1). The study also found that [18F] DCFPyL PET influenced the management of 44% of relapsed patients, compared to 29% of those who only underwent [18F] choline PET.

Although the data analysis in our study was conducted with a robust methodological design and demonstrated a high positivity rate for [18F] PSMA-1007 PET compared to other diagnostic methods, it is important to acknowledge some limitations. One limitation is the lack of pathological confirmation for positive imaging results

which could lead to false positives. Another potential limitation is the imbalance in the number of positive (65 patients) versus negative (12 patients) cases within the [18F] PSMA-1007 PET group which could introduce random bias in statistical analysis.

In conclusion, our analysis revealed a low concordance between [18F]-PSMA-1007 PET and CT, BS, and [18F] choline PET in detecting PC metastases in patients with BRPC. This low concordance can be attributed to the higher positivity rate of [18F]-PSMA-1007 PET compared to the other diagnostic methods.

Furthermore, [18F]-PSMA-1007 PET demonstrated superior efficacy in localizing RCCP in patients with BRPC, in contrast to CT, BS, and [18F] choline PET. This capability allowed for improved restaging of BRPC patients compared to CT, BS, and [18F] choline PET. Moreover, [18F]-PSMA-1007 PET exhibited superior lesion detection, identifying more lesions than the other diagnostic methods.

Additionally, correlating PSA levels with the detection rate of RCCP using CT, BS, [18F] Choline PET, and [18F]-PSMA-1007 PET revealed that [18F]-PSMA-1007 PET diagnosed 50% of RCCP cases with PSA values < 0.5 ng/mL and 100% of cases with PSA values > 2 ng/mL.

Conflict of interest: None to declare

References

1. Sung H, Ferlay J, Siegel R L, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; 71: 209–49.
2. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh P C. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA* 1999; 281: 1591–7.
3. Hamdy FC, Donovan JL, Lane JA, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. *N Engl J Med* 2016; 375: 1415–24.
4. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically localized prostate cancer: AUA/ASTRO Guideline, Part I: Introduction, Risk Assessment, Staging, and Risk-Based Management. *J Urol* 2022; 208: 10–8.
5. Lowrance WT, Breau RH, Chou R, et al. Advanced prostate cancer: AUA/ASTRO/SUO Guideline PART I. *J Urol* 2021; 205: 14–21.
6. Okotie OT, Aronson WJ, Wieder JA, et al. Predictors of metastatic disease in men with biochemical failure following radical prostatectomy. *J Urol* 2004; 171: 2260–4.
7. Fanti S, Minozzi S, Castellucci P, et al. PET/CT with (11)C-choline for evaluation of prostate cancer patients with biochemical recurrence: meta-analysis and critical review of available data. *Eur J Nucl Med Mol Imaging* 2016; 43: 55–69.
8. Castellucci P, Fuccio C, Rubello D, et al. Is there a role for ^{11}C-choline PET/CT in the early detection of metastatic disease in surgically treated prostate cancer patients with a mild PSA increase <1.5 ng/ml? *Eur J Nucl Med Mol Imaging* 2011; 38: 55–63.
9. Perera M, Papa N, Roberts M, et al. Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer-updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: a systematic review and meta-analysis. *Eur Urol* 2020; 77: 403–17.
10. Horoszewicz JS, Leong SS, Kawinski E, et al. LNCaP model of human prostatic carcinoma. *Cancer Res* 1983; 43: 1809–18.
11. Evans JC, Malhotra M, Cryan JF, et al. The therapeutic and diagnostic potential of the prostate specific membrane antigen/glutamate carboxypeptidase II (PSMA/GCPII) in cancer and neurological disease. *Br J Pharmacol* 2016; 173: 3041–79.
12. Saule L, Radzina M, Liepa M, et al. Recurrent prostate cancer diagnostics with 18F-PSMA-1007 PET/CT: a systematic review of the current state. *Diagnostics (Basel)* 2022; 12: 3176.
13. Giesel FL, Hadaschik B, Cardinale J, et al. F-18 labelled PSMA-1007: biodistribution, radiation dosimetry and histopathological validation of tumor lesions in prostate cancer patients. *Eur J Nucl Med Mol Imaging* 2017; 44: 678–88.

14. Alonso O, Dos Santos G, García Fontes M, et al. 68Ga-PSMA and 11C-Choline comparison using a tri-modality PET/CT-MRI (3.0 T) system with a dedicated shuttle. *Eur J Hybrid Imaging* 2018; 2: 9.
15. Cantiello F, Crocerossa F, Russo GI, et al. Comparison between 64Cu-PSMA-617 PET/CT and 18F-choline PET/CT imaging in early diagnosis of prostate cancer biochemical recurrence. *Clin Genitourin Cancer* 2018; 16: 385–91.
16. Schwenck J, Rempp H, Reischl G, et al. Comparison of 68Ga-labelled PSMA-11 and 11C-choline in the detection of prostate cancer metastases by PET/CT. *Eur J Nucl Med Mol Imaging* 2017; 44: 92–101.
17. Morigi JJ, Stricker PD, van Leeuwen PJ, et al. Prospective comparison of 18f-fluoromethylcholine versus 68Ga-PSMA PET/CT in prostate cancer patients who have rising PSA after curative treatment and are being considered for targeted therapy. *J Nucl Med* 2015; 56: 1185–90.
18. Afshar-Oromieh A, Zechmann CM, Malcher A, et al. Comparison of PET imaging with a (68)Ga-labelled PSMA ligand and (18)F-choline-based PET/CT for the diagnosis of recurrent prostate cancer. *Eur J Nucl Med Mol Imaging* 2014; 41: 11–20.
19. Treglia G, Pereira Mestre R, Ferrari M, et al. Radiolabelled choline versus PSMA PET/CT in prostate cancer restaging: a meta-analysis. *Am J Nucl Med Mol Imaging* 2019; 9: 127–39.
20. Oprea-Lager DE, Gontier E, García-Cañamaque L, et al. [18F]DCFPyL PET/CT versus [18F]fluoromethylcholine PET/CT in biochemical recurrence of prostate cancer (PYTHON): a prospective, open label, cross-over, comparative study. *Eur J Nucl Med Mol Imaging* 2023; 50: 3439-51.