18F-Fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) is accurate for high-grade prostate cancer bone staging when compared to bone scintigraphy

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Abstract

Introduction: In this study, we compared 18F-FDG-postron emission tomography/computed tomography (PET/CT) and bone scintigraphy accuracies for the detection of bone metastases for primary staging in high-grade prostate cancer (PCa) patients to determine if 18F-FDG-PET/CT could be used alone as a staging modality.
Methods: Men with localized high-grade PCa (n=256, Gleason 8–10, International Society of Urological Pathology [ISUP] grades 4 or 5) were imaged with bone scintigraphy and 18F-FDG-PET/CT. We compared on a per-patient basis the accuracy of the two imaging modalities, taking intermodality agreement as the standard of truth (SOT).
Results: 18F-FDG-PET/CT detected at least one bone metastasis in 33 patients compared to only 26 with bone scan. Of the seven false-negative bone scintigraphies, four (57.1%) were solitary metastases (monometastatic), three (42.9%) were oligometastatic (2–4 lesions), and none were plurimetastatic (>4 lesions). Compared to SOT, 18F-FDG-PET/CT showed higher sensitivity and accuracy than bone scintigraphy (100% vs. 78.8%, and 98.7% vs. 98.2%) for the detection of skeletal lesions.
Conclusions: 18F-FDG-PET/CT appears similar or better than conventional bone scans to assess

for bone metastases in patients newly diagnosed with high-grade PCa. Since intraprostatic FDG-uptake is also a biomarker of failure to radical prostatectomy and that FDG-PET/CT has been shown to be accurate in detecting PCa lymph node metastasis, FDG-PET/CT has the potential to be used as the sole preoperative staging modality in high-grade PCa.

Introduction

Prostate cancer (PCa) is the third most common cause of cancer-related deaths in men [1] and bone metastases represent the most common site of distant metastases [2]. Conventional imaging modalities, such as bone scintigraphy and computed tomography (CT), are still the reference standard for evaluating bone metastases and this technique is recommended by most international guidelines. [3-7]. The management of metastatic and non-metastatic PCa is based on the metastatic burden determined by these conventional imaging [8,9]. However, staging PCa with bone scintigraphy and CT necessitates two separate appointments and do not allow imaging of intraprostatic PCa nor normal size lymph nodes with high accuracy. 18F-FDG-PET/CT is a widely available molecular imaging technique that allows diagnosis, staging, and therapeutic assessment in a wide range of malignancies [10], but it is not recognized as an accurate tool in localized PCa management. Therefore, it is not currently routinely performed. However, a closer look at literature revealed that PCa could switch to a high glycolytic rate in the advanced stage of the disease [11-14]. We and others have shown that 18F-fluorodeoxyglucose (18F-FDG) uptake in the primary tumor, lymph node, or bone metastasis was associated poor prognosis after therapy [12,14-21]. Thus, in an aggressive PCa cohort of 148 patients (Gleason ≥8 at biopsy), we demonstrated that PCa patients exhibiting high intraprostatic FDG-uptake on 18F-FDG-PET/CT had an increased risk of biochemical recurrence (median time to recurrence =11.3 vs 49.5 months for low uptake) and castration resistance [20,21]. 18F-FDG-PET/CT could also predict lymph node metastasis with an accuracy of 73% compared to histopathology at radical prostatectomy. However, there is limited literature on the clinical utility and safety to use 18F-FDG-PET/CT to stage newly diagnosed PCa patients for bone metastasis. The purpose of the present study was to compare the diagnostic performances of conventional bone scintigraphy and 18F-FDG-PET/CT imaging for the detection of bone metastases in high-risk PCa patients in order to determine if 18F-FDG-PET/CT could be used as a standalone for staging technique in this population.

Methods

Patient characteristics
Patients newly diagnosed with an adenocarcinoma of the prostate with a Gleason score ≥8 at biopsy (ISUP grade 4 or 5) between 2010 and 2016 at the CHU de Québec-Université Laval were included in the study (Figure 1). Patients with a prior history of malignancy within 5 years of PCa

diagnosis or who had previous therapies for PCa were excluded. The institutional Ethics committee approved this retrospective study (2021-5014).

¹⁸F-FDG-PET/CT imaging

PET/CT imaging was performed as previously described [19-21]. Following a fasting period of 6 h, ¹⁸F-FDG-PET/CT imaging was performed from the base of the skull to the upper thighs on a Biograph 6 PET/CT system (Siemens Healthcare, Erlangen, Germany) approximately 75 min after the administration of a bolus of 300–500 Mbq of ¹⁸F-FDG with oral contrast.

Bone scintigraphy

Bone scintigraphy was performed using dual-head gamma cameras (Siemens, Munich, Germany) equipped with low energy, high resolution collimators. Simultaneous anterior and posterior whole-body images as well as SPECT +/- CT images were acquired approximately 3 h after intravenous administration of 740 MBq ^{99m}Tc-methylene diphosphonate (^{99m}MDP). Static additional planar images were also acquired at the discretion of the attending nuclear physician.

Images interpretation

Bone scintigraphy and PET/CT were interpreted according to clinical routine by experienced nuclear medicine physicians using a 2-point scale scoring system (metastasis or no metastasis, per patient basis). A bone lesion on bone scintigraphy was considered positive if it showed either focal or diffuse uptake typical for bone metastases excluding lesions with a location or underlying morphological feature typical for a benign entity. Focal uptake on PET/CT with ¹⁸F-FDG-uptake visually exceeding the skeletal background, in the absence of underlying benign entity on the accompanying low dose CT scan, were interpreted as metastases.

Standard of truth definition

The metastatic status for each patient and imaging modality was determined by intermodality agreement. In case of disagreement between bone scintigraphy and ¹⁸F-FDG-PET/CT, a standard of truth (SOT) definition was used. Definite per-patient bone metastasis status was determined if at least one of the following criteria were met: (1) bone biopsy of a lesion diagnostic for PCa, (2) new metastasis detected on a follow-up imaging, (3) metastasis detected on a concomitant or follow-up MRI/CT imaging or, (4) clinical/biochemical follow-up compatible with bone metastasis. The diagnostic performance of each modality, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy, were calculated based on SOT.

Statistical analyses

Students' t-test for statistical significance assessment of the differences between age and PSA level was used. Comparison of bone scintigraphy and ¹⁸F-FDG-PET/CT for the detection of bone

metastases was evaluated with confidence intervals using the McNemar test. As imaging performance could varies across patient's subgroups, phenomena called spectrum bias, we evaluated sensibility and specificity by stratifying the patients according to the number of lesions, PSA level or Gleason score. Statistical analysis was performed with the GraphPad Prism v.8 Software (San Diego, CA, USA).

Results

Patient characteristics
Table 1 shows the cohort's clinicopathological characteristics. A total of 256 patients with Gleason ≥8 at biopsy (ISUP grades 4 or 5) were included in the study. The mean patient age was 65.9 ± 7.9 years and the median PSA was 8.5 ng/mL at the time of biopsy. One hundred forty-nine patients had Gleason score 8 at biopsy, 97 had Gleason score 9 and 7 had Gleason score 10. A total of 180 patients underwent radical prostatectomy (RP) and bilateral pelvic lymph node dissection (70%), while 72 patients (30%) received hormonal therapy alone or in combination with radiotherapy and/or chemotherapy as initial therapy. Patients underwent a bone scintigraphy and ^{18}F-FDG-PET/CT imaging within an average of 14.5 ± 86.2 days as a staging procedure prior to management.

Detection rate comparison between bone scintigraphy and ^{18}F-FDG-PET/CT
Bone metastases were diagnosed in 33 patients (33/256, 13%, Table 2). Patients with bone metastases were significantly older (68.8 ± 10.1 vs 65.4 ± 7.4; p=0.02), presented with higher PSA (165.5 ± 327.5 vs 13.8 ± 25.6; p<0.0001) and a higher Gleason score (9-10 vs 8; p<0.0001). In patients with bone metastases, 8 had a single lesion (monometastatic), 9 had between 2 and 4 lesions (oligometastatic) and 16 had 5 lesions or more (plurimetastatic). All 223 patients (223/256, 87%) without bone metastases had no clinical or radiographic evidence of metastatic spread for at least 6 months following initial staging. Bone scintigraphy detected 26 patients with bone lesions suspicious of metastases (detection rate 10%, 26/256) while ^{18}F-FDG-PET/CT detected a metastatic lesion for all the patients diagnosed as metastatic by standard of truth (SOT, detection rate 13%, 33/256). Figures 2 and 3 show representative images of a patient with concordant and discordant bone scintigraphy and ^{18}F-FDG-PET/CT imaging, respectively. There were 7 patients with negative bone scintigraphy and a positive ^{18}F-FDG-PET/CT. All of them met the SOT criteria for metastasis based on a per-patient basis (Tables 3-4). Six of the 7 patients had a confirmatory follow-up progressive bone scintigraphy (range from 2 to 36 months after initial staging) and/or clinical progression (rising PSA, bone pain), supporting the diagnosis of bone metastases. The remaining patient underwent a follow-up MRI (14 months after staging) confirming the presence bone metastases. False negative bone scintigraphy (n=7) represented 57.1% and 43.9% of patients with single (4/7) or oligometastatic (3/7) lesions, respectively. All plurimetastatic patients were detected by both imaging techniques (16/16) (Table 5).

Based on SOT, bone scintigraphy correctly identified 219 patients (98.2%, 219/223) as true negative while ^{18}F-FDG-PET/CT identified 220 patients (98.7%, 220/223). For the 4 patients with false positive bone scintigraphy, bone scintigraphy and CT follow-up (24 to 57 months) as well as clinical follow-up after radical prostatectomy or re-imaging showed no evidence of disease recurrence. For the 3 patients with false positive ^{18}F-FDG-PET/CT, ^{18}F-FDG-PET/CT and clinical follow-up (7 to 54 months) showed no sign of disease recurrence.

Table 6 summarizes the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ^{18}F-FDG-PET/CT and bone scintigraphy determined by SOT. Using the McNemar test, sensitivity of ^{18}F-FDG-PET/CT was significantly better than that of bone scintigraphy. ^{18}F-FDG-PET/CT correctly classified all patients with bone metastases, thus demonstrating a sensitivity of 100% (95% CI: 89.4-100), whereas the sensitivity of bone scintigraphy was 78.8% (95% CI: 61.1-91.0). The PPV was 86.7% (95% CI: 70.8-94.4%) for bone scintigraphy and 97.1% (95% CI: 82.4-99.6%) for ^{18}F-FDG-PET/CT. The NPV for bone scintigraphy was 96.9% (95% CI: 94.2-98.4%) and 100% (95% CI: n/a) for ^{18}F-FDG-PET/CT. The overall accuracy was 95.7% (95% CI: 92.4-97.8%) for bone scintigraphy and 98.8% (95% CI: 96.6-99.8%) for ^{18}F-FDG-PET/CT.

Sensitivities of bone scintigraphy and ^{18}F-FDG-PET/CT were also evaluated by stratifying the patients according to the number of lesions, PSA level or Gleason score. For patients with a single metastasis, ^{18}F-FDG-PET/CT and bone scintigraphy sensitivities were 100% (95% CI: 59.0-100) and 50.0% (95% CI: 15.7-84.3), respectively, while it was 88.0% (95% CI: 68.8-97.5) and 100% (95% CI: 86.3-100) for the oligo- and plurimetastatic patients (Table 7). Of the 8 patients with PSA < 20 ng/mL (8/33), bone scintigraphy missed bone metastases in 3 while ^{18}F-FDG-PET/CT correctly identified all metastatic patients, thus resulting in a sensitivity of 62.5% (95% CI: 24.5-91.5) and 100% (95% CI: 59.0-100), respectively (Table 7). In the 25 metastatic patients with PSA ³ 20 ng/mL (25/33), 21 patients were correctly identified with bone metastatic disease by bone scintigraphy, which resulted in a sensitivity of 84.0% (95% CI: 63.9-95.5). ^{18}F-FDG-PET/CT sensitivity was 100% (95% CI: 86.3-100) in this group. For patients with biopsy Gleason score of 8 or 9-10, bone scintigraphy sensitivity was 75.0% (95% CI: 34.9-96.8) and 79.1% (95% CI: 57.9-92.9) respectively, whereas ^{18}F-FDG-PET/CT showed a sensitivity of 100% for both groups (95% CI: 63.1-100 and 85.8-100) (Table 7).

Table 8 shows comparison between metastatic patients with true positive and false negative bone scintigraphy. Although it is not significant, false negative patients presented lower PSA levels and fewer lesions.

Discussion

In this study, we show that ^{18}F-FDG-PET/CT detected all metastatic patients identified by bone scintigraphy and more. In addition, based on our previous paper, it could detect lymph node and visceral metastasis, in addition to providing intra-prostatic biological information. As such, it can replace scintigraphy to stage newly diagnosed high-risk PCa. In a previous study, we exploited the ability of ^{18}F-FDG-PET/CT to image intraprostatic tumor biology of high grade PCa in order to discriminate high risk from very high-risk prostate cancer patients based on their risk of recurrence after radical prostatectomy [20]. We demonstrated that the accuracy of ^{18}F-FDG-PET/CT for lymph node metastasis detection was 73%. The next question was to determine if ^{18}F-FDG-PET/CT could stage PCa bone compartment instead of bone scintigraphy. In the current retrospective study on 256 patients with high-risk and high grade PCa (including the 148 described above), we compared the accuracy of bone scintigraphy and ^{18}F-FDG-PET/CT for bone metastasis detection. We observed that ^{18}F-FDG-PET/CT showed higher sensitivity and accuracy than bone scintigraphy for the detection of bone lesions. These results are in agreement with recent smaller studies [22-24]. Therefore, ^{18}F-FDG-PET/CT positions itself as a potential effective alternative to bone scintigraphy in patients with high-grade PCa by improving the detection rate while being highly specific for node metastasis. If sodium fluoride (NaF) is injected concomitantly with the FDG as published recently by Sonni et al., it is possible that a higher detection rates for bone metastasis could be reached without compromising the nodal or intraprostatic cancer detection by ^{18}F-FDG-PET/CT [25]. Given the poor accuracy of CT scan for imaging lymph node metastasis and our previously published data, FDG PET/CT can be considered as a single imaging technique to image high grade prostate cancers [20].

The slight superiority of ^{18}F-FDG-PET/CT could be explained by the mechanisms involved in ^{99m}MDP and ^{18}F-FDG-uptake, which are very different. ^{99m}MDP is adsorbed onto the mineral phase of forming bone, thus is an indirect sign of the presence of a metastatic lesion, while ^{18}F-FDG is captured by cells with high glucose metabolism, which in the bone regions are represented by cancer cells and represents a direct sign of metastatic cells. In this study, bone scintigraphy missed identifying metastases in 7 patients who all had positive ^{18}F-FDG-PET/CT, suggesting that not all ^{18}F-FDG positive lesions involved osteoblastic turnover or that ^{18}F-FDG-PET/CT could detect cancer cells in the bone before bone remodeling occurs.

The advantage of ^{18}F-FDG-PET/CT over bone scintigraphy is especially pertinent for two sub-groups of high-risk PCa patients: those with single metastases and those with low PSA levels. In these populations, bone scintigraphy only detected half of the patients that were metastatic on ^{18}F-FDG-PET/CT. This is not surprising as it is known that bone scintigraphy suffers from low sensitivity, especially at low PSA levels [26]. As expected, an increased detection rate of bone metastases with rising PSA value was observed and sensitivity reached 84.0% at a median PSA of 51.

Recently, PSMA-tracer PET imaging has emerged as the best imaging modality to stage or re-stage PCa (Fendler et al. 2017). However, the significance of a PSMA-avid lesion that is negative on conventional imaging remains to be convincingly determined. Because ^{18}F-FDG-PET/CT has a sensitivity similar to that of conventional imaging, metastatic cancer classification into high volume/high risk can still apply and management decided based on the conventional imaging algorithms [8,9]. Moreover, ^{18}F-FDG-PET/CT is available worldwide which means that it could therefore be used as a single imaging modality to stage high-risk PCa and guide management based on findings even if the patient is metastatic. This is especially important in the context of the COVID-19 pandemic in which it is recommended to limit in-hospital patient's visits. Finally, in our opinion, PSMA-PET/CT will be broadly indicated for restaging prostate cancer before salvage therapies. However, for initial staging, we think that the indication of PSMA-PET/CT compared to conventional imaging or FDG-PET/CT will rely on the strength of evidence showing that acting on supplemental findings from PSMA-PET/CT will make a change in outcome.

Our study has some limitations. Foremost the study is subject to all known biases of retrospective studies as selection and information bias. In addition, we do not have the histological confirmation of all discordant metastatic lesions. Even in prospective studies, this limitation cannot be easily overcome, as bone biopsies are painful, uncommonly performed in patients and notoriously challenging. Thus, false positive and false negative findings for both imaging modalities cannot be ruled out, and therefore may affect sensitivity and specificity, which need to be interpreted carefully. However, clinical and imaging follow-up remain valid approaches for evaluation of diagnostic accuracy, as it has been extensively used in other comparative imaging studies in PCa [27-29].

Despite these limitations, strengths of our study are its relative homogeneity of the study patients fulfilling the inclusion criteria, as we focused on high-grade PCa with homogeneous requirements in terms of diagnostic. This approach was chosen because the end points of our study are purely diagnostic. Another strength of the current study is its sample size which is significantly larger than that of other similar comparative studies [23,24,30,31]. Finally, the short time range (14.5 days) between bone scintigraphy and ^{18}F-FDG-PET/CT reduces the risk of metastatic development between examinations.

Conclusions
In high-grade prostate cancer patients at biopsy (Gleason 8-10; ISUP 4 and 5), our data shows that ^{18}F-FDG-PET/CT can be used alone to stage patients for bone metastasis.

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Figures and Tables

Fig. 1. Flowchart of the patient recruitment and selection process. PCa: prostate cancer; PET: positron emission tomography.
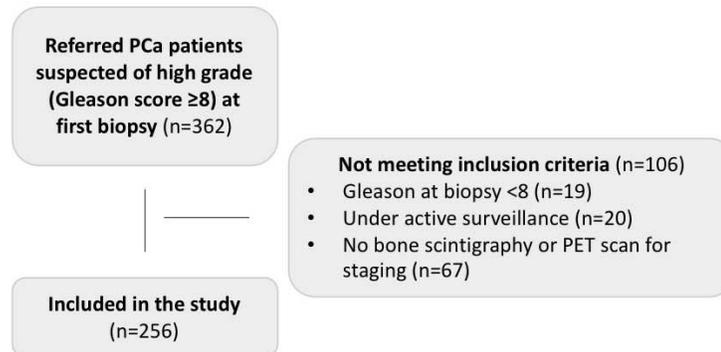

Fig. 2. Representative images of concordant bone scintigraphy and ^{18}F-FDG-PET/CT for bone metastasis detection in a 71-year-old patient with newly diagnosed prostate cancer (PSA 1.2 ng/ml; Gleason score 8 [4 + 4]). *(A)* Coronal, sagittal and axial ^{99m}Tc-MDP bone scan views showing metastatic lesion in D11 vertebra. *(B)* Coronal, sagittal and axial fused PET/CT images showing high ^{18}F-FDG-uptake (SUV$_{max}$=6.9) in D11 vertebra. PET/CT: positron emission tomography/computed tomography; PSA: prostate-specific antigen; SUV$_{max}$: maximum standardized uptake value.
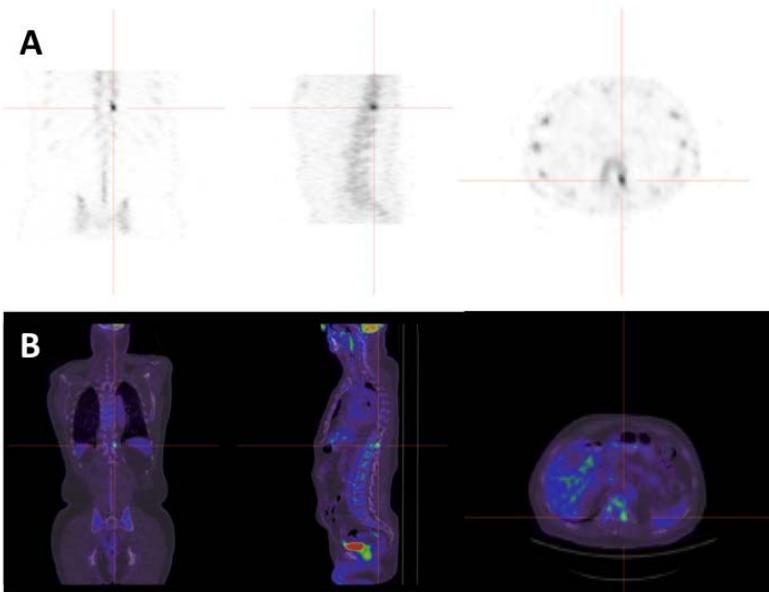
Fig. 3. False-negative bone scintigraphy versus ^{18}F-FDG-PET/CT for bone metastasis detection in a 78-yr-old patient with newly diagnosed PCa (PSA 9.0 ng/ml; Gleason score 8 [4 + 4]). *(A)* Coronal, sagittal and axial ^{99m}Tc-MDP bone scan views showing no obvious metastatic lesion. *(B)* Coronal, sagittal and axial fused PET/CT showing high ^{18}F-FDG-uptake (SUV$_{max}$=17.1) in D11 vertebra. PET/CT: positron emission tomography/computed tomography; PSA: prostate-specific antigen; SUV$_{max}$: maximum standardized uptake value.
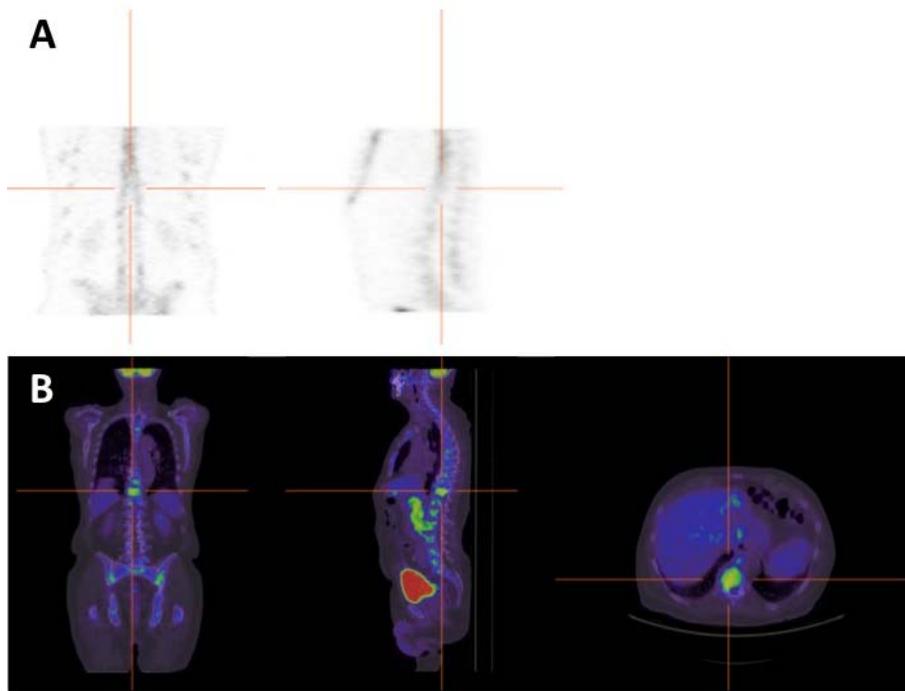
Table 1. Patients and clinicopathologic characteristics of the cohort	
Characteristics	**Value**
Patients, n	256
Age (years), mean ± SD	65.8±7.9
Gleason (biopsy)	
8	147
9	97
10	7
PSA (ng/mL), median	8.5
Clinical T stage	
cT1–2	176
cT3–4	29
NCCN risk category	
High	231
Very high	21
Treatment	
Radical prostatectomy	180
Radiotherapy + ADT	39
ADT	28
ADT + Chemotherapy	3
NA	6

ADT: androgen deprivation therapy; NA: not available; NCCN: National Comprehensive Cancer Network; PSA: prostate-specific antigen; SD: standard deviation.

Table 2. Metastatic burden at diagnosis by any modality

Characteristics	No metastasis	Metastasis	p	Mono	Oligo	Pluri	p
				Metastatic burden			
Patient, n (% of all)	223 (87)	33 (13)	–	8 (3)	9 (4)	16 (6)	–
Age (y), mean ± SD	65.4±7.4	68.8±10.1	0.02	69.8±9.9	64.6±10.9	70.8±9.6	0.33
Gleason at biopsy, n (%)			<0.0001				0.05
8	139 (63)	8 (33)		5 (63)	1 (11)	2 (13)	
9–10	80 (37)	24 (66)		3 (38)	8 (89)	13 (87)	
PSA (ng/mL), median	7.7	45.0	<0.0001	15.7	29.0	84.0	0.08

PSA: prostate-specific antigen; SD: standard deviation.

Table 3. Sensitivity for bone metastasis based on metastatic burden

	Bone scintigraphy	^{18}F-FDG-TEP/CT	Total
All	26 (78,8%)	33 (100%)	33
Plurimetastatic	16 (100%)	16 (100%)	16
Oligometastatic	6 (66,7%)	9 (100%)	9
Monometastatic	4 (50,0%)	8 (100%)	8

Table 4. Concordance between bone scintigraphy and ¹⁸F-FDG-PET/CT imaging for bone metastasis detection			
	Bone scintigraphy (+)	Bone scintigraphy (-)	Total
¹⁸F-FDG-PET/CT (+)	27	9	36
¹⁸F-FDG-PET/CT (-)	3	217	220
Total	30	226	256

Table 5. Description of patients with discordant PET/CT and bone scan					
Patient	PSA	Gleason	BS (n of meta)	PET/CT (n of meta)	Confirmation test
1	9.0	8	0	1	pT3N1 and postop PSA=2, no immediate confirmation test, BS performed years later and metastasis found on the suspected vertebra
2	10.8	9	0	1	Bone pain few months postop at the meta site & BS positive
3	13.0	9	0	3	Positive bone biopsy
4	20.7	8	0	1	Positive control CT scan
5	29.0	9	0	2	Positive control CT scan
6	45.0	9	0	1	Positive control BS, CT scan and clinical progression
7	125.0	9	0*	2	Positive control BS

*One lesion that cannot be classified. BS: bone scintigraphy; CT: computed tomography; PSA: prostate-specific antigen.

Table 6. Diagnostic performance of bone scintigraphy and ¹⁸F-FDG-PET/CT		
	Bone scintigraphy % (95% CI)	¹⁸F-FDG-TEP/CT % (95% CI)
Sensitivity	78.8 (61.1–91.0)	100 (89.4–100)
Specificity	98.2 (95.5–99.5)	98.7 (96.1–99.7)
PPV	86.7 (70.8–94.6)	91.7 (78.1–97.1)
NPV	96.9 (94.2–98.4)	100 (n/a)
Accuracy	95.7 (92.4–97.8)	98.8 (96.6–99.8)
False negative	7	0
False positive	4	3

CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

Table 7. Stratification of bone scintigraphy and ¹⁸F-FDG-PET/CT accuracy							
Stratification			**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
Number of lesions	Mono	BS	50.0 (15.7–84.3)	98.2 (95.5–99.5)	50.0 (23.7–76.7)	98.2 (96.5–99.1)	96.5 (93.3–98.5)
		FDG-TEP/CT	100 (59.0–100)	98.7 (96.1–99.7)	70.0 (43.1–87.8)	100 (n/a)	98.7 (96.2–99.7)
	Oligo-Pluri	BS	88.0 (68.8–97.5)	98.2 (95.5–99.5)	84.6 (67.3–93.5)	98.7 (96.2–99.5)	97.2 (94.3–98.9)
		FDG-TEP/CT	100 (86.3–100)	98.7 (96.1–99.7)	89.3 (73.0–96.3)	100 (n/a)	98.8 (96.5–99.8)
PSA levels	<20	BS	62.5 (24.5–91.5)	98.2 (95.5–99.5)	55.6 (29.2–79.1)	98.7 (96.8–99.4)	97.0 (93.9–98.8)
		FDG-TEP/CT	100 (59.0–100)	98.7 (96.1–99.7)	70.0 (43.1–87.8)	100 (n/a)	98.7 (96.2–99.7)
	≥20	BS	84.0 (63.9–95.5)	98.2 (95.5–99.5)	84.0 (66.2–93.4)	98.2 (95.7–99.3)	96.8 (93.7–98.6)
		FDG-TEP/CT	100 (86.3–100)	98.7 (96.1–99.7)	89.3 (73.0–96.3)	100 (n/a)	98.8 (96.5–99.8)
Gleason sum	8	BS	75.0 (34.9–96.8)	98.2 (95.5–99.5)	60.0 (34.4–81.1)	99.1 (97.1–99.7)	97.4 (94.4–99.0)
		FDG-TEP/CT	100 (63.1–100)	99.6 (97.5–100)	88.9 (53.1–98.3)	100 (n/a)	99.6 (97.6–100)
	9–10	BS	79.1 (57.9–92.9)	98.2 (95.5–99.5)	82.6 (63.8–92.8)	97.8 (95.3–99.0)	96.4 (93.2–98.3)
		FDG-TEP/CT	100 (85.8–100)	99.6 (97.5–100)	96.0 (77.3–99.4)	100 (n/a)	99.6 (97.6–100)

BS: bones scan; NPV: negative predictive value; PPV: positive predictive value; PSA: prostate-specific antigen.

Table 8. Comparison between metastatic patients with true positive and false negative bone scintigraphy		
	Bone scintigraphy	
	True positive	**False negative**
Patient, n	26	7
PSA (ng/mL), median	68.5	20.7
Gleason (biopsy), n		
8	6	2
9–10	19	5
Metastatic status, n		
Mono	4	4
Oligo	6	3
Pluri	16	0
Time between BS and PET (days)	47.1±106.9	26±22.5

BS: bone scan; PET: positron emission tomography; PSA: prostate-specific antigen; SD, standard deviation