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Nuclear Medicine Imaging in Prostate Cancer: Current Evidence and Clinical Applications

Slikovna dijagnostika u nuklearnoj medicini kod karcinoma prostate: aktualna saznanja i klinička primjena

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Abstract. Prostate cancer (PCa) is the most commonly diagnosed malignancy in men, and a leading cause of cancer-related death. Accurate imaging is essential for diagnosis, staging, and therapy planning. Prostate-specific membrane antigen (PSMA)-targeted radiotracers provide superior sensitivity and specificity across clinical scenarios. In biochemical recurrence, PSMA positron emission tomography/computed tomography (PET/CT) offers the highest detection rates, especially at low prostate-specific antigen (PSA) levels. Choline and fluciclovine PET/CT remain valuable alternatives. Bone scintigraphy, fluoride PET/CT, and MRI contribute to skeletal staging. Molecular imaging has significantly advanced PCa management, enabling more precise diagnosis and treatment. This review summarizes recent advances in PSMA-targeted nuclear imaging.

Keywords: nuclear medicine; prostate cancer; scintigraphy; theranostics

Sažetak. Rak prostate (engl. *prostate cancer*, PCa) najčešće je dijagnosticirana zloćudna novotvorina u muškaraca i jedan od vodećih uzroka smrti povezanih s rakom. Precizna slikovna dijagnostika ključna je za dijagnozu, određivanje stadija bolesti i planiranje terapije. Radiofarmaci usmjereni na prostata-specifični membranski antigen (PSMA) pokazuju visoku osjetljivost i specifičnost u različitim kliničkim kontekstima. U slučaju biokemijskog recidiva, PSMA pozitronska emisijska tomografija s kompjutoriziranom tomografijom (engl. *positron emission tomography/computed tomography*, PET/CT) omogućuje najvišu stopu detekcije, osobito pri niskim razinama prostata-specifičnog antigena (PSA). PET/CT s kolinom i fluciklovinom i dalje su vrijedne dijagnostičke alternative. Scintigrafija kostiju, PET/CT s fluoridom i magnetska rezonancija pridonose procjeni koštanih metastaza. Molekularno oslikavanje značajno je unaprijedilo dijagnostiku i liječenje raka prostate, omogućujući personaliziran pristup bolesniku. Ovaj rad donosi pregled najnovijih dostignuća u nuklearnoj medicini usmjerenoj na PSMA.

Ključne riječi: nuklearna medicina; rak prostate; scintigrafija; teranostika

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INTRODUCTION

Medical imaging is essential in modern oncology, facilitating cancer detection, accurate staging, treatment planning, and disease monitoring[1]. This is particularly important in prostate cancer (PCa), whose high prevalence has led some authors to describe it as an age-related physiological phenomenon[2]. PCa is the most frequently diagnosed malignancy and the second leading cause of cancer-related death among men[3, 4]. Therefore, not only is early detection crucial, but so is accurate imaging—especially in cases of suspected recurrence or metastasis[5]. Current guidelines recommend various imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and bone scintigraphy. However, their sensitivity is often limited, especially when prostate-specific antigen (PSA) levels are low[3, 6, 7]. Positron emission tomography/computed tomography (PET/CT) has gained increasing importance due to its ability to provide specific molecular imaging of malignant tissue. Among molecular targets, prostate-specific membrane antigen (PSMA) stands out for its high expression in PCa cells[8]. Radiotracers targeting PSMA, particularly those used in PET/CT, have shown excellent sensitivity and specificity in detecting recurrent and metastatic PCa[6, 9]. Notably, gallium-68-labeled PSMA-11 (^{68}Ga-PSMA-11), fluorine-18-labeled piflufolastat (^{18}F-DCFPyL), and fluorine-18-labeled PSMA-1007 (^{18}F-PSMA-1007) are the Food and Drug Administration (FDA)-approved PSMA-targeted PET tracers[10]. Due to limited availability of PET/CT, PSMA-targeted agents for single-photon emission computed tomography (SPECT), such as technetium-99m-labeled PSMA (^{99m}Tc-PSMA), have also been developed[11]. Given the rapid evolution of molecular imaging and the range of available radionuclides, it is important to assess various imaging modalities and both PSMA- and non-PSMA-targeted approaches in PCa diagnostics. The aim of this review is to provide an overview of the most advanced nuclear medicine techniques currently used in the diagnosis and staging of PCa, with a critical evaluation of the characteristics, feasibility, diagnostic performance, and clinical relevance of both PSMA-targeted and non-PSMA radiotracers.

BIOLOGY AND CLASSIFICATION OF PROSTATE CANCER

PCa is the most frequently diagnosed malignancy in men worldwide, representing a significant public health concern. The majority of PCa cases, confirmed by prostate biopsy, are classified as acinar adenocarcinoma, while the prostatic ductal adenocarcinoma (PDA) subtype occurs less frequently[12]. Other histological variants, such as neuroendocrine tumors, are extremely rare[12].

Conventional imaging often lacks sensitivity in detecting early recurrence and small-volume metastases in PCa, particularly at low PSA levels. PSMA PET/CT has demonstrated superior accuracy in diagnosis, staging, and treatment monitoring, influencing clinical decisions and offering clearer detection of disease compared to CT, MRI, and bone scintigraphy.

Due to its glandular origin, PCa is graded based on glandular architectural patterns. The most widely used grading systems include the Gleason Score and the more recently developed Grade Group classification[13, 14].

Accurate staging is crucial for treatment planning and prognosis. PCa is typically staged using the Tumor, Node, Metastasis (TNM) classification system and is broadly categorized as localized, locally advanced, or metastatic. Localized cancer remains confined to the prostate, while locally advanced disease may involve high-risk features without distant metastases[15]. Metastatic PCa most commonly spreads to the bones, observed in up to 90 % of cases[16].

NUCLEAR MEDICINE IMAGING IN PROSTATE CANCER

PET/CT integrates metabolic and anatomical imaging by employing radiotracers that target specific tumor-related processes. After intravenous administration, these tracers accumulate in cancerous tissues and emit positrons, which upon annihilation with electrons produce gamma photons. These are detected to create functional images, while the CT component provides anatomical detail, allowing for accurate localization

of pathological uptake[17]. In PCa diagnostics and workup, there are three main groups of radiotracers used, prostate-specific PSMA-targeted, prostate specific non-PSMA-targeted and non-specific tracers. Selecting the appropriate radiotracer is essential for accurate PCa management with PET/CT[7, 18–20].

PROSTATE-SPECIFIC PSMA-TARGETED RADIOTRACERS

PSMA is highly overexpressed in most prostate adenocarcinomas and their metastases, making it an ideal molecular target for diagnostic imaging[7, 18]. PSMA is a membrane-bound enzyme, also known by names such as glutamate carboxypeptidase II and NAALADase I. Its expression correlates with disease stage and tumor aggressiveness, offering high sensitivity in the detection of PCa across all stages[6]. The possibility of labeling PSMA with radionuclides, whether positron-emitting (^{68}Ga, ^{18}F) or conventional, (^{99m}Tc), enables visualization of cancer tissue.

Gallium-68 PSMA-11

^{68}Ga-PSMA-11 was approved by the FDA in 2020 for PCa imaging[20, 21]. It consists of a targeting ligand (Glu-NH-CO-NH-Lys(Ahx)), a chelator (HBED-CC), and the positron-emitting isotope ^{68}Ga[20]. ^{68}Ga has a half-life of 67.7 minutes and decays via β+ emission, allowing for PET imaging. Its short half-life necessitates onsite production but minimizes radiation exposure[20, 22]. While PSMA PET/CT can be used for initial staging, particularly in select intermediate- and high-risk cases where available, it is not routinely recommended for all patients due to limited availability, high costs, and the current "weak" strength of recommendation in the European Association of Urology (EAU) guidelines. Its use is more commonly indicated for the detection of recurrent or persistent disease, assessment of metastatic spread, monitoring of treatment response, guidance of biopsies, and planning of PSMA-targeted therapy[10]. Physiological uptake occurs in kidneys, salivary glands, and liver[10, 23, 24].

Fluorine-18 DCFPyL

Approved by the FDA in 2021 as PYLARIFY®, fluorine-18-labeled piflufolastat (^{18}F-DCFPyL) is a PSMA-targeted tracer with a longer half-life (110 minutes) compared to ^{68}Ga, allowing for broader distribution and reduced radiation dose. Its ligand structure is based on a urea motif that binds strongly to PSMA[25]. Since ^{18}F is cyclotron-produced in large batches, it is more efficient for imaging multiple patients[26]. ^{18}F-DCFPyL shares similar biodistribution to ^{68}Ga PSMA-11 but demonstrates lower renal uptake, which may be beneficial in specific clinical scenarios[21, 27].

Fluorine-18 PSMA-1007

^{18}F-PSMA-1007 was introduced by Giesel et al. to identify patients suitable for lutetium-177-labeled PSMA-617 (^{177}Lu-PSMA-617) therapy due to the structural similarities of the theranostic ligand[28]. Since ^{18}F-PSMA-1007 is mainly excreted by hepatobiliary clearance, radiation dose to the urinary bladder wall is lower compared to other PSMA tracers, possibly related to lower accumulation in the proximity of the bladder[29, 30].

Technetium-99m PSMA SPECT/CT Imaging

In settings where PET/CT is unavailable, technetium-99m-labeled PSMA (^{99m}Tc-PSMA) radiotracers offer an alternative via SPECT/CT[31]. Although less sensitive than PET, SPECT/CT remains widely accessible due to gamma camera availability[32, 33]. One such radiotracer, introduced in 2016, commercially known as ^{99m}Tc-PSMA I&S (Imaging & Surgery), consisting of a ^{99m}Tc isotope, a chelator, and a PSMA-targeting ligand, accumulates in gallbladder, kidneys, and salivary glands[34, 35]. While it may detect metastases comparably to PET/CT, it is less effective for visualizing intraprostatic tumors.

PROSTATE-SPECIFIC NON-PSMA-TARGETED RADIOTRACERS

In addition to PSMA-targeted agents, several other radiotracers are used in PCa imaging.

Fluorine-18 Choline

Fluorine-18-labeled choline (^{18}F-Choline) consists of the radioactive isotope ^{18}F and a methylcholine molecule[36, 37]. It targets choline metabolism, critical for cell membrane synthesis. After entering cells via choline transporters, it is phosphorylated by choline kinase (CK)—an enzyme often overexpressed in malignant tissue, including

PCa[31, 38]. After cellular uptake via choline transporters, it is phosphorylated but not further metabolized, leading to intracellular accumulation[31, 38]. The tracer shows physiological uptake in the salivary and lacrimal glands, liver, pancreas, spleen, and urinary tract[31, 39].

Fluorine-18 Fluciclovine

Approved as AXUMIN®, fluorine-18-labeled fluciclovine (^{18}F-Fluciclovine) is a synthetic amino acid analogue targets upregulated amino acid transporters in PCa [40, 41]. It is not metabolized intracellularly and accumulates in malignant tissue[42]. Many tumor cells have an upregulated uptake of essential amino acids (AAs) because of the increased nutrients demand of cancer cells[43]. Physiologically, the liver and pancreas show the highest uptake, followed by the pituitary gland, salivary gland and Waldeyer ring, thyroid gland, breast parenchyma, esophagus, stomach, bowel and renal parenchyma[44].

NONSPECIFIC RADIOTRACERS

Fluorine-18 Fluorodeoxyglucose (FDG)

Fluorine-18-labeled fluorodeoxyglucose (^{18}F-FDG) is a glucose analogue taken up by metabolically active tissues and does not specifically bind to PCa tissue[45]. Although widely used in oncology, its role in PCa is limited due to typically low glycolytic activity and high false-positive rates in inflammation. It is more applicable in high-grade or advanced tumors[46, 47].

Fluorine-18 Sodium Fluoride

Fluorine-18-labeled sodium fluoride (^{18}F-NaF) PET/CT only assesses the presence of bone metastases. The tracer was reported to have similar specificity and superior sensitivity to bone scintigraphy for detecting bone metastases in patients with newly diagnosed high-risk PCa[48, 49].

Technetium-99m Bone Scintigraphy

Bone scintigraphy using technetium-99m-labelled diphosphonates is a highly sensitive conventional imaging technique, evaluating the distribution of active bone formation in the skeleton related to malignant and benign disease especially skeletal metastases[50]. These radiotracers accumulate in areas of increased osteoblastic activity but are limited by low specificity and reduced sensitivity for early marrow involvement[50]. The addition of 3D hybrid SPECT/CT imaging method has partly overcome these limitations, by improving discrimination of benign and equivocal findings.

PET/CT IMAGING IN A CLINICAL SETTING

Diagnosis

The basic diagnostic procedures for suspected PCa include evaluation of PSA levels in the blood and a digital rectal examination (DRE). In patients with PSA values between 3 and 20 nmol/L, multiparametric MRI of the prostate is recommended to improve diagnostic accuracy and improve cancer detection rates, along with the targeted prostate biopsy.

PSMA PET/CT imaging can help in guiding biopsies, with reported sensitivity of 0.89 and specificity of 0.5651. When combined with MRI, sensitivity further increases (97% compared to 83% for MRI alone), but specificity decreases (40% vs. 53%)[52].

Clinical staging – T

For primary tumor staging, DRE and morphological imaging modalities such as ultrasound (US), including transrectal US, CT, and MRI are commonly utilized[53–55].

Clinical staging – N

The high spatial resolution of CT and MRI allows for detailed assessment of lymph node involvement based on nodal size and morphology; additionally, MRI may detect metastases in lymph nodes that appear normal in size. However, metastatic infiltration does not necessarily alter lymph node dimensions and negative MRI finding cannot reliably exclude lymph node metastases. Consequently, the sensitivity of these methods remains below 40%[56–58]. Given the ability of nuclear medicine techniques to visualize small volumes of pathological metabolic activity, their role is particularly valuable in this context.

PSMA-based PET/CT

In lymph node staging, both ^{68}Ga-PSMA-11 and ^{18}F-DCFPyL PET/CT demonstrated similar sensitiv-

ity (0.40) and specificity (0.95)[59–62]. Sensitivity is significantly improved after elective lymph node dissection performed during radical prostatectomy (RP), reaching 77% sensitivity and 97% specificity. Compared to MRI and CT, PSMA PET/CT shows superior sensitivity in N-staging, although small lymph node metastases may still go undetected[63, 64].

Choline PET/CT

In patients at risk for lymph node involvement, the sensitivity of choline PET/CT is estimated at 18.9% increasing to 50 % in high-risk patients and up to 71 % in very high-risk groups[65, 66]. When combined with conventional imaging, choline PET/CT improves sensitivity for lymph node metastases compared to conventional imaging

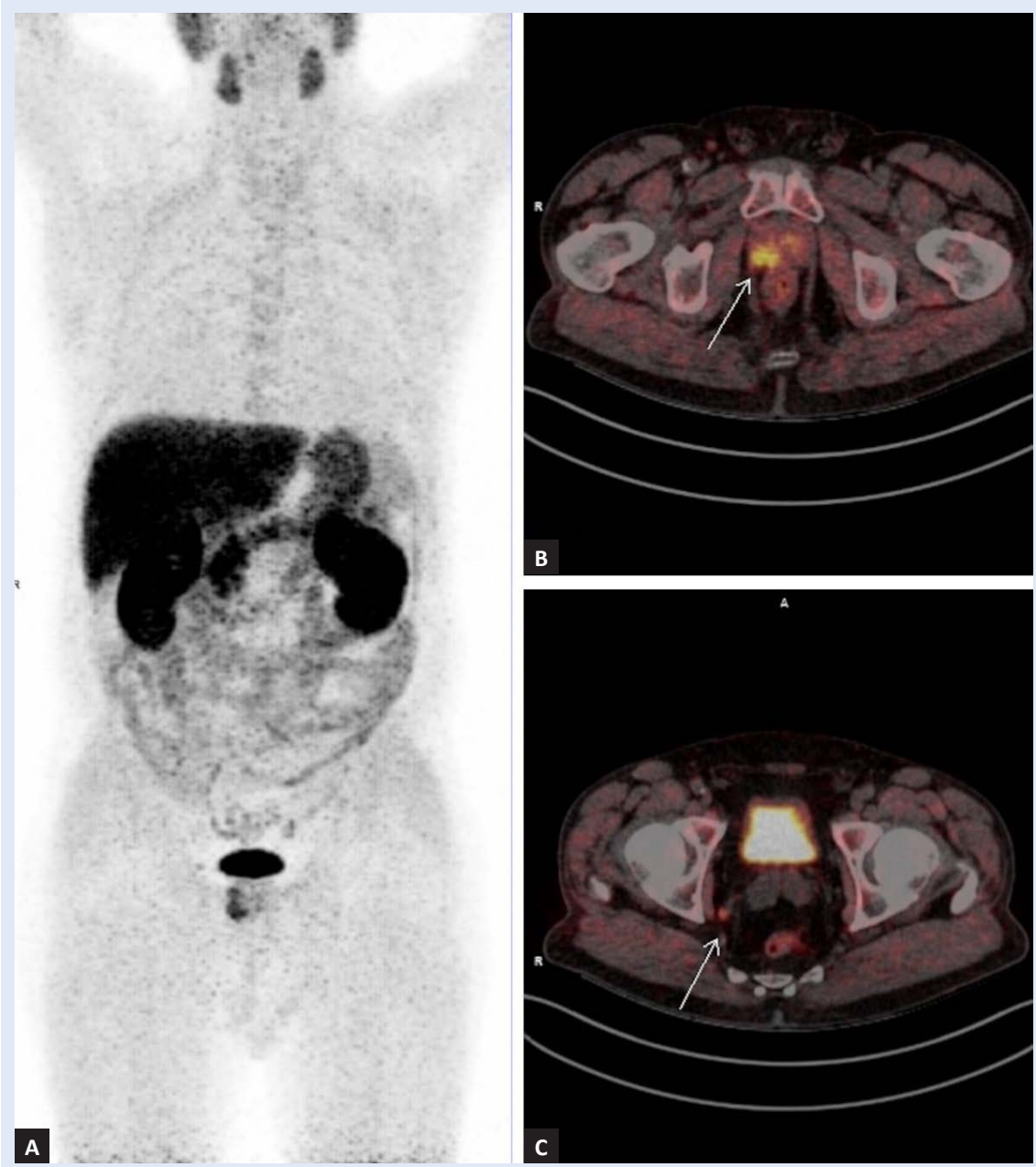

Figure 1. Fluorine-18 choline PET/CT imaging of 65 years old patient referred for primary staging of prostate cancer (PSA 31,7 ng/mL, Gleason score 4+3), demonstrating primary tumor and regional lymph node involvement. A: Whole body MIP (Maximum intensity projection) PET image, B-C: Axial PET/CT images showing high choline uptake in the right prostate lobe and in a small right pararectal lymph node. From the archives of the Clinical Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb, Zagreb, Croatia.

alone, 77.78% vs. 28.57% and 65.62% vs. 17.65% (regarding as the reference standard final pathology finding or final pathology with serial PSA evaluations)[67] (Figure 1).

Clinical staging – M

^{99m}Tc-Bone scintigraphy

Bone scintigraphy demonstrates sensitivity of 79% and specificity of 64.5% for the detection of bone metastases[50, 68]. It is indicated in symptomatic patients regardless of PSA level, tumor grade, or clinical stage[69]. The addition of SPECT/CT can improve differentiation of indeterminate findings.

Fluoride PET/CT

^{18}F-NaF PET/CT is used to detect bone metastases and demonstrates superior sensitivity and similar specificity compared to bone scintigraphy, especially in high-risk PCa patients[48, 70]. Intra-individual comparisons have confirmed the superior sensitivity of ^{18}F-NaF PET/CT[49].

Choline PET/CT

Compared to conventional imaging, choline PET/CT shows higher per-patient diagnostic accuracy in patients with intermediate- and high-risk PCa, and has the advantage of detecting both visceral and lymph node metastases[67, 71–73].

MRI

MRI is more sensitive than bone scintigraphy and choline PET/CT for detection of bone metastases and as a whole-body technique can also detect both visceral and lymph node metastases[74]. However, choline PET/CT shows the higher specificity[68].

PSMA PET/CT

PSMA PET/CT demonstrates superior detection rates compared to conventional imaging (bone scintigraphy and CT), with sensitivity and specificity of 85 % and 98 %, respectively, compared to 38% and 91% for conventional imaging[75]. PSMA PET/CT also leads to more frequent changes in clinical management (28% vs.15%), results in fewer equivocal findings (7% vs. 23%), and reduces radiation exposure[76].

Summary of evidence and practical considerations on initial N/M staging

Current evidence indicates that choline PET/CT, PSMA PET/CT, and whole-body MRI provide greater sensitivity for detecting lymph node and bone metastases compared to conventional imaging modalities such as bone scintigraphy and CT. PSMA PET/CT has demonstrated detection of extra-prostatic disease in 32 % of advanced PCa cases despite previously negative conventional imaging and improves accuracy for detecting pelvic lymph node metastases by 32% compared to standard imaging[63, 76].

Biochemical Recurrence and PSA-only Recurrence

In patients with rising PSA levels after definitive treatment, recurrence or progression of disease is suspected. In the literature, two partially overlapping terms are used: biochemical recurrence (BCR), which refers to rising PSA levels with or without radiological or pathological confirmation of recurrence, and PSA-only recurrence, where the sole evidence of disease is a rising PSA level. While BCR may warrant more aggressive treatment approaches, PSA-only recurrence often allows for active surveillance and monitoring[77].

Choline PET/CT

In the setting of BCR, choline PET/CT demonstrates combined sensitivities and specificities of 86–89% and 89–93%, respectively, for detecting recurrence at any site[78, 79]. Choline PET/CT may detect bone metastases in up to 15% of patients with BCR after radical prostatectomy and a negative bone scan and offers higher specificity compared to bone scintigraphy[68, 80]. Detection of lymph node metastases remains limited by the moderate sensitivity of choline PET/CT; however, sensitivity increases to 67–100% when PSA levels exceed 5 ng/mL. Despite these limitations, choline PET/CT findings lead to changes in clinical management in approximately 18-48% of patients with BCR following primary treatment[81–83].

Fluciclovine PET/CT

^{18}F-fluciclovine PET/CT offers slightly higher sensitivity than choline PET/CT for detecting sites of relapse in BCR[84]. Sensitivity remains below 50%

for PSA levels < 1 ng/mL. In post-prostatectomy recurrence, management changes occur in approximately 35.4 % of patients based on fluciclovine PET/CT findings[85]. Compared to conventional imaging (CT or MRI plus bone scan), ^{18}F-fluciclovine PET/CT demonstrates significantly higher positivity rates for the whole body (79.7% vs. 13.9%), prostate bed (69.6% vs. 5.1%), and pelvic lymph nodes (38.0% vs. 10.1%)[85].

PSMA-based PET/CT

^{18}F-PSMA PET/CT shows sensitivity, specificity, and area under the curve (AUC) values of 0.93, 0.94, and 0.96, respectively, for diagnosing recurrence or metastases in PCa[86]. PSMA PET/CT is significantly more sensitive than choline PET/CT, particularly at PSA levels < 1 ng/mL (61.8% vs. 39.5%), and demonstrates an overall detection rate of 84% compared to 69% for choline PET/CT[87, 88] (Figure 2, Figure 3).

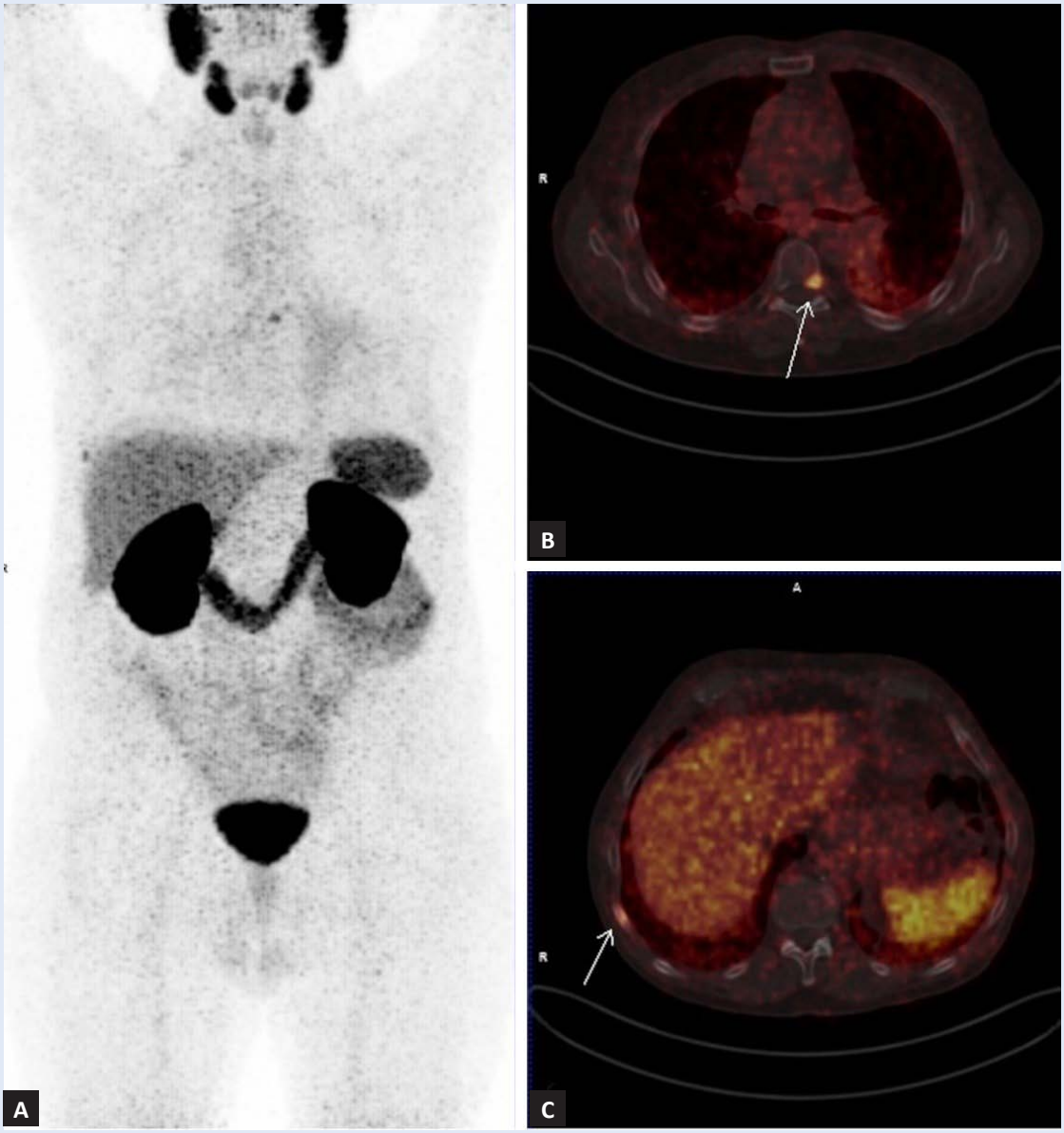

Figure 2. Gallium-68 PSMA-11 PET/CT imaging of 69 years old patient referred two years after radical prostatectomy due to biochemical recurrence (PSA 0,86 ng/ml), demonstrating bone metastases. A: Whole body MIP (Maximum intensity projection) PET image, B-C: Axial PET/CT images showing high PSMA uptake in Th7 vertebra and in 9th right rib. From the archives of the Clinical Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb, Zagreb, Croatia.

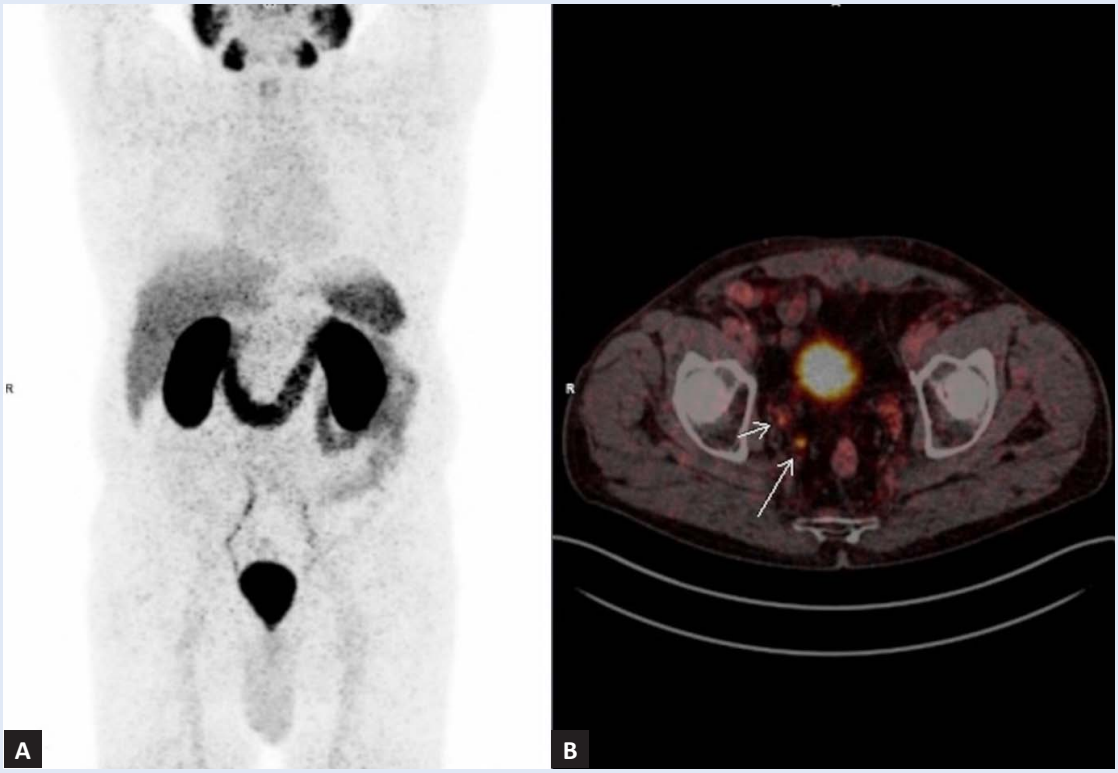

Figure 3. Gallium-68 PSMA-11 PET/CT imaging of 67 years old patient referred after radical prostatectomy due to biochemical recurrence (PSA 0,21 ng/ml), demonstrating lymph node metastasis. A: Whole body MIP (Maximum intensity projection) PET image, B: Axial PET/CT image showing PSMA uptake in the right internal iliac lymph node metastasis (long arrow) and physiological activity in right ureter (short arrow). From the archives of the Clinical Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb, Zagreb, Croatia.

PSMA-based Therapy

The increasing use of PSMA PET as a diagnostic tool, and the recognition that it enables the detection of a greater number of metastatic lesions, have led to the development of therapeutic approaches based on the same target, by substituting the diagnostic isotope with a therapeutic one that accumulates at sites of tumor activity (theranostics)[89].

Following target identification, usually performed with diagnostic ^{68}Ga-labeled PSMA, therapeutic radiotracers labeled with β-emitting isotopes such as Lutetium-177 (^{177}Lu) or Yttrium-90 (^{90}Y), or α-emitting isotopes such as Actinium-225 (^{225}Ac), may be employed to treat metastatic PCa. In a multicenter randomized controlled trial, radiographic progression-free survival (rPFS) was significantly longer in the ^{177}Lu-PSMA-617 group (11.60 months; 95% CI: 9.30–14.19) compared to the androgen receptor pathway inhibitor (ARPI) change group (5.59 months)[90].

DISCUSSION

Accurate imaging is a cornerstone in the management of PCa, guiding diagnosis, staging, and treatment decisions throughout the disease course. The rapid development of molecular imaging techniques, particularly PSMA-targeted PET/CT, has significantly improved the sensitivity and specificity for detecting both primary and recurrent disease.

^{68}Ga-PSMA-11 is an FDA-approved PSMA-targeted tracer that demonstrates high sensitivity and specificity, even at low PSA levels, making it applicable across various clinical scenarios[24]. It is conveniently produced on-site using commercial generator kits, and its short half-life (68 minutes) reduces radiation exposure and allows for timely imaging[20]. However, the short half-life also limits its distribution range, as it requires proximity to a ^{68}Ga generator. Additionally, a single generator supports imaging for only a few patients per day.

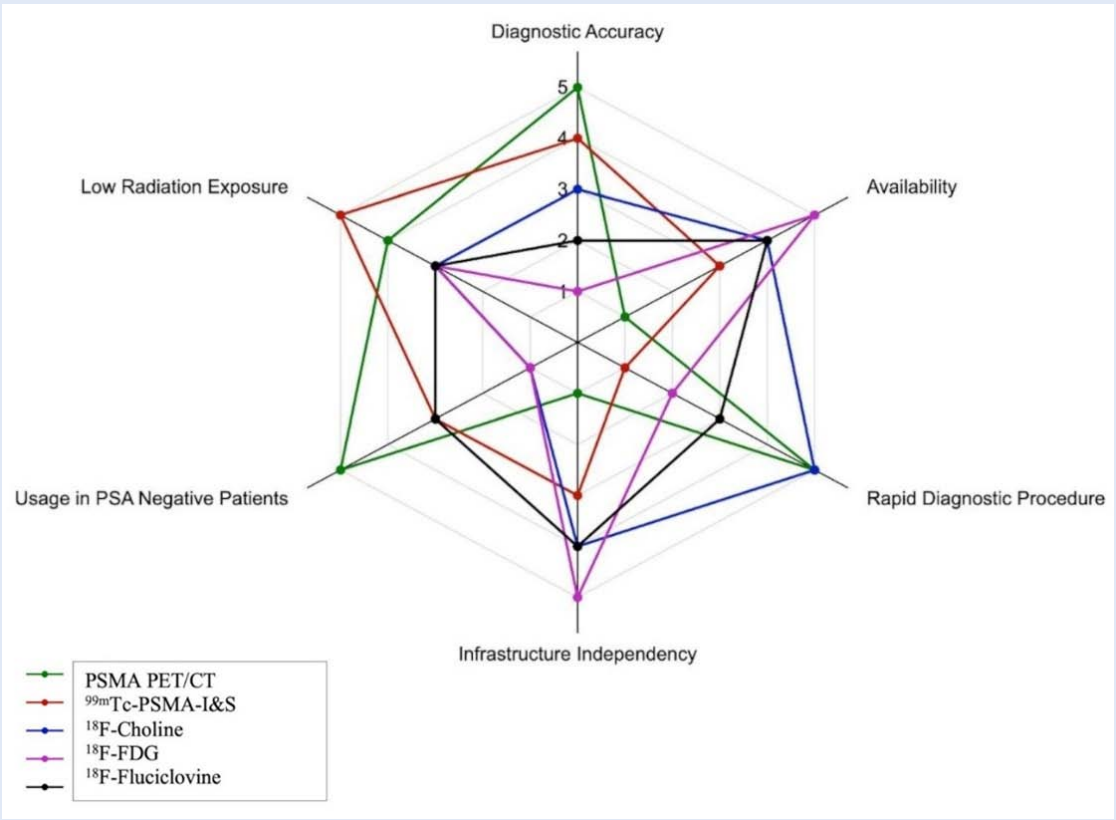

Figure 4. A comparative radar chart illustrating key parameters of diagnostic methods for the detection of prostate cancer: PSMA PET/CT, ^{99m}Tc-PSMA-I&S, ^{18}F-Choline, ^{18}F-FDG, and ^{18}F-Fluciclovine. The following parameters were compared: diagnostic accuracy, availability, speed of diagnostic procedure, infrastructure independency, effectiveness in PSA-negative patients, and level of radiation exposure. Radiotracers are rated from 1 ("does not apply") to 5 ("fully applies"). Source of the diagram: Rechner Club – Create Radar Chart [Internet]. Available from: https://www.rechner.club/diagramm/netzdiagramm-erstellen [accessed 16.06.2025.]

Limitations of PSMA PET/CT include restricted availability, high costs, and limited sensitivity in PSMA-negative or rare tumor subtypes. Future research should focus on improving access, developing alternative tracers, and expanding theranostic applications to ensure broader clinical use and enhance personalized treatment strategies across diverse healthcare settings.

To address these limitations, ^{18}F-PSMA-1007 offers logistical advantages. With a longer half-life of 110 minutes, it enables centralized production and wider distribution[91] (Figure 4).

The current evidence indicates that PSMA-targeted radiotracers offer superior diagnostic accuracy across multiple clinical settings. In primary staging, PSMA PET/CT outperforms conventional imaging modalities, particularly for detecting lymph node and distant metastases[76]. In biochemical recurrence, molecular imaging plays an increasingly pivotal role. Imaging can detect both local recurrences and distant metastases; however, the sensitivity largely depends on PSA levels. After radical prostatectomy, PSMA PET/CT demonstrates the highest sensitivity even at low PSA levels (< 0.5 ng/mL), enabling differentiation between local and systemic disease. Following radiotherapy, MRI remains highly effective for identifying local recurrence, while distant metastases may be detected using PSMA, choline or fluciclovine PET/CT, with PSMA PET/CT being the most sensitive option[87, 88]. In regions without access to PET/CT, SPECT/CT imaging using gamma-emitting PSMA tracers provides a practical alternative. ^{99m}Tc-PSMA I&S is especially valuable in such settings. SPECT/CT is more widely available and cost-effective. Technetium-99m, with its

6-hour half-life and 140.5 keV gamma emission, is suitable for delayed imaging and results in relatively low radiation exposure[92]. However, SPECT/CT offers lower spatial resolution than PET/CT, which may limit its sensitivity for small lesions[93, 94] (Figure 4).

Non-PSMA targeted radiotracers such as choline and fluciclovine retain value in certain clinical settings. Choline PET/CT performs better at higher PSA levels (>5 ng/mL), while fluciclovine PET/CT shows slightly improved sensitivity compared to choline, but remains limited at PSA <1 ng/mL[83, 85] (Figure 4).

For bone metastases, ^{18}F-NaF PET/CT and whole-body MRI demonstrate superior sensitivity compared to bone scintigraphy, which remains widely available due to its accessibility and cost-effectiveness, especially when combined with SPECT/CT.

The introduction of PSMA-based theranostics, particularly ^{177}Lu-PSMA-617, represents a significant therapeutic advance, offering improved progression-free survival compared to conventional systemic therapies in metastatic castration-resistant PCa[90].

Overall, the integration of advanced molecular imaging modalities into clinical practice has led to more precise and individualized management strategies for PCa patients.

CONCLUSION

Nuclear medicine imaging has revolutionized PCa management, offering highly sensitive and specific modalities for diagnosis, staging, and treatment monitoring. PSMA-targeted PET/CT currently represents the most advanced technique across all disease stages, while non-PSMA radiotracers and conventional imaging still retain roles depending on the clinical context and availability. The expanding field of PSMA-based theranostic further underlines the growing importance of molecular imaging in providing personalized care to PCa patients.

Conflicts of Interest: Authors declare no conflicts of interest.

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