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Actual impact of ^{68}Ga-PSMA-11 PET/CT on the management of prostate cancer patients with biochemical recurrence

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ABSTRACT

Purpose: In this prospective survey of referring physicians, we investigated whether and how Gallium-68 Prostate Specific Membrane Antigen Positron Emission Tomography/Computed Tomography (PSMA-11 PET/CT) affects the actually implemented management of prostate cancer patients wih biochemical recurrence (BCR). **Methods**: We conducted a prospective survey of physicians (NCT02940262) who referred 161 patients with prostate cancer BCR (median Prostate Specific Antigen (PSA) value 1.7 ng/ml (range 0.05-202)). Referring physicians completed one questionnaire prior to the scan to indicate the treatment plan without PSMA-11 PET/CT information (Q1; n=101); one immediately after the scan to denote intended management changes (Q2; n=101); and one 3 to 6 months later to document the final implemented management (Q3; n=56). Implemented management was also obtained via electronic chart review and/or patient contact (n=45). **Results**: Complete documented management strategy (Q1+Q2+implemented management) was available in 101/161 patients (63%). Seventy-six of these (75%) had a positive PSMA-11 PET/CT study. The actually implemented management differed from the pre-scan intended treatment plan (Q1) in 54/101 patients (53%). The post-scan intended management (Q2) differed from the pre-scan intended management (Q1) in 62/101 patients (61%); however, these intended changes were not implemented in 29/62 patients (47%). Pelvic nodal and extra-pelvic metastatic disease on PSMA-11 PET/CT (PSMA T0N1M0 and PSMA T0N1M1 patterns) were significantly associated with implemented management changes (p=0,001, 0.05). **Conclusion**: PSMA-11 PET/CT results in actually implemented management changes in more than 50% of prostate cancer patients with BCR (54/101; 53%). However, intended

management changes early after PSMA-11 PET/CT frequently differ from actually implemented management changes.

INTRODUCTION

PSMA-11 PET/CT is superior to conventional imaging for detecting sites of prostate cancer BCR (*1*–*4*), is sensitive for detecting regional and distant metastatic disease (*3*,*5*), is highly specific (*4*) and is associated with a low inter-reader variability (*6*).

Health Care providers and government agencies frequently judge the value of novel diagnostic tests by measuring their impact on patient management. Often, this impact has been estimated from survey information after the index test information becomes available to treating physicians (*7*). However, intended management early after imaging results become available do not necessarily translate into actually implemented management (*8*–*11*). The rate of implemented management changes related to PSMA-11 PET/CT has not been determined prospectively in patients with BCR. Two retrospective studies attempted to determine rates of *implemented* management changes (*12*,*13*), while 3 prospective studies evaluated the impact of PSMA-11 PET/CT on *intended* management changes (*1*,*14*,*15*).

Here we investigated prospectively the impact of PSMA-11 PET/CT on the actually implemented management of prostate cancer patients with BCR.

MATERIALS AND METHODS

Patients, Registration and Authorization

We were granted an Investigational New Drug Application (IND) by the Food and Drug Administration (FDA) for a prospective study to evaluate the diagnostic perfomance of PSMA-11 PET/CT for localization of BCR (NCT02940262). The primary endpoint of this study is the accuracy for lesions identified by PSMA-11 PET. Here we report on a secondary endpoint in a consecutively recruited subgroup of patients: the impact of PSMA-11 PET/CT on patient management. The University of California, Los Angeles (UCLA) Institutional Review Board (IRB) approved the protocol, informed consent forms, participant information forms and the prospective referring physician questionnaires (IRB#16-001095). From October 2016 to June 2017, we enrolled 161 patients with proven prostate adenocarcinoma and BCR after prostatectomy (PSA > 0.2 ng/mL,> six weeks after surgery) or definitive radiotherapy (PSA rise ≥ 2 ng/mL above the nadir). All patients provided written informed consent.

Survey Design

The survey design is depicted in Figure 1. We asked referring physicians to complete and return 3 questionnaires by email or fax. One questionnaire prior to the scan was required to indicate the treatment plan without PSMA-11 PET/CT information (Q1). A second questionnaire inquired about intended management immediately after receipt of the written clinical report and the images (Q2). A final third questionnaire emailed 3 to 6 months later verified whether intended management changes were in fact implemented (Q3). Up to 3 email reminders were sent to referring physicians if questionnaires were not

returned. To further document the actually implemented management strategy, we conducted an electronic chart review and and followed-up with patients.

The management options and changes are categorized in Table 1. We did not consider adding or removing androgen deprivation therapy (ADT) to the treatment strategy a significant management change except when active surveillance was intended/implemented.

Intended management changes between Q1 and Q2 represent the initial impact of imaging findings resulting in *intended* management changes that may however not necessarily represent the *implemented* management change. Changes between Q2 and Q3/chart review/patient contact represent the difference between the intended post-scan and actually implemented management plan. Changes between Q1 and Q3/chart review/patient contact represent the changes from pre-scan to the actually implemented management plan.

PSMA-11 PET/CT Protocol

PSMA-11 PET/CT imaging was performed according to recent guidelines (*16*) with a 64-detector PET/CT device (Biograph True Point 64 or Biograph mCT; Siemens). ^{68}Ga-PSMA-11 (Glu-NH-CO-NH-Lys-(Ahx)-[^{68}Ga(HBED-CC)]) was used as the PSMA ligand (*17*). The median injected dose was 196 MBq (range 93-241 MBq). To reduce bladder activity patients received 20 mg of furosemide at the time of tracer injection if there was no contraindication. The median uptake period was 62 min (range 52-96 min). A diagnostic CT scan (200-240 mAs, 120 kV) was performed after intravenous injection of contrast agent (if no contraindication) followed by the whole body PET image acquisition (2-4 min/bed position). Standard image reconstruction parameters were used (*16*,*18*).

^{68}Ga-PSMA-11 PET/CT Image Analysis

PSMA-11 PET/CT images were analyzed according to recent guidelines during clinical readouts by an experienced nuclear medicine physician who had unlimited access to all medical records (*16*,*18*,*19*): any focal uptake of PSMA-11 PET/CT above background and not associated with physiological uptake or known pitfalls (*6*,*18*) was considered PSMA-positive.

We routinely adopt an image based TNM staging system and analyze the following regions for recurrence: prostate/ prostate bed/ seminal vesicle remnants (T), pelvic lymph nodes (N) (internal iliac, obturator, external iliac, perirectal, pre-sacral, common Iliac, other), extra-pelvic lymph nodes (M1a) (retroperitoneal, inguinal, chest, other), bone (M1b) and visceral organs (M1c).

Statistics

All variables were summarized by descriptive statistics (median, range). The comparisons for management change rates between PSMA-positive and -negative patients were conducted using Chi-squared test. Post-scan intended management change (Q1->Q2), non-implementation of post-scan intended management (Q2->implemented) and actually implemented management change (Q1->implemented) were considered as three primary binary outcome variables in this study. Four potential predictor parameters were studied: National Comprehensive Cancer Network (NCCN) risk group, serum PSA level prior PSMA-11 PET/CT, prior primary treatment (surgery or radiotherapy) and PSMA-11 PET/CT TNM pattern. Multiple logistic regression analysis

was carried out to investigate the potential association between these four predictors and above three primary outcome variables. All statistical analyses were conducted in R (*20*).

RESULTS

Referring Physicians and Questionnaires

The flowchart is depicted in Figure 2. Fifty-seven physicians referred 161 patients for PSMA-11 PET/CT imaging. Complete documented management strategy (Q1+Q2+actual implemented management) was available in 101/161 patients (63%). Forty-two different physicians (10 from UCLA, 32 from other institutions) referred the 101 patients (38 from UCLA, 63 from other institutions).

Q1 and Q2 were completed in all 101 while Q3 was completed in 56/101 patients (55%). In 19 of these patients electronic chart verification (n=11), patient contact (n=8), were used to further verify the accuracy of Q3 information. In the remaining 45/101 patients (45%) Q3 was not completed but electronic chart review (n=32), patient contact (n=10) or both (n=3) were used to document the actually implemented management strategy (Fig. 2).

Referring physicians completed Q1 within a median of 18 days before the scan (range 0-93 days). Q2 was completed within a median of 9 days after the scan (range 1-89 days). We obtained Information about the actually implemented treatment within medians of 105 days after the scan (range 30-259 days) and 94 days after Q2 completion, respectively (range 26-246 days).

Patient Population

Patient demographics are presented in Table 2. Briefly, in the 101 patients with complete documented management strategy the median serum PSA value prior to PSMA-11 PET/CT was 1.7 ng/ml (range 0.05-140). 87/101 patients (86%) had prior prostatectomy while 14/101 (14%) had prior definitive radiotherapy. The median time between primary treatment and PSMA-11 PET/CT was 4.2 years (range 0.12-18) and 21/101 patients (21%) had ADT within 6 months prior to PSMA-11 PET/CT.

In the 60 patients without complete documented management strategy median serum PSA value prior to PET/CT was 2.25 ng/ml (range 0.2-202).

PSMA-11 PET/CT Findings

PSMA-11 PET/CT findings are detailed in Table 3. In brief, 76/101 patients (75%) had a positive PET/CT study: 64/101 (64%) had PSMA-positive intra-pelvic lesions while 37/101 (37%) had PSMA-positive extra-pelvic lesions. Thus far, histopathological verification was available in 18 of the 76 PSMA-positive patients (24%). PSMA-positive lesions corresponded to prostate adenocarcinoma in 14/18 patients (78%): in 4/7 (57%) with local recurrence, in 7/7 (100%) with pelvic LN recurrence, in 1/1 with retroperitoneal LN recurrence and in 2/3 (66%) with lung metastases reported by PET. The remaining 4/18 cases (22%) may reflect PSMA-11 PET/CT false positive or biopsy false negative findings.

Forty-seven/ 60 patients (78%) without complete documented management strategy had a positive PSMA-11 PET/CT study.

Impact on Patient Management

Management changes are detailed in Table 4. Implemented management changes (Q1->implemented) were recorded in 54/101 patients (53%). These consisted of conversion to focal treatment/new focal treatment in 29/101 (29%), conversion to systemic treatment in 13/101 (13%), change of the systemic treatment approach in 5/101 (5%), and conversion to active surveillance in 7/101 patients (7%).

PSMA-11 PET/CT (Q1->Q2) resulted in intended management changes in 62/101 patients (61%): these included conversion to focal treatment/new focal treatment in 40/101 (40%), conversion to systemic treatment in 12/101 (12%), change in systemic treatment in 5/101 (5%), and conversion to active surveillance in 5/101 patients (5%).

Intended treatment as indicated in Q2 was implemented in 66/101 patients (67.5%): implementation of the intended strategy occurred in 33/62 patients (53%) with and 33/39 patients (85%) without intended management changes. Non-implementation of intended management changes following the PSMA-11 PET/CT study (Q2) occurred in 35/101 (35%) patients. Tumor board or other medical decisions (13/35; 37%), patient choice (11/35; 31%), and second opinions at other institutions (5/35; 14%) accounted for non-implementation. Reasons remained unknown in 6/35 (17%). Figures 3 and 4 depict patients in whom subsequent decisions led to non-implementation of intended management.

Predictors of Management Changes

Among four tested parameters (NCCN risk group, PSA level prior PET/CT, prior primary treatment and PSMA-11 TNM pattern) the PSMA-11 PET/CT TNM pattern was the only significant predictor of intended (Q1->Q2) and implemented (Q1->implemented) management changes.

Specifically, the probability of having *intended* management change was higher in patients with pelvic nodal disease only (PSMA T0N1M0) than in patients with negative scans (p=0.02). Furthermore, *intended* management changes occurred more frequently in patients with positive PSMA-11 PET/CT (52/76; 68%) than in those with negative scans (10/25; 40%) (p= 0.02). Figure 5 illustrates a PSMA T0N1M0 pattern.

The probability of having *actually implemented* management changes (Q1->implemented) was higher in patients with PSMA T0N1M0 (p=0.001) and T0N1M1 patterns (p=0.05) than in those with negative scans. Finally, implemented management changes (Q1-> implemented) occurred more frequently in patients with positive PSMA-11 PET/CT (48/76; 63%) than in those with negative scans (6/25; 24%) (p<0.002).

None of the four parameters predicted non-implementation of the intended management after the PSMA-11 PET/CT study (Q2->implemented).

DISCUSSION

This prospective survey enabled a systematic assessment of how referring physicians respond to the diagnostic information provided by PSMA-11 PET/CT imaging. The actually implemented management differed from the pre-scan treatment plan (Q1) in 54/101 patients (53%). PSMA T0N1M0 and PSMA T0N1M1 patterns were significantly associated with higher likelihood for actually implemented management changes (p=0.001 and 0.05 respectively) (Fig. 5). These two patterns frequently lead to focal therapy with surgery or radiation therapy (especially pelvic node only recurrence), a strategy that can only be considered after scan findings are available.

A significant impact of any diagnostic test on management suggests value for patients and is a prerequisite for widespread acceptance (*7*). However, one concern about

studies using intended management changes as endpoint is that these changes may not be implemented (*8*–*11*). The actually implemented management reflects the true impact of an index test (*8*,*9*). In fact, implemented management changes are the most reliable source for cost or cost-effectiveness analyses (*8*,*21*,*22*). Implemented management can be assessed retrospectively for instance from large databases (*22*). However, intended management before image information becomes available can only be determined prospectively. Thus, reliable information must arise from information that is prospectively recorded prior to and after the index test is performed.

We documented actual management changes in 53% of prostate cancer patients with BCR in response to PSMA-11 PET/CT imaging. These findings are in line with the mean pooled rate of 57.3% (range 39-76%) from retrospective studies (*12*,*13*). The current rate of intended management changes in 61% of patients is also consistent with the pooled rate of 55.8% (range 51-63%) from prospective studies (*1*,*14*,*15*). Other studies enrolled patients prospectively for other reasons but management changes were not assessed prospectively (*23*).

We demonstrated that in 1/3 of the patients, the intended management changes (Q2) were not implemented consistent with previous studies (*8*). Prostate cancer patients are offered multiple treatment options, including ADT, surgery, RT or combinations. Clinical decisions are often based on imaging information, tumor boards, expert opinions and patient preference. The timing of surveys conducted early after the index test, in our case Q2, precludes consideration of other factors that can affect final decision-making. Imaging is obviously not the only determinant of management decisions. These are often based on tumor board or expert opinions, second opinions, patient preference and others. Thus, intended management changes, used as study endpoints in many studies, do not

provide actual patient management information. In the current study intended management, changes were often either not implemented or changed to yet other management plans after more information became available to referring physicians. Interestingly, the rate of non-implementation was much higher in patients with intended changes after the scan (47%) than in patients without intended changes (15%). The current findings underscore a severe limitation of surveys using *intended* management changes as endpoint: surveys are blind to changes induced by tumor board/expert opinions, patient preference and others. To clearly define the actually implemented management, verification of the management plan using other sources such as electronic chart review, patient and clinician informations is a prerequisite for appropriate assessment.

Limitations

We cannot rule out a responder bias as complete information was available in 101/161 patients (63%) (*24–26*). A less than 100% completion rate may have introduced a responder bias. However, as 96/161 patients (60%) were referred from different external institutions we considered a 63% completion rate as satisfactory. In addition, the large number of participating physicians (n>40) argues against a significant bias. Furthermore, imaging findings and clinical parameters were comparable between the 101 patients with complete documented management strategy and the 60 patients without (detection rate of 75% vs. 78%; median PSA levels of 1.7 ng/ml (range 0.05-140) vs. 2.25 ng/ml (range 0.2-202)). The relatively low completion rate of Q3 is a negligible problem as we verified implemented management strategies via other means (electronic chart review and contact with patients).

CONCLUSION

This prospective referring physician based survey shows a significant impact (54/101; 53%) of PSMA-11 PET/CT on the actual management of prostate cancer patients with BCR. Importantly, intended management changes after PSMA-11 PET/CT were further modified in almost 50% of the patients underlining limitations of survey-based management assessment.

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FIGURE LEGENDS

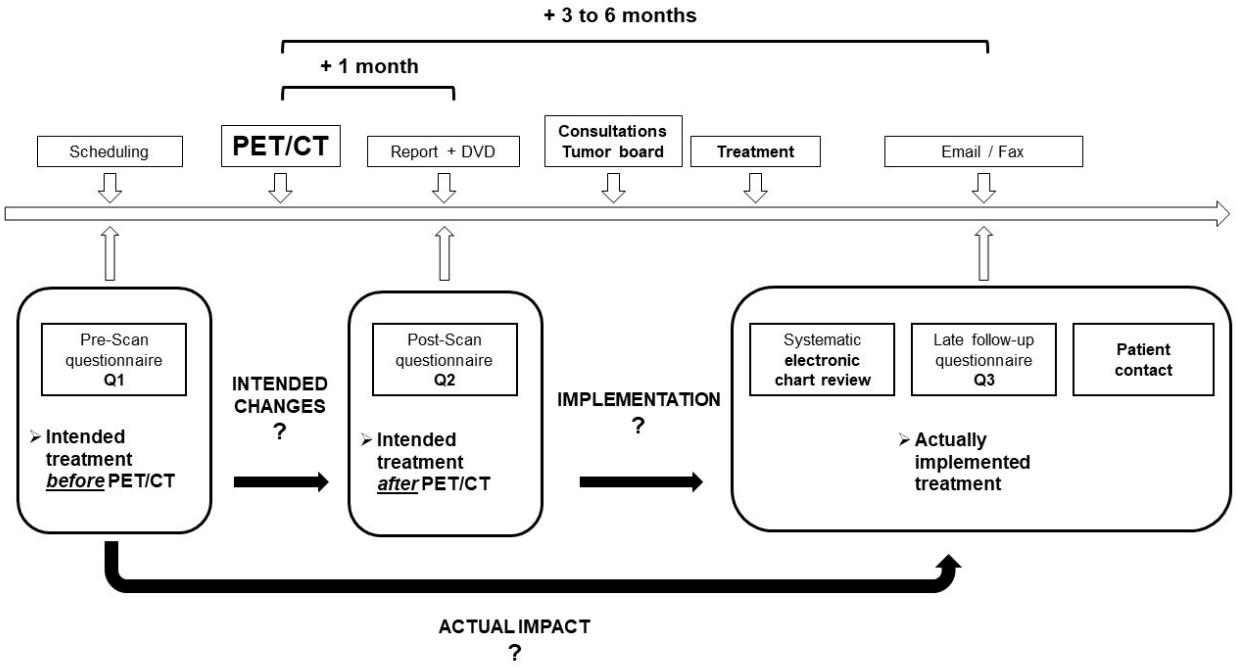

Figure 1: Study design

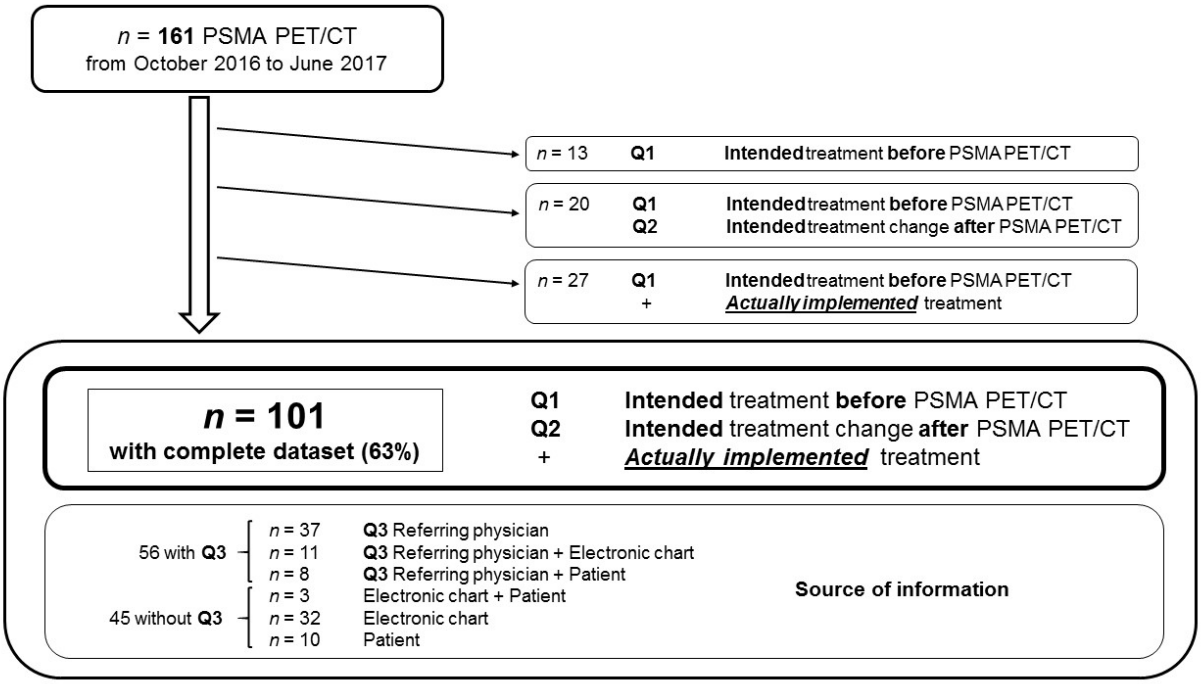

Figure 2: Flowchart

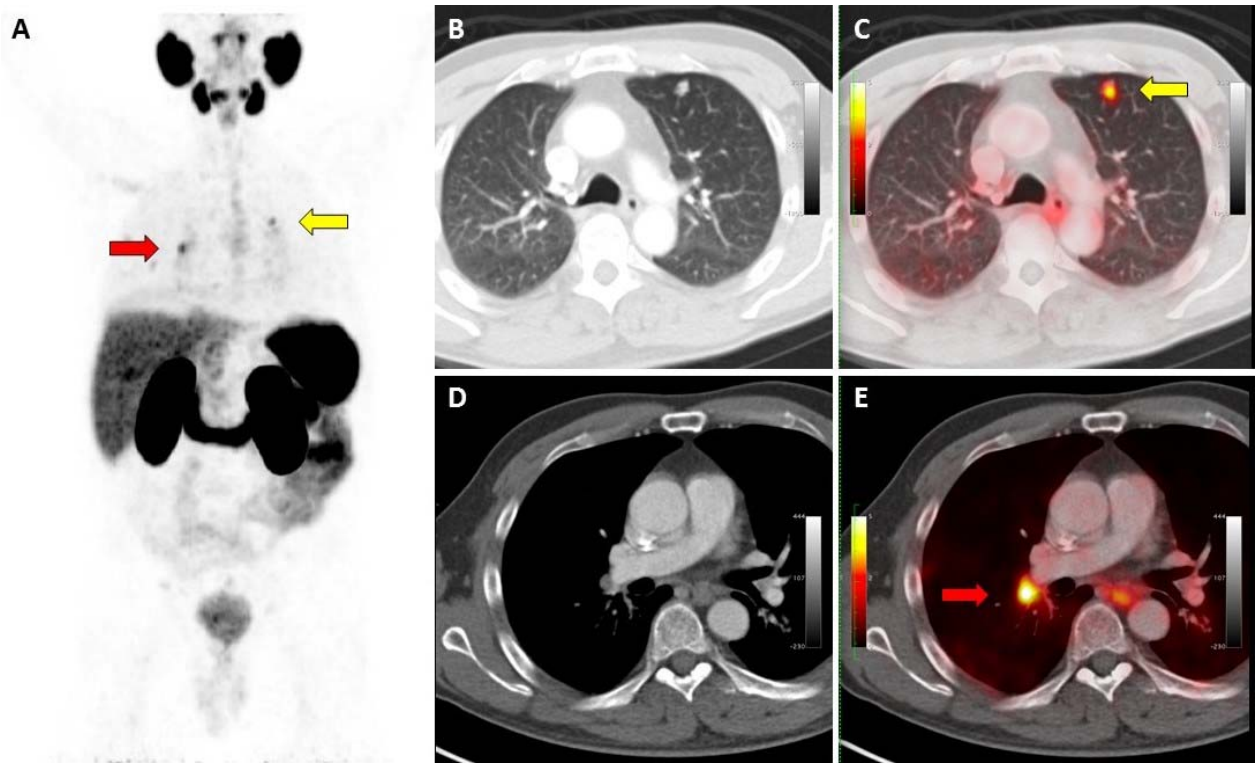

Figure 3: 67-year-old man with BCR (PSA 10.7 ng/ml, doubling time 9.3 months) of an initially high-risk prostate cancer (Gleason 9; pT3a) eight years after primary radical prostatectomy and adjuvant prostate bed irradiation. The intended pre-scan treatment was ADT. PSMA-11 PET/CT showed intense PSMA-11 uptake (SUVmax 7) in multiple lung nodules (yellow arrows) and thoracic lymph nodes (red arrows). The intended post-scan treatment (Q2) was chemotherapy + ADT. The CT-guided biopsy of the upper left lung nodule confirmed metastatic prostatic adenocarcinoma. Patient elected to forgo chemotherapy because of the potential side effects and thus the intended post-scan management (Q2) was not implemented. The actual management was ADT alone and thus there was no change from the pre-scan intended management as recorded on Q1.

Panel A: PSMA-11 PET Maximum-Intensity-Projection (MIP) images; Panel B: Axial CT, lung window; Panel C: Fused axial PSMA-11 PET/CT, lung window; Panel D: axial CT, mediastinal window; Panel E: Fused axial PSMA-11 PET/CT, mediastinal window.

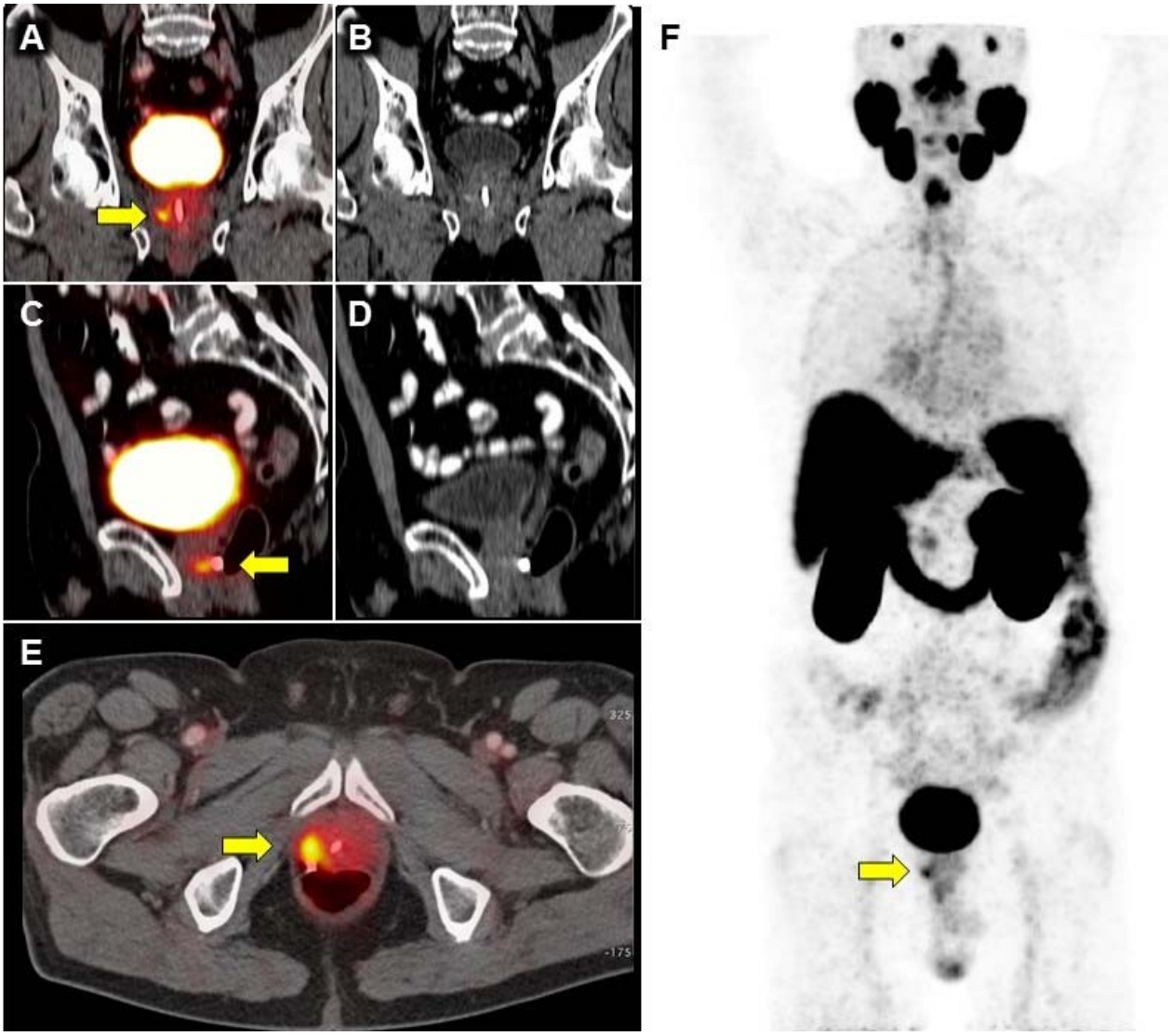

Figure 4: PSMA-11 PET/CT in a 75-year-old patient with BCR (PSA 2.88 ng/ml, doubling time 4.5 months) of an initially high-risk prostate cancer (Gleason 8; pT3) four years after primary radiotherapy without ADT. Q1 listed ADT as planned treatment. PSMA-11 PET/CT showed focal PSMA-11 uptake (SUVmax 3.9) in the right prostate lobe (yellow arrows). The intended treatment after PSMA-11 PET/CT (Q2) was surgery, which the patient refused because of the potential side effects. The actual management was thus ADT as indicated on Q1 (no management change).

Panel A: Fused coronal PSMA-11 PET/CT; Panel B: Coronal CT; Panel C: Fused sagittal PSMA-11 PET/CT; Panel D: sagittal CT; Panel E: Fused axial PSMA-11 PET/CT; Panel F: PSMA-11 PET Maximum-Intensity-Projection (MIP) images; Yellow arrow denotes focal tracer uptake consistent with intraprostatic recurrence.

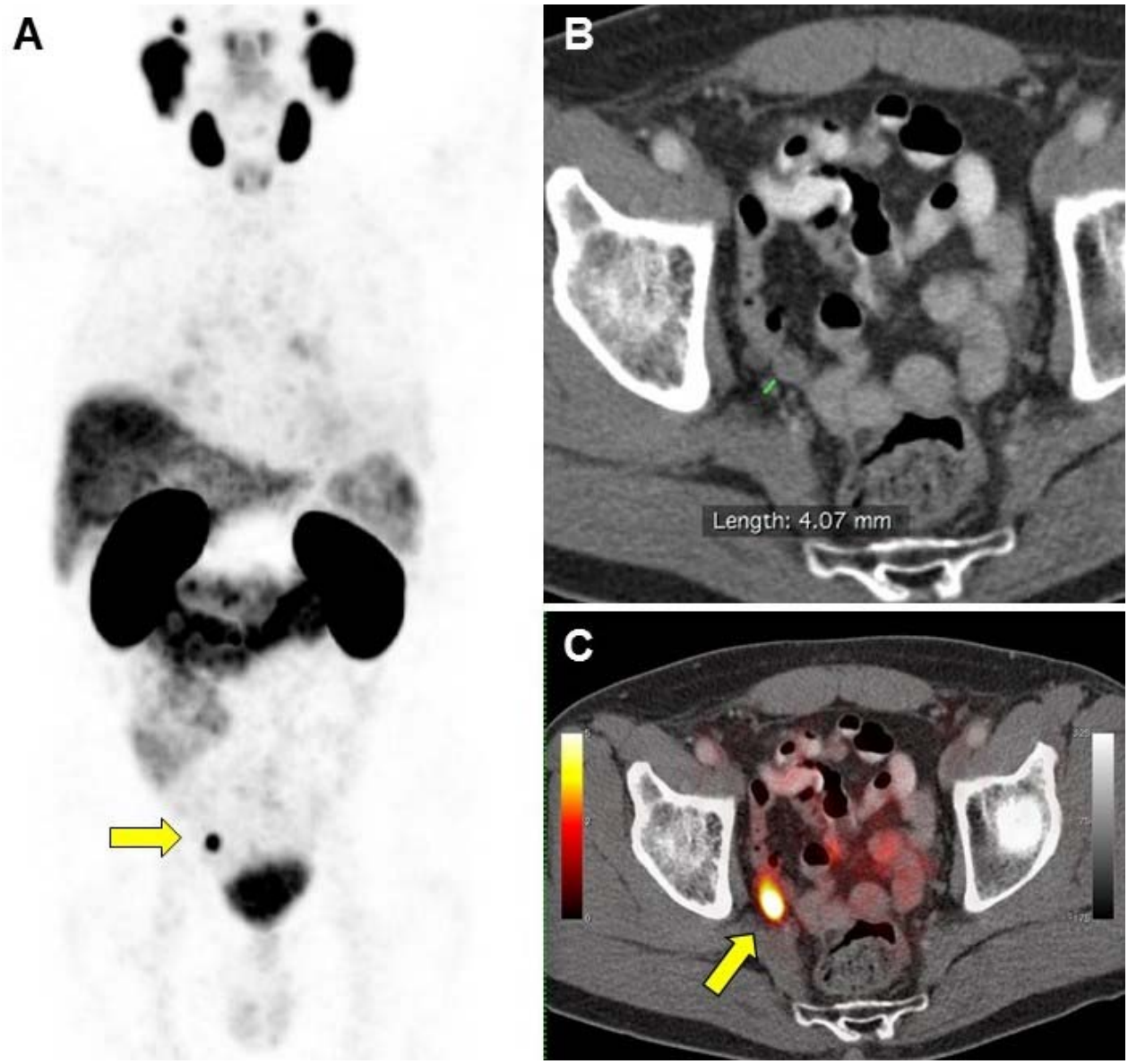

Figure 5*:* PSMA-11 PET/CT scan in a 70-year-old man with BCR (PSA 1.06 ng/ml, doubling time 7 months) of an initially high-risk prostate cancer (Gleason 8, pT2c) one year after primary radical prostatectomy. Intended treatment before PSMA-11 PET/CT was active surveillance (Q1). PSMA-11 PET/CT showed intense PSMA-11 uptake (SUVmax 10.8) in a 4 mm right internal iliac pelvic lymph node (yellow arrows). Intended treatment after PSMA-11 PET/CT (Q2) was surgery. The intended change was

implemented: patient underwent pelvic lymph node dissection 2 months later, which confirmed metastatic prostatic adenocarcinoma.

Panel A: PSMA-11 PET Maximum-Intensity-Projection (MIP) images; Panel B: Axial CT; Panel C: Axial fused PSMA-11 PET/CT.

TABLES AND TABLE LEGENDS

Table 1: Management options categories.

Multiple treatment options were possible.

	Treatment Options
1	Surgery
2	Salvage Radiation Therapy (SRT)
3	Stereotactic Body Radiation Therapy (SBRT)
4	Androgen Deprivation Therapy (ADT)
5	Chemotherapy (CTx)
6	Bone radionuclide therapy (RNT)
7	PSMA radionuclide therapy (RNT)
8	Other systemic treatment (vaccine therapy, immunotherapy)
9	Active Surveillance

	Management Change Category
1	Conversion to focal treatment / New focal treatment (for either prostate bed, lymph node or metastasis ablation)
2	Conversion to systemic treatment
3	Change in Systemic Treatment (adding a new systemic treatment or removing a systemic treatment)
4	Conversion to active surveillance.

Table 2: Patient characteristics.

		Total Population *n* = 101
Initial characteristics		
Initial PSA at diagnosis, median (ng/ml)		6.8 (range 0.25-33.3)
	< 10	52 (52%)
	≥ 10 < 20	10 (10%)
	≥ 20	9 (9%)
	Unknown	30 (30%)
Gleason Score	≤ 7	32 (32%)
	≥ 8	66 (66%)
	Unknown	3 (3%)
Primary Tumor Stage (T)	T1-T2	35 (35%)
	T3-T4	35 (35%)
	Unknown	31 (31%)
Initial NCCN Risk Group	Low	5 (5%)
	Intermediate	42 (42%)
	High	44 (44%)
	N1	8 (8%)
	Unknown	2 (2%)
Prior Treatment		
Primary Surgery		87 (86%)
	Surgery Only	47 (47%)
	Surgery + ADT	10 (10%)
	Surgery + SRT ± ADT	27 (27%)
	Surgery + SBRT ± ADT	1 (1%)
	Surgery + Chemotherapy ± ADT	2 (2%)
Primary Radiation Therapy (RT)		14 (14%)
	RT only	5 (5%)
	RT + ADT	6 (6%)
	RT + SBRT ± ADT	2 (2%)
	RT + Chemotherapy ± ADT	1 (1%)
PET/CT		
Age at PET/CT, median (years)		69 (range 43-88)
Time between primary treatment and PET/CT, median (years)		4.2 (range 0.12-18)
ADT within 6 months prior to imaging		21 (21%)
Serum PSA prior to PET/CT, median (ng/ml)		1.7 (range 0.05-140)

Abbreviations: NCCN: National Comprehensive Cancer Network; ADT: Androgen Deprivation Therapy; SRT: Salvage Radiation Therapy; SBRT: Stereotactic Body Radiation Therapy

Table 3: PSMA-11 PET/CT findings

	Population n = 101 (%)
PSMA-11 PET/CT +	77 (76%)
Prostate/Prostate Bed (T+)	23 (23%)
Pelvic LN (N1)	47 (47%)
Extra-pelvic LN (M1a)	21 (21%)
Bone (M1b)	19 (19%)
Visceral (M1c)	7 (7%)
PSMA-11 TNM Pattern	
PSMA T+ N0 M0	12 (12%)
PSMA T0 N1 M0	25 (25%)
PSMA T+ N1 M0	2 (2%)
PSMA T+ N0 M1	6 (6%)
PSMA T0 N0 M1	12 (12%)
PSMA T0 N1 M1	17 (17%)
PSMA T+ N1 M1	3 (3%)

Table 4: Individual management changes

	Q1 -> Q2		Q2 -> Implemented		Q1 -> Implemented	
MANAGEMENT CHANGES	**62**	**(61%)**	**35**	**(35%)**	**54**	**(53%)**
Conversion to Focal Treatment / New Focal Treatment	**40**	**40%**	**14**	**14%**	**29**	**29%**
Active surveillance -> Surgery ± ADT	5	5%	0	0%	5	5%
Active surveillance -> SRT ± ADT	9	9%	2	2%	3	3%
Active surveillance -> SBRT ± ADT	0	0%	0	0%	1	1%
ADT -> Surgery ± ADT	3	3%	0	0%	1	1%
ADT -> Surgery + SRT + ADT	0	0%	0	0%	1	1%
ADT -> SRT ± ADT	4	4%	1	1%	2	2%
ADT -> SRT + CTx + ADT	1	1%	0	0%	0	0%
ADT -> SBRT ± ADT	4	4%	0	0%	4	4%
ADT -> SBRT + CTx + ADT	0	0%	0	0%	1	1%
CTx + ADT -> Surgery	1	1%	0	0%	0	0%
CTx + ADT -> SRT ± ADT	1	1%	1	1%	1	1%
CTx + ADT -> SBRT ± ADT	1	1%	0	0%	2	2%
PSMA-RNT -> SRT + ADT	0	0%	1	1%	0	0%
SRT ± ADT -> Surgery	5	5%	2	2%	2	2%
SRT ± ADT -> SBRT ± ADT	5	5%	1	1%	5	5%
SRT ± ADT -> SBRT + SRT ± ADT	0	0%	1	1%	1	1%
SRT ± ADT -> SBRT + CTx + ADT	0	0%	1	1%	0	0%
SRT + CTx + ADT -> SBRT + ADT	0	0%	1	1%	0	0%
SBRT + ADT -> Surgery	1	1%	0	0%	0	0%
Surgery + ADT -> SRT + ADT	0	0%	2	2%	0	0%
Surgery + ADT -> Surgery + SRT + ADT	0	0%	1	1%	0	0%
Conversion to systemic treatment	**12**	**12%**	**7**	**7%**	**13**	**13%**
Active surveillance -> ADT	4	4%	1	1%	4	4%
Active surveillance -> Other systemic treatment + ADT	0	0%	0	0%	3	3%
Surgery ± ADT -> ADT	0	0%	3	3%	0	0%
SRT + CTx ± ADT -> ADT	1	1%	0	0%	1	1%
SRT ± ADT -> ADT	5	5%	2	2%	5	5%
SRT ± ADT -> CTx + ADT	1	1%	0	0%	0	0%
SBRT + ADT -> Other systemic treatment + ADT	1	1%	1	1%	0	0%
Unknown -> ADT	0	0%	0	0%	0	0%
Conversion to active surveillance	**5**	**5%**	**7**	**7%**	**7**	**7%**
Surgery ± ADT -> Active Surveillance	0	0%	3	3%	0	0%
SRT ± ADT -> Active Surveillance	4	4%	2	2%	4	4%
SRT + CTx -> Active Surveillance	0	0%	0	0%	0	0%
ADT -> Active Surveillance	1	1%	2	2%	3	3%
Change in Systemic Treatment	**5**	**5%**	**7**	**7%**	**5**	**5%**
ADT -> CTx ± ADT	3	3%	0	0%	0	0%
ADT -> Other Systemic Treatment ± ADT	0	0%	4	4%	2	2%
CTx ± ADT -> ADT	0	0%	3	3%	1	1%
CTx + Bone RNT + ADT -> ADT + CTx	0	0%	0	0%	0	0%

CTx + Bone RNT + ADT -> CTx + PSMA-RNT + ADT	0	0%	0	0%	0	0%
CTx + Bone RNT + ADT -> PSMA-RNT	1	1%	0	0%	1	1%
Bone RNT + ADT -> CTx + ADT	1	1%	0	0%	1	1%
Bone RNT + ADT -> PSMA-RNT	0	0%	0	0%	0	0%

Abbreviations: ADT: androgen deprivation therapy; CTx: chemotherapy; SRT: Salvage radiation therapy; SBRT: stereotactic body radiation therapy; RNT: radionuclide therapy; Q1: intended treatment before PSMA PET; Q2: intended treatment after PSMA PET;