

Diagnostic efficacy of F-18-rhPSMA-7.3 PET imaging for N-staging in Intermediate and High-Risk Prostate Cancer patients validated by histopathology

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Introduction and Objectives

⁶⁸Ga-prostate-specific membrane antigen (PSMA) positron emission tomography (PET) has become a common method for primary staging of prostate cancer. ¹⁸F-labeled PSMA ligands are increasingly used because in comparison with ⁶⁸Ga-labeled counterparts they have a longer half-life, larger batch production and lower positron range resulting in higher image resolution. Radiohybrid PSMA (rhPSMA) ligands are a new class of diagnostic/therapeutic PSMA-targeting agents, which can be efficiently labeled with F-18 and radiometals and show only minimal renal excretion. Promising preliminary data have been reported for F-18-rhPSMA-7, which comprises four isomers. Based on preclinical findings, F-18-rhPSMA-7.3 was selected as the lead rhPSMA compound for clinical development. Here we report first data investigating its efficacy for primary N-staging in patients with intermediate and high-risk prostate cancer. Results were compared to morphological imaging and validated by histopathology.

Methods

Data from 56 consecutive patients with with intermediate or high-risk prostate cancer (defined by D’Amico) who had undergone F-18-rhPSMA-7.3 PET/CT-imaging before radical prostatectomy and extended pelvic lymph node dissection, were reviewed. An experienced reader carried out a template-based analysis using a 5-point scale to determine the presence of lymph node metastases. This was conducted independently for both the PET and morphological datasets. Patient-level, Right vs. Left (R vs. L) side-based and template-based results were both compared to histopathological findings.

Results

Patients’ characteristics are shown in Table 1. The median injected activity of ¹⁸F-rhPSMA7.3 was 349 MBq (range, 240–449 MBq), with a median uptake time of 72 min (range, 58–102 min). Lymph node metastases were present in 18/56 patients (32.1%) located in 33 of 319 templates (10.3%) (Figure 1). On the patient-based analysis, the sensitivity, specificity and accuracy of ¹⁸F-rhPSMA7.3 PET were 81.3%, 87.5% and 85.7%, respectively, while those for morphological imaging were 33.3%, 89.5% and 71.4%, respectively. For the right vs. left analysis the sensitivity, specificity and accuracy of F-18-rhPSMA7.3-PET were 70.8%, 96.6% and 91.1%, and for morphological imaging 25.0%, 95.5% and 80.4%, respectively. On the template-based analysis, the sensitivity, specificity and accuracy of ¹⁸F-rhPSMA7.3 PET were 63.6%, 97.9% and 94.4%, respectively and those for morphological imaging were 15.2%, 99.3% and 90.6%, respectively (Table 2). On ROC analyses, F-18-rhPSMA7.3-PET showed a significantly better performance than morphological imaging on patient-, R vs. L and template-based analyses, yielding AUC values of 0.842 vs. 0.697 (p<0.05), 0.843 vs. 0.631 (p<0.001) and 0.801 vs. 0.639 (p<0.001), respectively.

Table 1: Characteristics of patient cohort (n = 56)

Age at PET	Median (years)	66 (50-81)
PSA at PET	Median (ng/mL)	11.0 (2.4-296.0)
pT	≤pT2	20 (35.7 %)
	pT3a	7 (12.5 %)
	≥pT3b	29 (51.8 %)
pN	pN0	38 (67.9 %)
	pN1	18 (32.1 %)
LN removed / pt.	Median	21 (7-50)
LN with mets / pt.	Median	0 (0-19)
Gleason Score	7a (3+4)	7 (12.5 %)
	7b (4+3)	28 (50.0 %)
	8	7 (12.5 %)
	9	13 (23.2 %)
	10	1 (1.8 %)

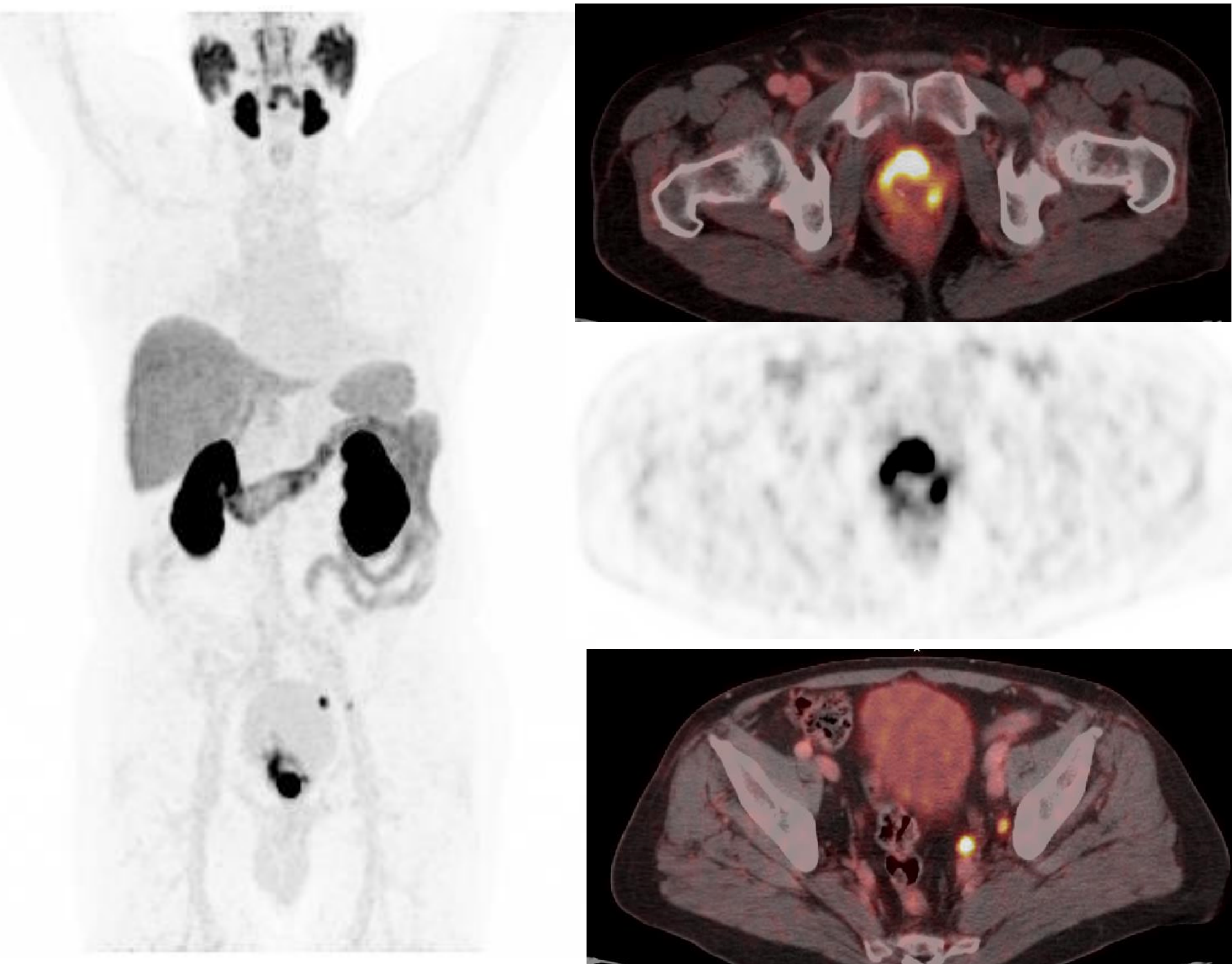


Figure 1: 72 y/o patient with high risk prostate cancer (iPSA= 44 ng/ml): ¹⁸F-rhPSMA-7.3 PET/CT detected the primary tumor and pelvic lymph node metastases histologically confirmed by radical prostatectomy (pT3b pN1 (2/34) Gleason score 3+4=7b)

Table 2: Imaging results from ¹⁸F-rhPSMA7 PET (n = 56)

Site of disease	Local	Pelvic LN	Extrapelvic LN	Bone mets	Visceral mets
No. pos. (%)	56 (100)	15 (26.8)	0 (0)	3 (5.4)	0 (0)
patient-based analysis	Morphological imaging			¹⁸ F-rhPSMA7.3 PET	
	Estimate in %	95%CI in %		Estimate in %	95%CI in %
Sensitivity	33.3	13.3 – 59.0		81.3	54.4 – 96.0
Specificity	89.5	75.2 – 97.1		87.5	73.2 – 95.8
PPV	60.0	32.6 – 82.3		72.2	52.6 – 85.9
NPV	73.9	66.8 – 80.0		92.1	80.7 – 97.0
Accuracy	71.4	57.8 – 82.7		85.7	73.8 – 93.6
AUC (p<0.05) (Standard error)	0.697 (0.073)	0.560 – 0.813		0.842 (0.061)	0.720 – 0.926
Difference (Standard error)	0.145 (0.072)	0.003 – 0.286			
Template-based analysis	Morphological imaging			¹⁸ F-rhPSMA7.3 PET	
	Estimate in %	95%CI in %		Estimate in %	95%CI in %
Sensitivity	15.2	5.11 – 31.9		63.6	45.1 – 79.6
Specificity	99.3	97.5 – 99.9		97.9	95.5 – 99.2
PPV	71.4	33.6 – 92.5		77.8	60.4 – 89.0
NPV	91.0	89.8 – 92.1		95.9	93.7 – 97.3
Accuracy	90.6	86.9 – 93.6		94.4	91.2 – 96.6
AUC (p<0.001) (SE)	0.639 (0.043)	0.584 – 0.692		0.801 (0.045)	0.753 – 0.843
Difference (SE)	0.162 (0.048)	0.068 – 0.256			

Conclusion

¹⁸F-rhPSMA7.3 PET is superior to morphological imaging for lymph node staging of primary intermediate and high risk prostate cancer. The efficacy of ¹⁸F-rhPSMA7.3 PET is in the same range as that previously reported in the literature for ⁶⁸Ga-PSMA11. However, ¹⁸F-rhPSMA7.3 exhibits the advantage of facilitated large batch production.