

A prospective comparative study of ¹⁸F-PSMA-1007 PET-CT for primary staging of high-risk prostate cancer using strict validation criteria - high sensitivity and limited specificity for bone lesions

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Introduction

Computed tomography (CT) and bone scintigraphy (BS) are the imaging modalities currently used for metastasis staging of prostate cancer (PCa). The objective was to compare standard staging modalities with potentially more accurate imaging modalities.

Materials

This prospective, single-center trial (NCT03537391) enrolled 80 patients with newly diagnosed high-risk PCa (March 2018-June 2019) to undergo primary metastasis staging with standard and advanced imaging. This study reports the results of the distant metastasis staging.

Results of BS and CT were compared with ^{99m}Tc-HMDP single-photon emission CT-CT (SPECT-CT), 1.5T whole-body magnetic resonance imaging using diffusion-weighted imaging (WBMRI) and ¹⁸F-prostate-specific membrane antigen-1007 positron emission tomography (PSMA PET-CT). Each modality was reviewed by two independent experts and lesions were classified as benign, equivocal or malignant. Pessimistic and optimistic analyses were performed to resolve equivocal status. Based on primary and follow-up imaging, the reference standard was defined. PSMA PET-avid lesions were rated malignant only if there was a corresponding anatomical finding at primary or follow-up imaging.

Results

The clinical characteristics of 79 men completing the trial are presented in Table 1. The median follow-up was 435 days (range:378-557). Metastatic disease was detected in 20 (25%) patients. PSMA PET-CT had superior sensitivity [reader 1; 0.86 (95%CI;0.71-1.00), reader 2; 0.95 (95%CI;0.86-1.00)] and the highest inter-reader agreement. The area under the receiver-operating characteristic curve (AUC) values for bone metastasis detection were 0.90 (95%CI;0.85-0.95) and 0.91 (95%CI;0.87-0.96) (reader 1, and reader 2, respectively) for PSMA PET-CT while the AUC values

for the other modalities ranged from 0.53-0.85. PSMA PET-CT detected metastatic disease in 11/20 patients where standard imaging was negative, and influenced clinical decision making in 14/79 (18%) patients. In 12/79 cases false positive oligometastatic bone disease was reported only by PSMA PET-CT.

Age, years; mean (sd)	70 (7)
PSA, ng/ml; median (IQR) (range)	12 (16) (3-2000)
Clinical T-stage; n (%) ¹	
cT1	7 (9)
cT2	38 (48)
cT3	27 (34)
cT4	8 (10)
Biopsy GGG; n (%)	
1 ²	3 (4)
2	1 (1)
3	29 (36)
4	13 (16)
5	34 (42)
Primary treatment methods; n (%) ³	
RALP	5 (6)
RALP + lymphadenectomy	17 (21)
EBRT	38 (48)
TULSA	2 (3)
ADT	17 (21)
Watchful waiting	1 (1)

Table 1. Patient demographics, disease characteristics and primary treatment methods.

Conclusions

Despite the high false positive rate for bone lesions, PSMA PET-CT outperformed all other imaging methods studied for primary detection of distant metastasis in high-risk PCa.

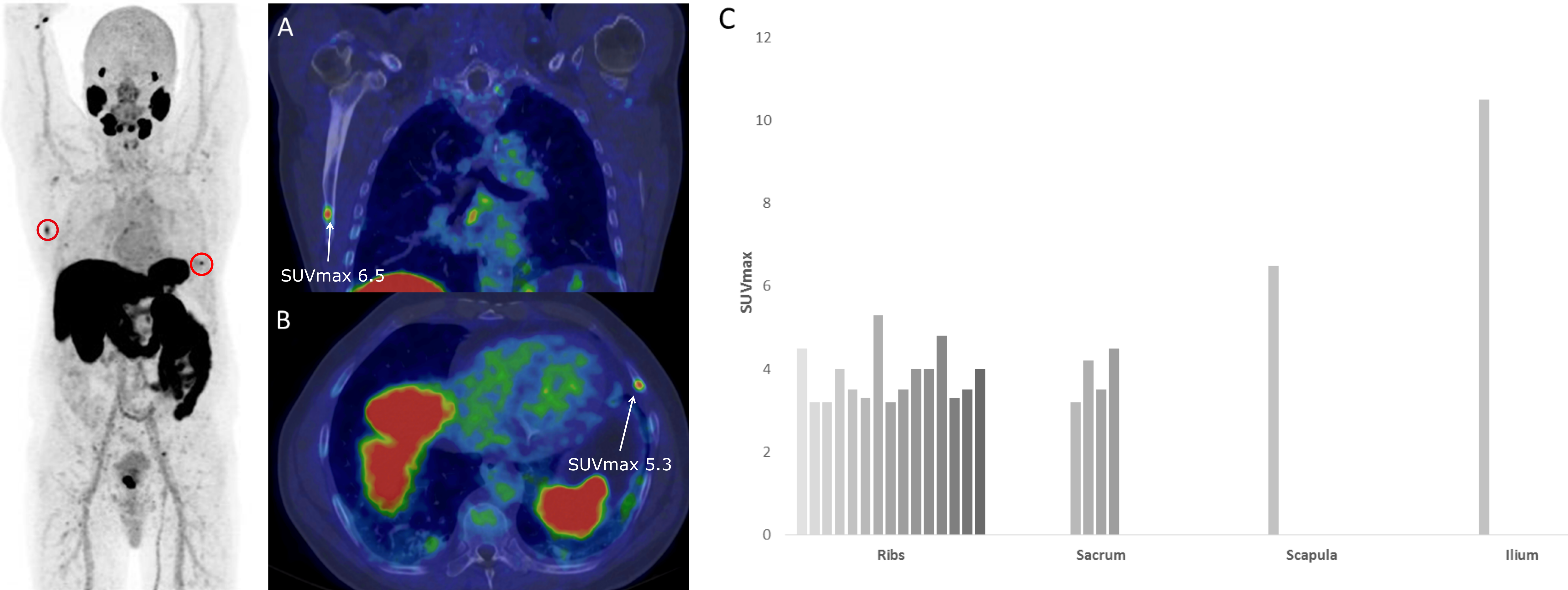


Figure 1. Maximum intensity projection and fused images of PSMA PET-CT in a study patient (GS 4+3 = 7, PSA 14 ug/l), showing two equivocal uptake foci (white arrows) in the right scapula (A) and 6th left rib (B). All other imaging modalities studied were reported as negative for bone metastases. The patient was treated with surgery, and 3 and 12 months after intervention PSA was < 0.006 ug/l without ADT. Ten out of 17 study patients treated with curative surgery (3-month PSA < 0.1 ug/l without ADT) presented with similar mild to moderate PSMA focal bone uptake (SUVmax) without anatomical correspondence as shown in the chart (C). The majority of PSMA uptake foci were located in ribs, followed by sacrum and, in one case, scapula and ilium. The mean SUVmax value was 4.3 (median: 4, range: 3.2-10.5, SD: 1.6).

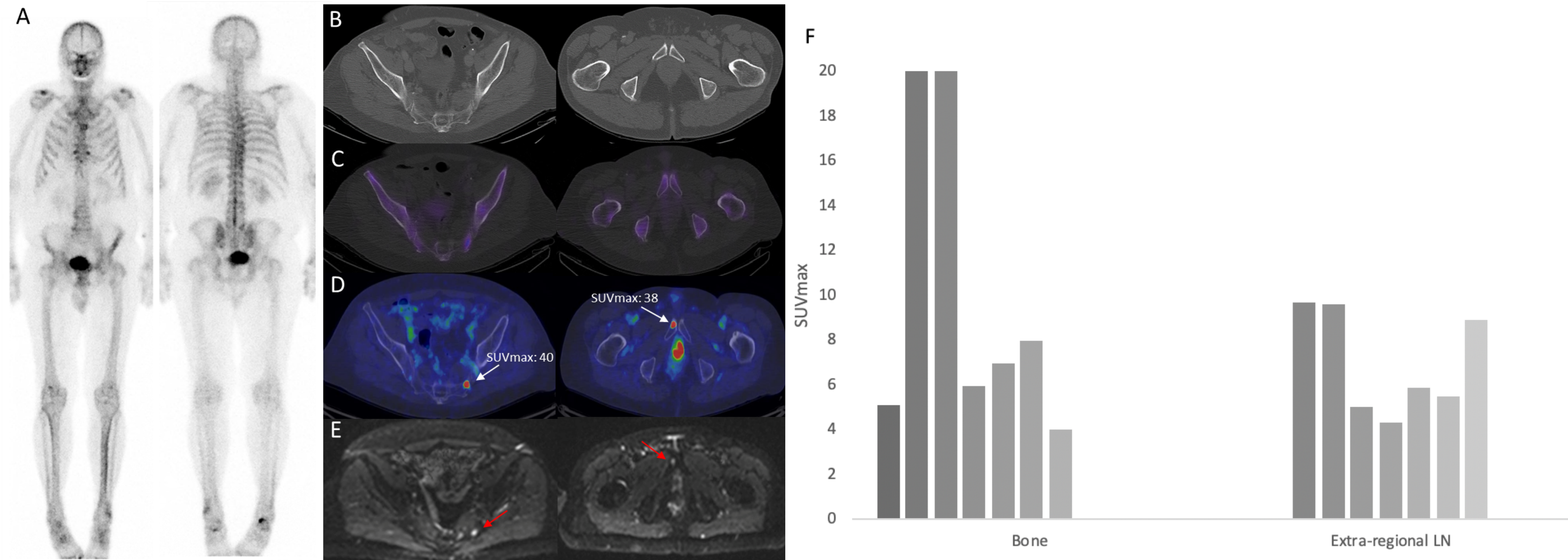


Figure 2. Images of BS (A), CT (B), SPECT-CT (C), PSMA PET-CT (D) and DWI (E) from a study patient (GS 5+4 = 9, PSA 10 ug/l). All imaging modalities were reported as negative for bone metastases in prospective reading, except PSMA PET-CT, in which two pathological uptake foci in the left sacrum and right pubic bone were observed (white arrows). DWI images, retrospectively analyzed, confirmed the presence of two lesions with diffusion restriction (red arrows). The chart (F) shows similar bone and extra-regional lymph node PSMA uptake reported as malignant in consensus reading in 6 patients with only PSMA PET-positive scans, that showed an anatomic correspondence and/or diffusion restriction in MRI, retrospectively analyzed. The mean SUVmax value was 10.5 (median: 6.4, range: 4-39.7, SD: 11.1).