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Original Article

Diagnostic scope of ^{18}F-PSMA-1007 PET/CT: comparison with multiparametric MRI and bone scintigraphy for the assessment of early prostate cancer recurrence

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Abstract: The aim of this study was to compare the diagnostic tools-^{18}F-PSMA-1007 positron emission tomography (PET/CT), magnetic resonance imaging (MRI) and bone scintigraphy for the evaluation of local recurrence, regional lymph nodes and bone metastases of recurrent prostate cancer (PCa). 28 PCa patients after radical prostatectomy and/or radiation therapy and with biochemical relapse were enrolled in this study. The evaluation of local recurrence and regional lymph node metastases was based on results of PET/CT and MRI. Local recurrent disease in 28 patients was detected by PET/CT in 36% (10/28) and by MRI in 32% (9/28) with sensitivity, specificity, accuracy of 90.9%, 100%, 96.4% and 81.8%, 100%, 92.9%, respectively (kappa 0.92, P<0.001). Nodal involvement was confirmed by PET/CT and MRI in 46% (13/28) and 25% (7/28) with sensitivity, specificity and accuracy for PET/CT 92.3%, 93.3%, 92.9% and for MRI-53.8%, 100%, 78.6%, respectively (kappa 0.57, P<0.001). The evaluation of skeletal metastases was based on PET/CT and bone scintigraphy. Bone metastases were seen on PET/CT and bone scintigraphy in 21% (6/28) and 20% (5/25) with sensitivity, specificity and accuracy of 100%; 91.7%; 92.9% and 50.0%; 85.7%; 80.0%, respectively (kappa 0.41, P<0.01). In conclusion, our comparative study demonstrates advantages of ^{18}F-PSMA-1007 PET/CT compared to MRI and scintigraphy for the evaluation of recurrent prostate cancer. Both methods, ^{18}F-PSMA-1007 PET/CT and MRI, detect local recurrence with high accuracy and excellent agreement, which may be attributed to the low urinary background clearance of ^{18}F-PSMA-1007.

Keywords: ^{18}F-PSMA-1007 PET/CT, MRI, scintigraphy, prostate cancer, recurrence

Introduction

According to American Cancer Society, 1 in 8 men will be diagnosed with prostate cancer (PCa) in his lifetime. 1 out of 41 men will die from prostate cancer [1]. As per the European Urology Association, prostate cancer remains the second most commonly diagnosed cancer in men, with an estimated 1.1 million diagnoses worldwide in 2012, accounting for 15% of all cancers diagnosed. The disease is characterized by morphological, genetic and clinical heterogeneity, from a slowly progressive localized tumor to an aggressive, treatment-resistant form with metastases, so its clinical course, response to therapy, and prognosis are directly dependent on its heterogeneous nature and specifically adapted treatment strategy. Clinically, prostate cancers are classified as low, moderate, and high-risk, depending on the stage, the prostate-specific antigen (PSA) level, and Gleason score [2]. The main radical treatment options for prostate cancer are surgery and radiation therapy. Still, recurrence of the disease is frequent and patients with clinically intermediate/high risk prostate cancer after ini-

tial radical treatment need clinical follow-up. While Prostate-specific antigen (PSA) is still the most commonly used biomarker for prostate cancer screening and follow-up, it is unspecific and does not reflect tumor localization or volume-on the other hand, patients with biochemical recurrence are best treated as early as possible and precise imaging of volume and localization of the lesions is mandatory for planning salvage therapy. However, accurate localization of recurrent prostate cancer at low PSA values is still a major challenge. Presently and with the currently available PET/CT tracers, a systematic combination of the available modalities for a multimodality comparative approach seems to offer the best options. Since the most significant reason for failure of salvage therapy is undetected metastatic disease, in particular lymph node metastases, anatomical and functional imaging plays a decisive role [3, 4].

This highlights the need for the further optimization of molecular imaging for biochemically recurrent prostate cancer (BRPCa). New radiopharmaceuticals have substantially increased the diagnostic scope of radionuclide imaging for recurrent prostate cancer and treatment strategy. Hybrid imaging with Positron emission tomography in combination with computer tomography (PET/CT) is a functional and anatomical non-invasive imaging modality used in the detection and staging of prostate cancer, in the evaluation of treatment efficacy and localization of recurrence. When compared with other diagnostic modalities, e.g. Magnetic Resonance Imaging (MRI), Computed Tomography (CT) or bone scintigraphy, the single PET/CT examination can be more accurate to find very tiny metastases in both-soft tissues and bones [4]. PSMA is an excellent tool for radionuclide diagnostics and prostate cancer treatment for several reasons: it is expressed in prostate cancer cells during all stages of the disease on the cell surface as an integral part of the membrane and does not go into blood circulation. Several radiolabeled PSMA probes have been developed, including that most widely used: ^{68}Ga-PSMA-11. Radiopharmarceutical ^{18}F-PSMA-1007 is a novel PSMA-based radiopharmaceutical that has several advantages over ^{68}Ga-PSMA-11 [5]. Comparing both, ^{68}Ga-PSMA-11 ligands have a drawback in the assessment of small local recurrences, which is their excretion via the kidneys and high accumulation in the urinary bladder [6]. ^{18}F-PSMA-1007 combines the same favorable properties (in respect to structure, biodistribution and uptake by prostate cancer cells) with partial hepatobiliary elimination and lower local accumulation in the urinary tract. Therefore, fewer overlays of the structures of interest may be expected. The aim of the presented study therefore was to further investigate the potential clinical value of ^{18}F-PSMA-1007 PET/CT compared to MRI and bone scintigraphy.

Materials and methods

Patients

Out of a cohort of 137 consecutive patients with primary or recurrent prostate cancer who underwent ^{18}F-PSMA-1007 PET/CT at our institution, a subgroup of 28 patients with biochemical PCa recurrence met the inclusion criteria for the study and was enrolled. Besides ^{18}F-PSMA-1007 PET/CT, all patients underwent pelvic multiparametric mpMRI and bone scintigraphy within ≤3 months before or ≤1 month after PET/CT as components of their clinical routine work-up. The study was approved by the ethics committee and informed written consent was obtained from all patients.

Inclusion criteria: Only patients who matched the criteria of the Eastern Cooperative Oncology Group (ECOG) 0 to 2 and for whom full access to previous clinical history (initial stage of disease, previous treatment, prostate biopsy histology results, Gleason score, at least two previous serum PSA level results) was available, were enrolled. Criteria for biochemical recurrence (within 10 years after initial therapy) were PSA 0.2-5.0 ng/ml after radical prostatectomy (subgroup 1) or prostatectomy with following radiation therapy in recurrence (subgroup 2), respectively.

Exclusion criteria were: decreased renal function (glomerular filtration rate <45 ml/min); pelvic radiation therapy within 6 months before PET/CT and MRI; chemotherapy before PET/CT and MRI and patients with history of additional oncological disease.

Imaging

PET/CT: All patients underwent ^{18}F-PSMA-1007 PET/CT using a commercially available clinical system equipped with 18 cm size PET detector

and integrated 64 row detector CT unit (Gemini TF64, Philips, Koninklijke Philips N.V., Best, Netherlands). The administered ^{18}F-PSMA-1007 dose per patient ranged from 1.8-2.2 MBq/kgBW (mean individual dose 363.93±69.40 MBq) and the CT part was acquired with intravenous contrast material application (1 ml/kgBW iodixanol (Visipaque, GE Healthcare, Boston, USA)). The scanning protocol was individually adjusted for patient size. Every scanning protocol contained a whole body PET/CT scan from head to middle thigh 52-78 minutes after radiotracer injection (mean time 54 min, IQR 43-60 min) with both arms elevated above the head as far as tolerated), starting with low-dose CT, followed by PET.

The criterion for local or distant recurrence was an increased ^{18}F-PSMA-1007 uptake taking into account normal distribution and pitfalls of ^{18}F-PSMA-1007 accumulation, as well as clinical information data. The standard uptake maximum values (SUV_{max}) were measured for each pathological lesion. Lesion sizes (e.g. lymph node size) were measured on the corresponding CT images. For all lesions, quantitative (SUV values, size, count) and qualitative (uptake grade, location) expression activity analysis were carried out. This was applied as well for the documentation of tracer accumulation in the urinary bladder as a measure of potential overcast of local recurrences.

MRI: Pelvic multi-parametric MRI (mp-MRI) was acquired using commercial 1.5 T (Magnetom/Avanto, Siemens, Germany) (14 pats.); and 3 T (Ingenia, Philips Healthcare, Best, Netherlands) (18 pats) systems. Anatomy-specific phased-array surface coils were used, all sequences with small FOV images covering the prostate position and one sequence with large FOV for the whole pelvis were obtained.

The standard MRI protocol comprised standard T1-SE non-contrast enhanced, T1-SE contrast-enhanced with fat signal suppression and T2-FSE images in coronal and transverse orientation (slice thickness 4 mm, FOV 300-350 mm, matrix 320×280). Functional imaging included diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) imaging after i/v bolus administration of 0.1 mmol/kg of Gadobutrol (Gadovist, Bayer Pharma) using a power injector (administration rate of 3-4 mL/s).

MR-criteria for local recurrence in the prostate area were (1) a mass or soft-tissue area on T2WI with increased signal intensity relative to muscle tissue, (2) a high focal signal intensity on the DWI with corresponding low signal intensity on the ADC or (3) early contrast enhancement on DCE images. Local recurrence was assumed when a corresponding positive MR finding was confirmed on at least two sequences.

Criteria for lymph node metastases were a round shape and/or inhomogeneous intranodal signal intensity on T2WI and/or irregular border and/or intensive enhancement.

Bone scintigraphy: 89% patients (n=25/28) underwent Tc99m-MDP whole body bone scintigraphy in anterior and posterior projections (dual headed gamma camera equipped with a low-energy, high-resolution parallel-hole collimator; Philips SKYLIGHT AZ gamma camera, Philips, Best, Netherlands). Patients were well hydrated prior to the examination. The radiopharmaceutical was administered intravenously with a single injection of 500-700 MBq depending on patient weight and protocol used in different centers. Scans were obtained 120-150 min. after injection. No specific image postprocessing was applied.

Images were read for increased focal tracer uptake as a marker for prostate cancer metastases, localisation, size, shape and intensity were reported.

Comparative image analysis

All images were read and interpreted by an interdisciplinary panel of board-certified nuclear medicine physicians, radiologists and urologists on consensus using a standardized molecular imaging tumor, node and metastasis scoring system [7]. The performance of ^{18}F-PSMA-1007 PET/CT was compared to MRI and bone scintigraphy on a per patient base. True positive, false positive, true negative or false negative results for local recurrence, lymph node metastases and bone metastases were evaluated against the standard of reference (defined on consensus including all available

Table 1. Patient characteristics

Characteristic	Value
Age (years)	
Mean ± SD	66.67±6.83
Median (range)	67 (52-84)
Gleason score	
Mean ± SD	7±1
Median (range)	7 (5-9)
Prior therapies, n (%)	
Prostatectomy	19 (68%)
Prostatectomy + Radiation beam therapy	9 (32%)
Increase of PSA per month (ng/ml/month)	
Median (range)	0.1 (0.001-0.6)
PSA Doubling time (months)	
Median (range)	7.9 (2.1-78.49)
PSA level at PET/CT (ng/ml)	
Median (range)	1.05 (0.21-5.0)
Median PSA level at PET/CT (ng/ml) (range) for prior therapy subgroups (ng/ml)	
Prostatectomy	0.58 (0.21-5.0)
Prostatectomy + Radiation beam therapy	1.6 (0.57-4.5)
Administered activity for ^{18}F-PSMA-1007 PET/CT (MBq)	
Mean ± SD	363.93±69.40
Median (range)	366 (210-505)
Diagnosis according to the standard of reference, n (%)	
local recurrence	11/28 (39%)
lymph node metastasis	13/28 (46%)
bone metastasis	4/28 (14%)
visceral metastases	0 (0%)

clinical data of the study participants, as well from history as from follow-up). Based on this, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated according to standard definitions. The agreement of modalities was calculated on a per lesion base and expressed as kappa values as and limits of error (*P*-value). In particular, PET/CT was compared to mpMRI for the assessment of local recurrence and lymph node metastases and to bone scintigraphy for bone metastases. Statistics were calculated using SPSS Data Analysis Software (version 20, IBM Corporation, USA).

Results

The characteristics of the included participants are summarized in **Table 1**. In brief, 28 patients with biochemical prostate cancer recurrence were prospectively enrolled into the study (mean age: 66.67±6.83 (range 52-84) years) with a median PSA value at the time of PET/CT of 1.05 ng/ml.

Local recurrence

According to the clinically defined standard of reference, local recurrence of prostate cancer defined by tumor growth in tissues adjacent to the prostate or in the seminal vesicles was present in 11/28 patients. A pathologic ^{18}F-PSMA-1007 uptake (an increased ^{18}F-PSMA-1007 uptake taking into account normal distribution and pitfalls of ^{18}F-PSMA-1007 accumulation, as well as clinical information data) in the prostate or prostate bed was observed in 10/28 patients (36%) with a mean SUV_{max} value of recurrent local lesions in PET/CT of 6.9, while MRI findings suggested prostate cancer recurrence on 9/28 scans (32%). Against the standard of reference, sensitivity, specificity, accuracy, positive predictive value and negative predictive value for local recurrence of ^{18}F-

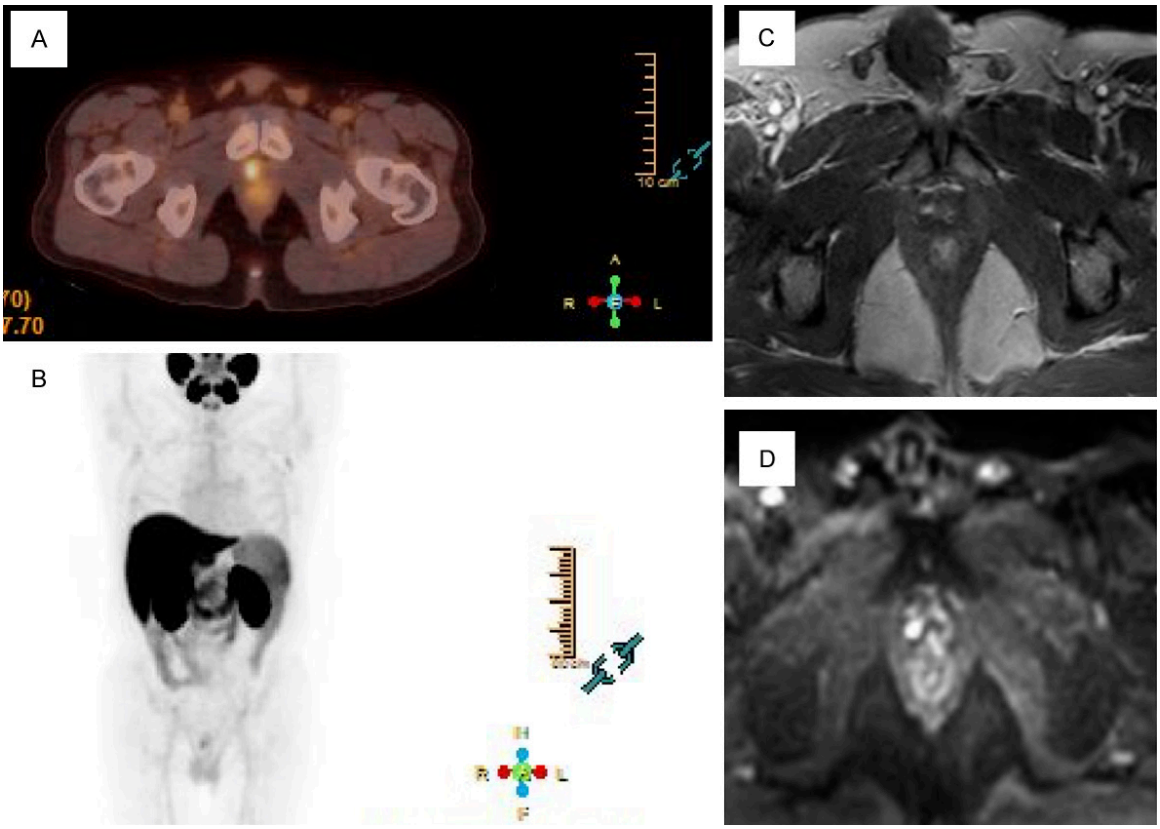

Figure 1. ^{18}F-PSMA-1007 PET/CT (A, B) and MRI (C, D) of a 57 years old patient 4 years after radical prostatectomy. The PSA level at the time of the study was 0.38 ng/ml. (A, B) ^{18}F-PSMA-1007 accumulation in the prostate bed, correlating with local recurrence. DCE (C) and DWI (D) MRI reveal a lesion in the prostate bed with early contrast enhancement and diffusion restriction, respectively.

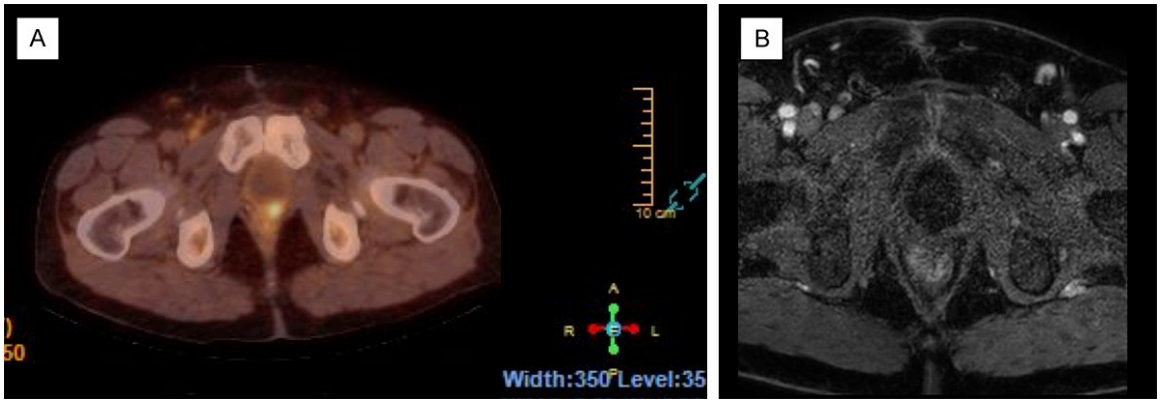

Figure 2. PET/CT and MRI examination of a 67 years old patient after radical prostatectomy one year ago, current PSA level-0.48 ng/ml. ^{18}F-PSMA-1007 accumulation in the left side of the prostate bed (A). This lesion can not be seen on the corresponding DCE-MRI series (B).

PSMA-1007 PET/CT were 90.9%, 100%, 96.4%, 100% and 94.4%, respectively. MRI reached 81.8%, 100%, 92.9%, 100% and 89.5%, respectively. Agreement of the two methods on a per lesion base was almost perfect (kappa 0.92, P<0.001).

Additional measurements of tracer accumulation in the urinary tract demonstrated a mean SUV_{max} in the bladder of 1.6±0.3.

Figures 1 and **2** show cases of local recurrence detected with both modalities, PET/CT and

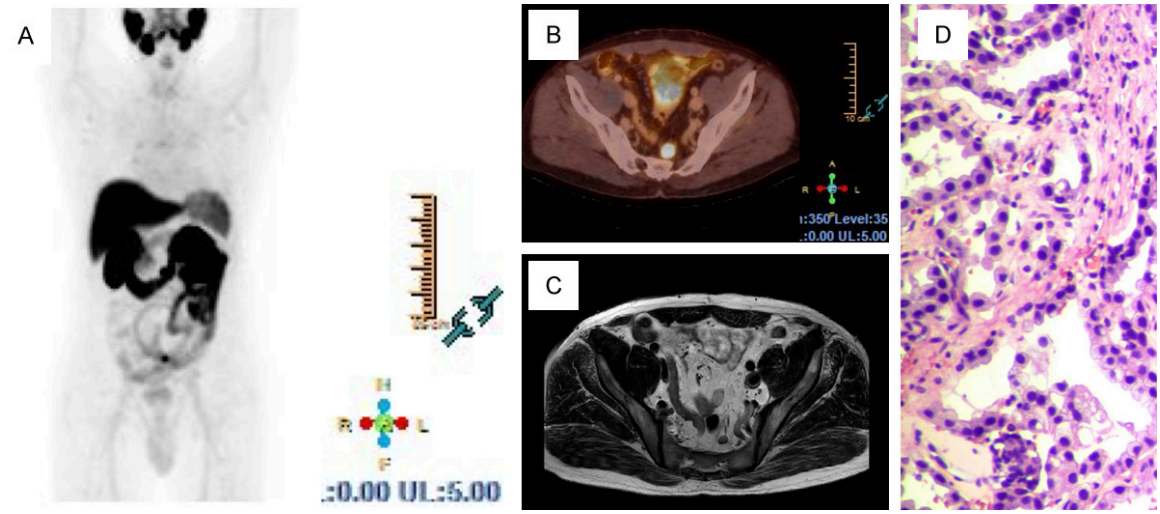

Figure 3. MRI and PET/CT examination of a patient (62 years old) after radical prostatectomy four years ago, Gleason Score 7, current PSA level 1.6 ng/ml. (A and B) show ^{18}F-PSMA-1007 uptake in an enlarged lymph node with SUV_{max}=15.9. The T2-weighted MRI sequence (C) shows the enlarged lymph node in rectosigmoid tissues. (D) Histopathology from the lymph node: Hematoxylin eosin (HE) stain, original magnification (OM) 200×-glandular structures with distinct cellular atypia.

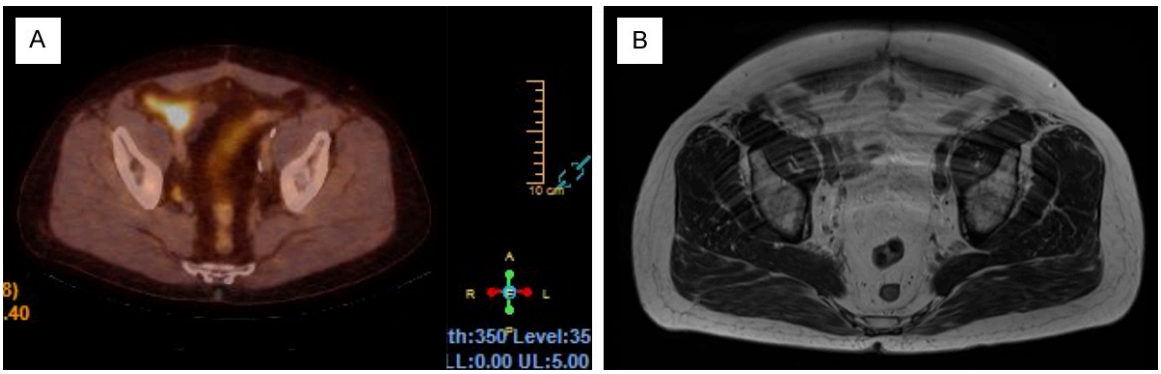

Figure 4. ^{18}F-PSMA-1007 PET/CT and MRI (T tse tra) of a 66 years old patient after radical prostatectomy one year ago. PSA level at the time of the study was 1.18 ng/ml. A. ^{18}F-PSMA-1007 accumulation in the right side lymph node, in front of the right internal iliac artery, confirming metastasis in regional lymph nodes. B. Pathologic lymph node was detected on MRI as nonspecific. After the studies, the patient received radiation therapy for the lymph node.

MRI, and with positive PET/CT, but not detected in MRI, respectively.

Lymph node metastases

Lymph node metastases were present in 13/28 patients according to the clinically defined standard of reference. Corresponding lesions were reported in 13/28 (46%) ^{18}F-PSMA-1007 PET/CT. In MRI lymph node metastases were observed in 7/28 patients (25%). All of the metastatic lymph nodes were smaller than 1 cm in short axis (mean short axis 0.72 cm).

Against the standard of reference, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of PET/CT for local lymph node metastases were 92.3%, 93.3%, 92.9%, 92.3% and 93.3%, respectively. With MRI, sensitivity, specificity, accuracy, PPV and NPV for lymph node metastases were 53.8%, 100%, 78.6%, 100% and 71.4%, respectively. Agreement of the two methods on a per lesion base were only moderate (kappa 0.57, P<0.001).

Figures 3 and **4** show examples of lymph node metastases detected with both modalities, PET/CT and MRI, and with positive PET/CT, but not detected in MRI, respectively.

Bone metastases

Bone metastases were confirmed in 4/28 study participants according to the clinically defined

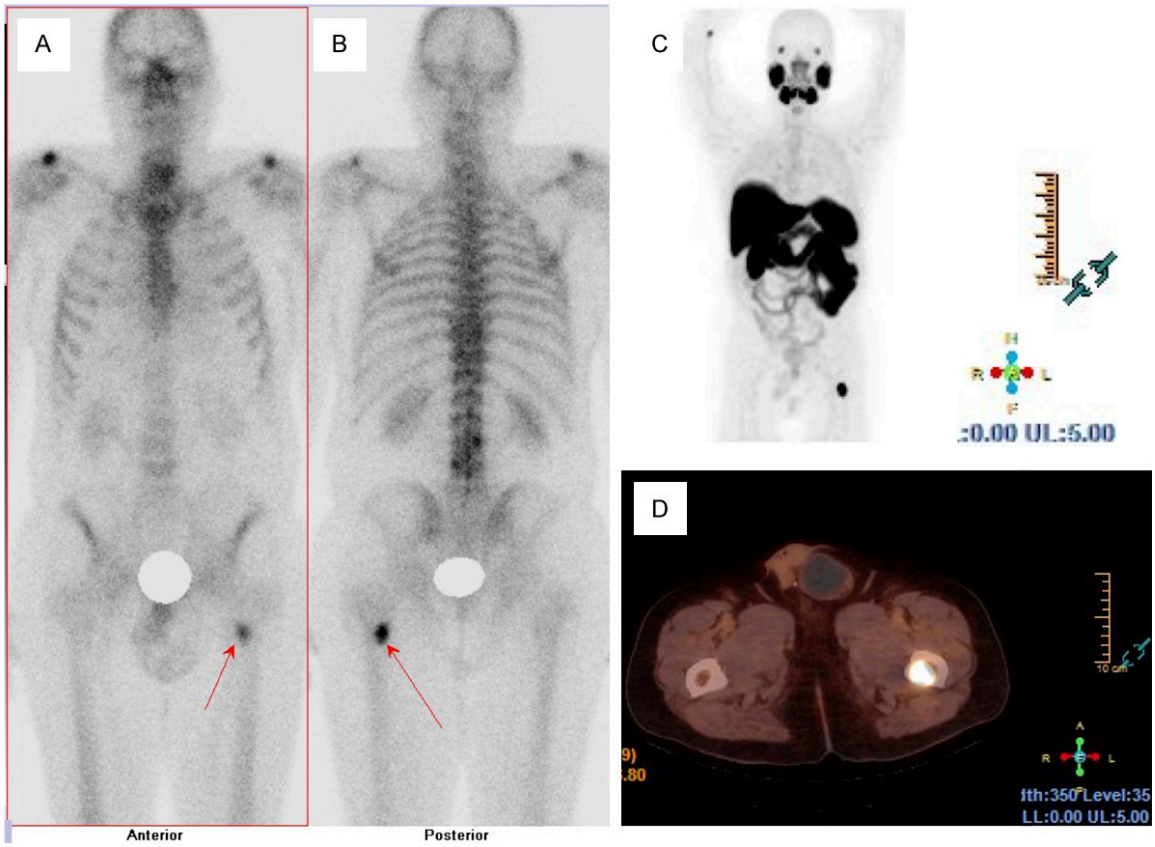

Figure 5. ^{18}F-PSMA-1007 PET/CT and bone scintigraphy of a 67 years old patient after radical prostatectomy and radiation therapy of the prostate bed six years ago. The PSA level at the time of the study was 4.35 ng/ml. A and B. A pathological ^{99m}Tc uptake (arrows) in the proximal left femur on bone scintigraphy. C and D. The corresponding pathological ^{18}F-PSMA uptake in PET/CT.

standard of reference. Corresponding lesions were reported in 6/28 (21%) ^{18}F-PSMA-1007 PET/CT including one case that was negative on bone scintigraphy. Bone scintigraphy revealed typical skeletal lesions in 5/25 patients (20%). In three patients with no lesions according to the standard of reference, PET/CT was negative, but bone scintigraphy was not available. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value for the assessment of bone metastases with PET/CT were 100%; 91.7%; 92.9%, 66.7% and 100%, respectively. Bone scintigraphy reached 50.0%; 85.7%; 80.0%; 40.0% and 90.0%, respectively. The agreement of the two methods on a per lesion base was only fair to just moderate (kappa 0.41, P<0.01).

Figure 5 shows example of bone metastasis detected with both modalities-PET/CT and bone scintigraphy.

Comparison of PET/CT with the combined examination MRI/bone scintigraphy

For a further estimation of the clinical value of ^{18}F-PSMA-1007 PET/CT, **Table 2** shows a comparison of the diagnostic accuracy PET/CT alone versus the combination of MRI and bone scintigraphy.

The median cohort's Gleason score was 7, range 5-9. Linear regression analysis estimates that an increase of PSA value by one unit at the PET/CT time point implies a decrease of PSA aoubling time by 1.27 (P=0.05) irrespective of the Gleason score (P=0.351). Also there was no significant difference in doubling time (months) between radical prostatectomy and prostatectomy and radiotherapy groups (P=0.383) analysed by Mann-Whitney test, see **Figure 6**.

Receiver Operating Characteristic (ROC) test statistics showed a non-significant (P>0.05)

Table 2. Diagnostic accuracy of ^{18}F-PSMA-1007 PET/CT and the combined examination using mpMRI and bone scintigraphy in recurrent prostate cancer

Finding	Modality	Sens. % [CI]	Spec. % (CI)	PPV	NPV	Acc % [CI]	*P* value
PCa Local recurrence	PET/CT	90.9 [58.7-99.8]	100 [80.5-100]	100	94.4	96.4 [81.6-99.9]	0.001
	MRI + scinti.	81.8 [48.2-97.7]	100 [80.5-100]	100	89.5	92.9 [76.5-99.1]	0.0001
Lymph nodes	PET/CT	92.3 [63.9-99.8]	93.3 [68.0-99.8]	92.3	93.3	92.9 [76.5-99.1]	0.001
	MRI + scinti.	53.8 [25.1-80.8]	100 [78.2-100]	100	71.4	78.6 [59.1-91.7]	0.01
Skeletal metastasis	PET/CT	100 [39.8-100]	91.7 [73.0-99.0]	66.7	100	92.9 [76.5-99.1]	0.01
	MRI + scinti.	50.0 [6.8-93.2]	85.7 [63.7-97.0]	40.0	90.0	80.0 [59.3-93.1]	0.001

PPV: positive predictive value, NPV: negative predictive value, Se: sensitivity, Sp: specificity, Acc: Accuracy, CI: confidence interval.

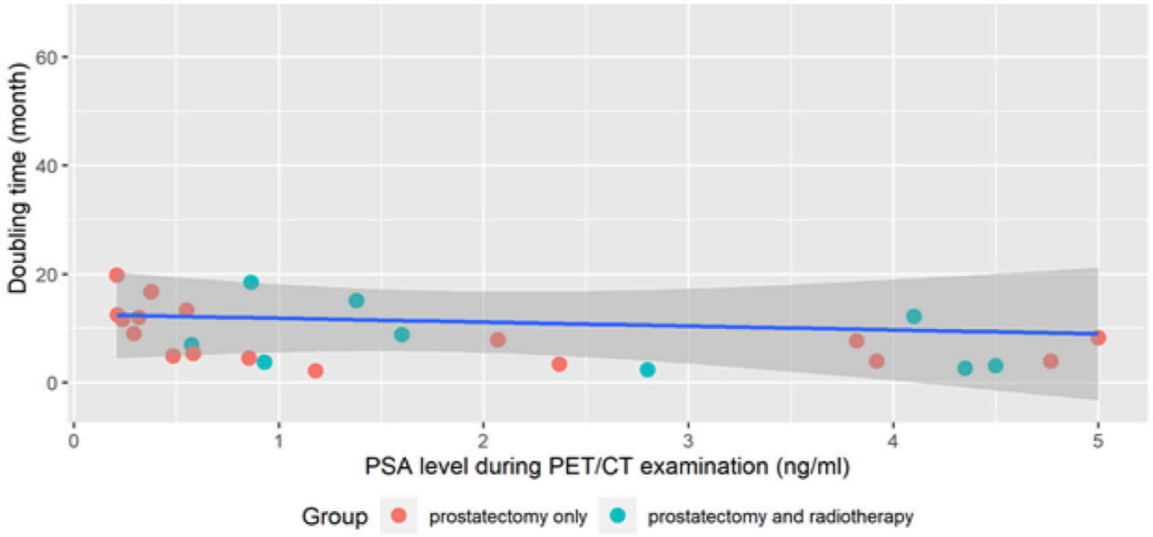

Figure 6. Linear regression analysis of PSA Doubling time (months) and PSA level at PET/CT examination (ng/ml).

tendency of threshold value for PET/CT positive finding in PSA Doubling time above 10.3 months including both therapy groups with sensitivity and specificity 0.70 and 0.63, respectively.

Discussion

The present study allows for the assumption of a high clinical value of ^{18}F-PSMA-1007 PET/CT for the assessment of early, biochemically recurrent prostate cancer. So far, the current guidelines of the European Urological Association already recommend PSMA PET/CT for patients after radical prostatectomy with increasing PSA level >0.2 ng/mL, but only at a recommendation level of 2b. This study was intended to improve the evidence of clinical benefit and should contribute to strengthen the level of recommendation, since further, additional work is warranted to refine selection criteria for PSMA PET/CT in the diagnostic algorithm [8].

Regarding sensitivity and overall diagnostic accuracy for local recurrence, PET/CT was shown to be at least fully equivalent to multiparametric MRI (mpMRI), which is so far the most precise available technique. At the current state of art, mpMRI can detect aggressive prostate cancer with a negative (NPV) and a positive predictive value (PPV) of 63 to 98%, and between 34 and 68%, respectively. Recent studies have shown that mpMRI can also be used to detect recurrence or residual disease. Although all types of PCa therapy leave treatment induced changes within the pelvis, thus complicating image interpretation, advances in technology have made mpMRI to be one of the most effective modalities in detection of local recurrent PCa after RP and RT even at low PSA levels [9],

possible limitations of MRI after RP are granulation tissue in the perianastomotic region where it can mimic the tumour recurrence, as well as sometimes it can be difficult to distinguish between local recurrence nodule and residual glandular healthy tissue [10]. MpMRI was therefore considered the benchmark for comparison with PET/CT.

The protocol applied in this studies fully complies with the protocols and diagnostic criteria for prostate mpMRI are described in the Prostate Imaging-Reporting and Data System Version 2 (PI-RADS™ v2)-the consensus of an international collaboration of the American College of Radiology (ACR), European Society of Uroradiology (ESUR), and AdMeTech Foundation, based on three main MRI protocol sequences (T2WI, DWI and T1WI with dynamic contrast enhancement) [11].

One of the major drawbacks of alternative tracers, i.e. ^{68}Ga-PSMA-11, is renal clearance which results in activity overcast of tracer accumulation in the urinary bladder over the prostate bed and the adjacent tissues. Since ^{18}F-PSMA-1007 is also eliminated by hepatobiliary clearance, a better diagnostic accuracy for local recurrence would be expected.

For the detection of regional lymph node metastases, ^{18}F-PSMA-1007 PET/CT outperformed mpMRI with superior sensitivity and overall diagnostic accuracy, in particular for small nodes. This is consistent with prior work from *Giesel et al.*, who reported that forty-four (88%) of 50 ^{18}F-PSMA-1007-positive lymph nodes had a short-axis diameter of less than 8 mm. In our study, all of the metastatic lymph nodes were smaller than 1 cm in short axis (mean short axis 0.72 cm). It confirms that metastatic lymph nodes can appear with non-specific characteristics on MRI [12].

In the evaluation of bone metastases, ^{18}F-PSMA-1007 PET/CT reached a higher sensitivity and overall higher diagnostic accuracy compared to bone scintigraphy. Generally, ^{99m}Tc-MDP whole-body bone scintigraphy is known as a sensitive imaging method that has been used for decades to evaluate PCa bone metastasis based on its availability and low cost; however, because of accumulation of this radiotracer in degenerative, inflammatory and traumatic lesions, the specificity is relatively low. For PSA values less than 7 ng/ml bone scintigraphy has a detection rate of only 5%, also CT, for comparison, has a similarly low sensitivity of 11-14% for detection of local recurrence and lymph node metastases in this group of patients [2].

Overall, these results are consistent with *Rahbar et al.*, that ^{18}F-PSMA-1007 PET/CT can detect recurrent PCa in a high percentage of patients with biochemical relapse, with improved accuracy (up to 96.4% for local recurrence and 92.9% for lymph nodes) and a mean PSA level of less than 1.05 ng/mL in our study [13]. Recent studies involving PSMA PET/CT in the setting of PCa recurrence showed higher sensitivity than other imaging modalities for detecting the sites of recurrence and metastatic disease, even at very low serum PSA values and overall appears superior to conventional imaging [14]. Our study observed that increase of PSA value by one unit at the PET/CT time point implies PSA Doubling time decrease by 1.27, regardless of Gleason score and with a tendency of PET/CT better detection if doubling time exceeds 10 months. Hence, dedicated cohort studies would be favourable to prove the concept. Performing ^{18}F-PSMA-1007 PET/CT at very low PSA levels potentially may allow more effective salvage treatment, because the prognosis is improved by the initiation of treatment before the PSA level has exceeded 0.5 ng/mL [15]. All these results are very much in favour of using ^{18}F-PSMA-1007 PET/CT as a one-stop-shopping approach for the assessment of patients with early, biochemically recurrent prostate cancer. However, besides radiation protection issues (double exposure from PET and CT) and expenses for equipment, also logistic aspects need to be considered. Regarding the cost-benefit ratio it needs to be mentioned that the study was conducted in a specified nuclear medicine center with cyclotron on site. This facilitates logistics regarding transportation and loss of activity due to decay during transportation. Regarding expenses for tracer purchase and reimbursement, any use in centers at a larger distance might make it more difficult to realize ^{18}F-PSMA-1007 PET/CT as a standard procedure from the economic perspective. Therefore, it might be still favourable for many sites to stick to the combined imaging protocol based on mpMRI and bone scintigraphy. Further studies will be needed to gain more insight into these aspects.

Limitations

First of all, it needs to be addressed that the study was conducted in a relatively small patient cohort. Furthermore, the definition of the ground truth by clinical evidence may be considered disputable, since in the majority of patients with local recurrence or pelvic lymph nodes, the clinical decision for local or systemic therapy was based on PSA levels and imaging results without histologic confirmation. A potential bias from over-diagnosis can therefore not be excluded.

A minor limitation was the lack of results of image data from 3 bone scintigrams, which slightly weakens the statistical comparison with PET/CT. However, as discussed above, these three cases included patients with no other evidence of bone metastases according to the standard of reference. Therefore the only possible error induced by these three cases would have been the overall unlikely possibility of false positive findings.

However, despite the relatively small number of included patients and other limitations as discussed above, this study still confirms the clinical value of ^{18}F-PSMA-1007 PET/CT in early prostate cancer recurrence, allows for a comparison with the established approaches and contributes valuable data for the further development of imaging concepts in this patient group.

Conclusions

For evaluation of early (biochemically) recurrent prostate cancer, this comparative study reveals potential advantages of ^{18}F-PSMA-1007 PET/CT over MRI and scintigraphy. Regarding local recurrence, both modalities, PET/CT and MRI, offer a high diagnostic accuracy with almost perfect agreement on a per lesion basis. The hypothesis, that a lower renal clearance of the tracer with less activity overcast from accumulation in the urinary bladder at least contributes to the full diagnostic equivalence of ^{18}F-PSMA-1007 PET/CT to mpMRI for the detection of local recurrence was confirmed by documentation of a lower accumulation in the urinary bladder. For the detection of regional lymph node metastases, ^{18}F-PSMA-1007 PET/CT provides superior sensitivity and overall diagnostic accuracy compared to MRI, in particular for small lymph nodes with non-specific characteristics on MRI. In the evaluation of bone metastases ^{18}F-PSMA-1007 PET/CT was more accurate compared to bone scintigraphy, as in particular the specificity of bone scintigraphy was relatively low. Compared to the combination of MRI and bone scintigraphy together, ^{18}F-PSMA-1007 PET/CT provided a superior diagnostic accuracy, except for the diagnosis of local recurrence, where it was at least fully equivalent to mpMRI. Based on these very promising results, further studies are warranted to more precisely quantify the clinical value and cost-benefit ratio of ^{18}F-PSMA-1007 PET/CT in long term oncologic outcomes.

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Disclosure of conflict of interest

None.

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