

Advantages of PSMA PET in APC imaging

Stefano Fanti



Disclosures

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Advantages of PSMA PET for imaging Prostate Cancer



Advantages of PSMA PET for imaging Prostate Cancer

STAGING

BIOCHEMICAL RECURRENCE

THERAPY PLANNING



STAGING

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5.3.5 Guidelines for staging of prostate cancer

Any risk group staging	LE	Strength rating
Do not use computed tomography and transrectal ultrasound for local staging.	2a	Strong
Use pre-biopsy mpMRI for staging information.	2a	Weak
Low-risk localised disease		
Do not use additional imaging for staging purposes.	2a	Strong
Intermediate-risk disease		
In ISUP grade ≥ 3 , include at least a cross-sectional abdominopelvic imaging and bone-scan for metastatic screening.	2a	Weak
High-risk localised disease/locally advanced disease		
Perform metastatic screening including at least cross-sectional abdominopelvic imaging and a bone-scan.	2a	Strong



5.3.3.3 Prostate-specific membrane antigen-based PET/CT

There is growing evidence on the performance of ^{68}Ga -PSMA PET/CT in initial staging. A recent SR including twelve studies and comprising a total of 322 patients reported high variation in sensitivity (range 33-99% median sensitivity on per-lesion analysis 33-92%, and on per-patient analysis 66-91%), with good specificity (per-lesion 82-100%, and per-patient 67-99%), with most studies demonstrating increased detection rates with respect to conventional imaging modalities (bone scan and CT) [316]. Table 5.3.1 reports the data of the five studies including histopathologic correlation.

Table 5.3.1: PSMA PET/CT results in primary staging alone [316]

Study	Sensitivity (per lesion)	Specificity (per lesion)	PPV (per lesion)	NPV (per lesion)
Budaus	33%	100%	100%	69%
Herlemann	84%	82%	84%	82%
Van Leeuwen	58%	100%	94%	98%
Maurer	74%	99%	95%	94%
Rahbar	92%	92%	96%	85%

NPV = negative predictive value; PPV = positive predictive value.



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5.3.4 Summary of evidence and practical considerations on initial N/M staging

The field of non-invasive nodal and metastatic staging of PCa is evolving very rapidly. Evidence shows that choline PET/CT, PSMA PET/CT and MRI provide a more sensitive detection of LN and bone metastases than the classical work-up associating bone scan and abdominopelvic CT. It could be tempting to conclude that bone scan and abdominopelvic CT must be replaced by more sensitive tests in all patients undergoing initial PCa staging. Yet, the clinical benefit of detecting metastases at an earlier time-point remains unclear [318].

The prognosis and ideal management of patients diagnosed as metastatic by these more sensitive tests is unknown. In particular, it is unclear whether patients with metastases, detectable only with PET/CT or MRI, should be managed using systemic therapies, or whether they should be submitted to aggressive local and metastases-directed therapies [319].

Results from RCTs evaluating the management and outcome of patients with (and without) metastases detected by choline PET/CT, PSMA PET/CT and MRI are awaited, before a decision can be made to treat patients based on the results of these tests [320].





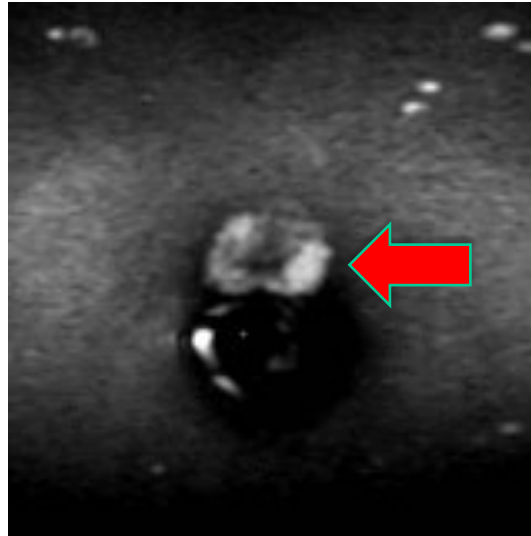
CLINICAL CASE

Alberto Briganti



- ✓ 61-year old patient, with family history of Prostate Cancer
- ✓ Total PSA (first assessment): 12.6 ng/ml (ratio f/t: 8%) (confirmed at a second, repeated measurement : 11.9 ng/ml – ratio f/t: 11%)
- ✓ Small hypoechoic lesion at TRUS in the left lobe (6 mm) – Prostate volume: 41 cc
- ✓ TRUS guided random prostate biopsy (12 cores) + US guided targeted biopsy of the nodule (2 cores)
- ✓ Adenocarcinoma Gleason score 8 (4 + 4) in 4 cores (left lobe)
- ✓ Adenocarcinoma Gleason 4+4 in 1 core (right lobe)

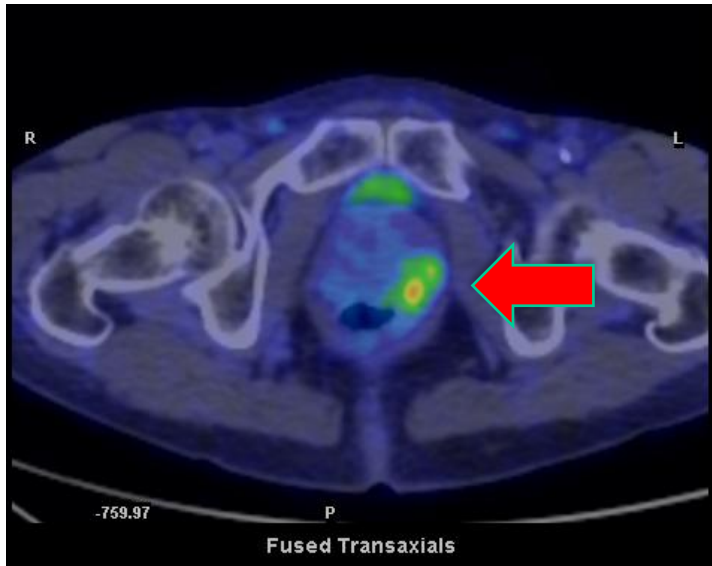
1.5 TESLA mp-MRI WITH ENDORECTAIL COIL FOR LOCAL STAGING



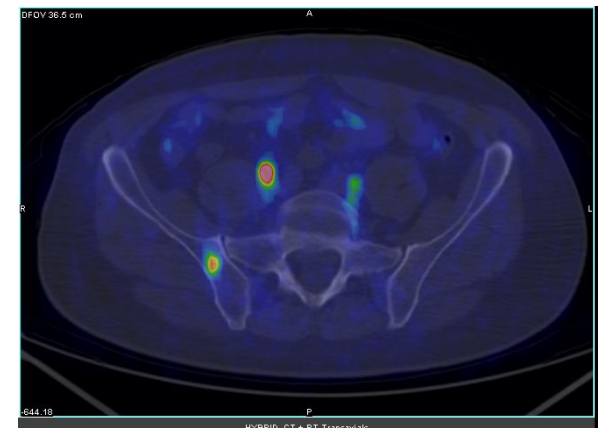
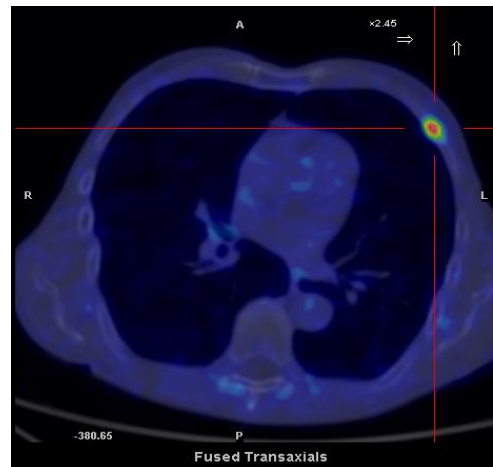
Left lobe: area of 20 x 14 x 12 mm, hypointense in T2, with restricted diffusion. Highly suspicious for ECE. No sign of SVI

Bone scintigraphy : NEGATIVE

CT abdomen + pelvis : NEGATIVE



^{68}Ga -PSMA



STAGING

PSMA PET in prostate cancer staging

Risk of metastatic disease on ^{68}Ga -prostate-specific membrane antigen positron emission tomography/computed tomography scan for primary staging of 1253 men at the diagnosis of prostate cancer

John W. Yaxley^{*†‡}, Sheliyan Raveenthiran^{†‡}, François-Xavier Nouhaud^{‡§}, Hemamali Samaratunga^{†¶}, William J. Yaxley^{†‡}, Geoff Coughlin^{*‡}, Anna J. Yaxley^{**}, Troy Gianduzzo^{†‡}, Boon Kua^{‡‡}, Louise McEwan^{‡‡} and David Wong^{‡‡}

Conclusion

We have identified the ability of ^{68}Ga -PSMA PET/CT to detect metastatic prostate cancer in 12.1% of men at initial diagnosis of prostate cancer. We recommend a ^{68}Ga -PSMA PET/CT scan as the investigation of choice in men with high-risk prostate cancer. The apparent improved detection ability of ^{68}Ga -PSMA PET/CT compared to standard radiology requires confirmation with a sufficiently powered randomised trial, to evaluate the diagnostic potential, the economic impact, and significant management impact of ^{68}Ga -PSMA PET/CT scan as first-line staging above standard radiology. One such prospective multicentre trial of high-risk and primary Gleason 4 intermediate-risk prostate cancer has just finished recruitment [23] and the results are expected in early 2020.



BIOCHEMICAL RECURRENCE


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6.3.4.4 Guidelines for imaging in patients with biochemical recurrence

Prostate-specific antigen (PSA) recurrence after radical prostatectomy	LE	Strength rating
Perform prostate-specific membrane antigen (PSMA) positron emission tomography (PET) computed tomography (CT) if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions.	2b	Weak
In case PSMA PET/CT is not available, and the PSA level is ≥ 1 ng/mL, perform fluciclovine PET/CT or choline PET/CT imaging if the results will influence subsequent treatment decisions.		Weak
PSA recurrence after radiotherapy		
Perform prostate multiparametric magnetic resonance imaging to localise abnormal areas and guide biopsies in patients fit for local salvage therapy.	3	Strong
Perform PSMA PET/CT (if available) or fluciclovine PET/CT or choline PET/CT in patients fit for curative salvage treatment.	2b	Strong



Diagnostic performance of ^{68}Ga -PSMA-11 (HBED-CC) PET/CT in patients with recurrent prostate cancer: evaluation in 1007 patients

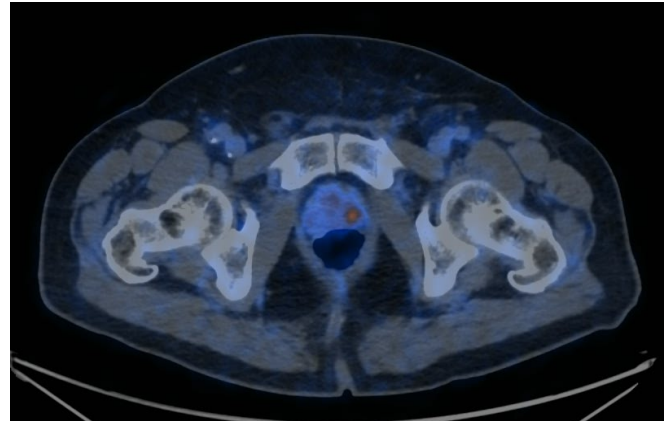
Ali Afshar-Oromieh^{1,2}  • Tim Holland-Letz³ • Frederik L. Giesel¹ • Clemens Kratochwil¹ • Walter Mier¹ • Sabine Haufe¹ • Nils Debus¹ • Matthias Eder² • Michael Eisenhut⁴ • Martin Schäfer⁴ • Oliver Neels⁴ • Markus Hohenfellner⁵ • Klaus Kopka⁴ • Hans-Ulrich Kauczor⁶ • Jürgen Debus⁷ • Uwe Haberkorn^{1,2}

Eur J Nucl Med Mol Imaging (2017) 44:1258–1268

In 801 of the 1007 patients (79.5%) at least one lesion characteristic of recurrent PCa was detected on ^{68}Ga -PSMA-11 PET/CT. The patient-based sensitivity was therefore 79.5% with a 95% confidence interval of 77.0% to 81.9%. The rates (including confidence intervals) of pathological PET/CT scans in relation to PSA levels and GSC are presented in Figs. 1 and 2, respectively.



- ü 2016 prostate cancer (GS 4+3) radically treated
- ü 2018 BCR (2,67 ng/mL)



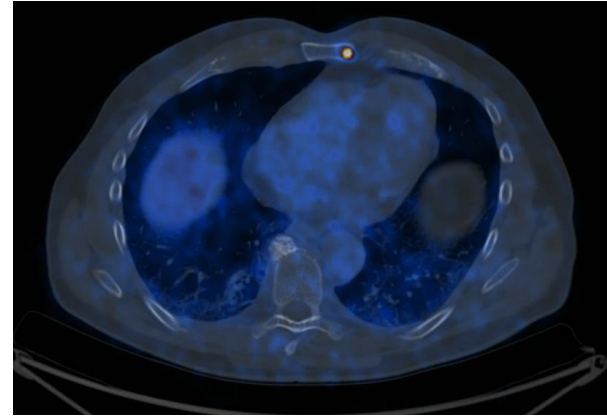
PSMA



ü 2013: RRP+ BPLND (GS 4+3, pT3bN0Mx; iPSA 17 ng/ml)

ü 2017: salvage EBRT

ü Sep 2018: PSA 0,46 ng/mL



PSMA



Imaging of PSMA-targeted Radiotracers for the Detection of Prostate Cancer Biochemical Recurrence After Definitive Therapy: A Systematic Review and Meta-analysis

Nelly Tan ✉, Niusha Bavadian, Jeremie Calais, Udochukwu Oyoyo, Johnathan Kim, I. Baris Turkbey,

Esther Mena, and Matthew S. Davenport

Results:

A total of 5113 patients from 43 studies were included in this systematic review. Fifteen (34.8%) of the studies were prospective. Three (6.9%) were multi-institutional and remainder were single centered. Eighteen (41.8 %) were in subjects post-RP, 2 (4.6%) were in subjects post-RT, and 23 (53.5%) were in subjects who were both post-RP and post-RT. The median PSA was 1.6 ng/ml (IQR 0.7-4.4) and the median age was 68 years (IQR 67-70). 33/43 (76.7%) of the studies evaluated 68Ga PSMA-11 (Ga-HBED-CC) PET/CT. The pooled detection rate was 70.2% (95% CI 65.0-75.4%) for the entire cohort. For PSA <0.5 ng/ml, 0.5-0.9 ng/ml, 1-1.9 ng/ml and ≥ 2 ng/ml, the pooled detection rates were 44.9% (36.0-53.9%), 61.3% (95% CI 52.3-70.3%), 78.2% (95% CI 70.8-85.6%), and 93.9% (95% CI 92.0-95.8%). A reference standard was confirmed positive in 684/715 (95.7%) of the patients. There were significant study heterogeneity and publication bias ($p < 0.01$).



PSMA-targeted radiotracers are likely effective for the detection of biochemically recurrent prostate cancer at low PSA levels. However, existing studies are limited by retrospective designs, limited reference standards, publication bias, and lack of inter-agent comparison.



A Systematic Review on the Role of Imaging in Early Recurrent Prostate Cancer

Pieter J.L. De Visschere^{a,*}, Chloë Standaert^a, Jurgen J. Fütterer^b, Geert M. Villeirs^a, Valeria Panebianco^c, Jochen Walz^d, Tobias Maurer^{e,f}, Boris A. Hadaschik^g, Frédéric E. Lecouvet^h, Gianluca Giannariniⁱ, Stefano Fanti^j

Table 5 – Summary of the roles of imaging modalities in the setting of early recurrent prostate cancer

Imaging modality	Number of studies	Percent related to total studies of 98		Imaging directed to	Role of imaging modality in the early recurrence setting
TRUS	5	5.1%		Local only	Readily available useful adjunct to PSA and DRE after RP, and has reasonable positivity at low PSA levels; after RT there are no studies in the early recurrence setting
CT	3	3.1%		Lymph nodes and bone	Traditionally used to restage patients with biochemical recurrence, but not sufficiently sensitive to localize recurrence at low PSA values
BS	3	3.1%		Bone only	Frequently used because of low cost and wide availability, but low sensitivity in the early recurrence setting and hampered by a high number of equivocal findings
SPECT					
¹¹¹ In-capromab pentetide (Prostascint)	4	4.1%		All in one	All studies published >10 yr ago; may have been useful in detecting the site of recurrence when conventional imaging is negative
^{99m} Tc PSMA	2	2.0%		All in one	Limited evidence; may detect more metastatic lesions and achieve higher detection rates than conventional imaging
PET-CT	93	80 (81.6%)			
¹⁸ F FDG		4	4.1%	All in one	Limited value in prostate cancer due to low glucose metabolism in most prostate cancer cells and disturbing tracer accumulation in the bladder hampering local recurrence detection
¹¹ C choline		26	26.5%	All in one	Widely available useful diagnostic tool in biochemical recurrence and also in the early setting
¹¹ C acetate		10	10.2%	All in one	Performs in a similar manner to ¹¹ C choline but is not as extensively used; higher detection rate for local recurrent PCa
¹⁸ F (fluoro)choline		23	23.4%	All in one	Alternative tracer for ¹¹ C choline, with advantages of ¹⁸ F labeling
¹⁸ F FACBC (fluciclovine)		3	3.1%	All in one	Relatively new tracer with sensitivity appearing to be higher than ¹¹ C choline
⁶⁸ Ga PSMA-11		21	21.4%	All in one	Higher detection rates than any other imaging modality, especially in the range of low PSA values (<0.5 ng/ml)
¹⁸ F DCFPyL		1	1.0%	All in one	Noninferior to ⁶⁸ Ga PSMA-11 while offering the advantages of ¹⁸ F-labeling
¹⁸ F DCFBC		1	1.0%	All in one	¹⁸ F labeled PSMA-targeted tracer but limited evidence in the early recurrence setting
PET-MRI		5	5.1%	All in one	Allows for improved anatomic correlation of PET tracer uptake in intraprostatic recurrence or in bone marrow metastasis, but longer scanning time and not as widely available as PET-CT
mpMRI	10	10.2%		Local only	Excellent technique for local recurrence, superior than PET-CT, even at low PSA, but provides no information about extrapelvic lymph nodes or bone metastases
wbMRI	4	4.1%		Lymph nodes and bone	Higher sensitivity than BS for the detection of bone metastases; dedicated scan sequences (such as diffusion-weighted imaging) allow for high detection rates of pathological lymph nodes



PSA PERSISTENCE

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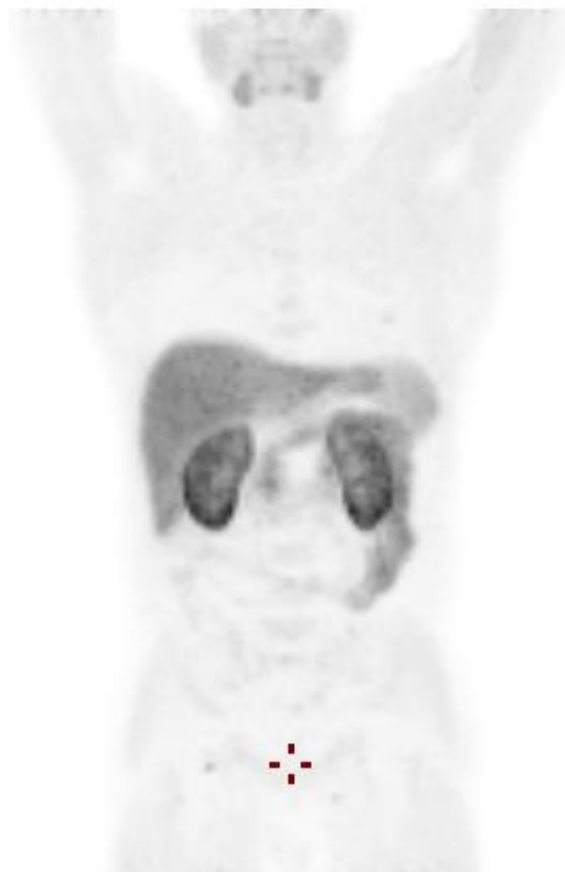
6.2.6.6 Recommendations for the management of persistent PSA after radical prostatectomy

Recommendations	Strength rating
Offer a prostate-specific membrane antigen positron emission tomography (PSMA PET) scan to men with a persistent PSA > 0.2 ng/mL to exclude metastatic disease.	Weak
Treat men with no evidence of metastatic disease with salvage radiotherapy and additional hormonal therapy.	Weak

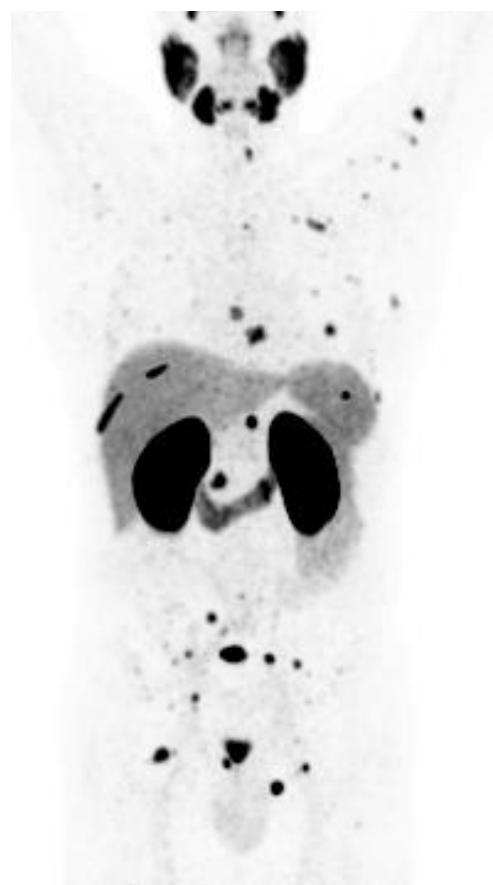


50yo; Gs 9 T3b iPSA 34ng/ml
Staging with pelvic MRI, CT and BS than RP December 2018 (T3b N1 M0)
January 2019: PSA nadir 0.3ng/ml (PSA persistence);

18 February 2019 C-Choline



27 February 2019 Ga-PSMA



BIOCHEMICAL RECURRENCE

Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer—Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis

Marlon Perera^{a,b,c,*}, Nathan Papa^a, Matthew Roberts^{b,c}, Michael Williams^b, Cristian Udovicich^d, Ian Vela^{b,e}, Daniel Christidis^a, Damien Bolton^{a,f}, Michael S. Hofman^g, Nathan Lawrentschuk^{a,f,h,i}, Declan G. Murphy^{h,i}

Evidence synthesis: A total of 37 articles including 4790 patients were analysed. For patients with biochemical recurrence, positive ⁶⁸Ga-PSMA PET scans increased with higher pre-PET prostate-specific antigen (PSA) levels. For PSA categories 0–0.19, 0.2–0.49, 0.5–0.99, 1–1.99, and ≥ 2 ng/ml, the percentages of positive scans were 33%, 45%, 59%, 75%, and 95%, respectively. No significant differences in positivity were noted between Gleason sums ≤ 7 and ≥ 8 . Significant differences in positivity after biochemical recurrence in the prostate bed were noted between radical prostatectomy (22%) and radiotherapy (52%) patients. On per-node analysis, high sensitivity (75%) and specificity (99%) were observed.

Conclusions: Ga-68-PSMA PET improves detection of metastases with biochemical recurrence, particularly at low pre-PET PSA levels of >0.2 ng/ml (33%) and 0.2–0.5 ng/ml (45%). Ga-68-PSMA-PET produces favourable sensitivity and specificity profiles on meta-analysis of pooled data. This analysis highlights different anatomic patterns of metastatic spread according to PSMA PET in the primary and biochemically recurrent settings.

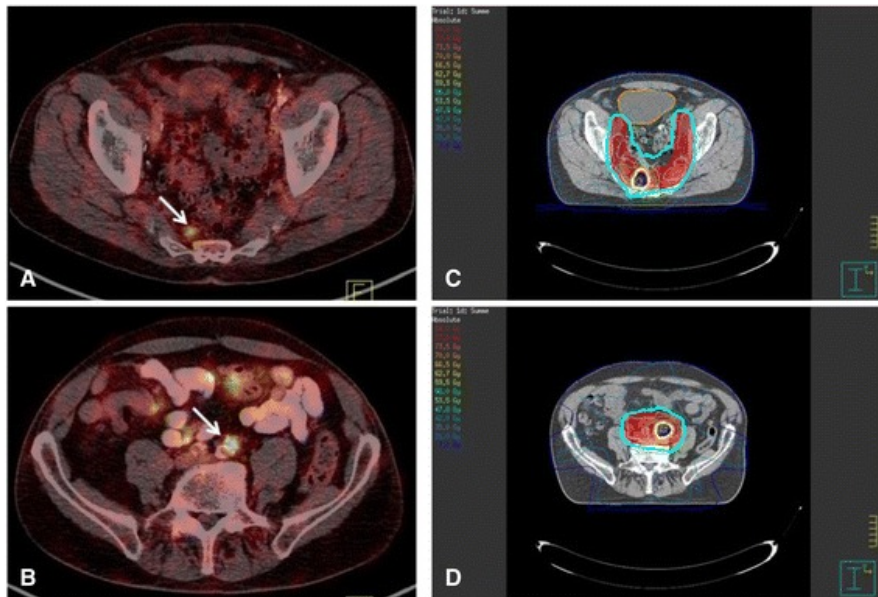


THERAPY PLANNING

EJNMMI Res. 2016 Dec;6(1):78. Epub 2016 Oct 26.

Impact of ^{68}Ga -PSMA PET/CT on salvage radiotherapy planning in patients with prostate cancer and persisting PSA values or biochemical relapse after prostatectomy.

Bluemel C^{1,2}, Linke F³, Herrmann K^{4,5}, Simunovic J⁶, Eiber M⁴, Kestler C⁷, Buck AK⁸, Schirbel A⁸, Bley TA⁷, Wester HJ⁹, Vergho D⁶, Becker A³.



A 74-year-old patient with biochemical recurrence (PSA 0.82 ng/ml; pT2aN0cM0; Gleason 6; iPSA 5.37 ng/ml) 8.4 months after radical prostatectomy and lymph node dissection. ^{68}Ga -PSMA PET/CT prior to salvage radiotherapy showed two PSMA-positive presacral (a, c) and retroperitoneal (b, d) LNMs. Salvage radiotherapy was extended to pelvic lymph nodes, including a dose escalation to the PSMA-positive lymph nodes. The patient was treated with IMRT (c, d IMRT plan). *red* PTV including pelvic lymph nodes (50.4 Gy), *blue* simultaneous and sequential boost (66 Gy) for iliac (d) and presacral (c) LNM. RT to prostate bed is not shown. The PSA level decreased to 0.02 ng/ml after SRT

THERAPY PLANNING

PSMA PET in prostate cancer RT planning

Prostate. 2017 Jun;77(6):920-927. doi: 10.1002/pros.23347. Epub 2017 Mar 20.

68 Ga-PSMA-PET for radiation treatment planning in prostate cancer recurrences after surgery: Individualized medicine or new standard in salvage treatment.

Habl G^{1,2}, Sauter K¹, Schiller K¹, Dewes S¹, Maurer T³, Eiber M^{4,5}, Combs SE^{1,2}.

Author information

Abstract

BACKGROUND: ⁶⁸ Ga-PSMA-PET imaging is a novel promising diagnostic tool to locate early biochemical failure after radical prostatectomy (RP) in prostate cancer (PC) patients. Exact knowledge of the relapse location may result in changes of the therapy concept aside from changes to the TNM stage. To gain data for this approach, we evaluated PC patients receiving ⁶⁸ Ga-PSMA-PET imaging before salvage radiotherapy (RT).

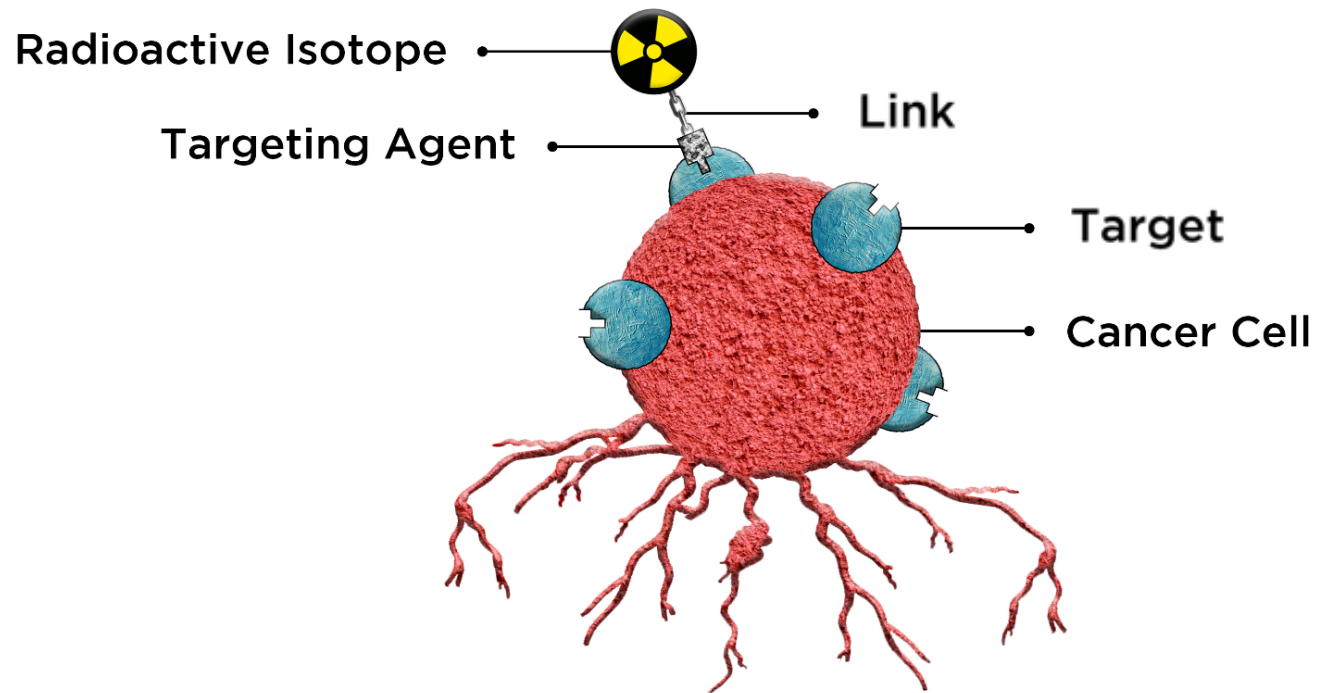
METHODS AND MATERIALS: In this study, 100 patients with biochemical failure after RP± prior RT who underwent ⁶⁸ Ga-PSMA PET/CT or PET/MRI were evaluated undergoing salvage RT in our department. We analyzed TNM staging changes due to ⁶⁸ Ga-PSMA-PET imaging and its influence on RT planning and treatment.

RESULTS: Uptake indicative for tumor recurrence in ⁶⁸ Ga-PSMA-PET was found in 76% of the patients with biochemical recurrent PC. Median PSA level was 1.0 ng/mL (range 0.12-14.7 ng/mL). Of these, 80% showed no morphological correlate in the corresponding CT or MRI. A 43% of all patients experienced a change in TNM stage due to ⁶⁸ Ga-PSMA-PET imaging. Patients had changes from Tx to rcT+ (28%), 12% from pN0 to rcN1, 1% from pN0/cM0 to rcM1a, and 8% from cM0 to rcM1b. Due to the additional knowledge of ⁶⁸ Ga-PSMA-PET imaging, initial planned RT planning was adapted in 59% of all cases. An additional simultaneous integrated boost (SIB) to the prostate bed or lymph nodes was given to 32% and 63%, respectively. Ten patients received stereotactic body RT (SBRT) to single bone metastases.

CONCLUSION: ⁶⁸ Ga-PSMA-PET imaging showed a high clinical impact on staging and RT management in patients with biochemically recurrent PC, even at low serum PSA levels. With 43% changes in staging and 59% in radiotherapy planning ⁶⁸ Ga-PSMA-PET could lead to an indispensable tool in guiding radiation treatment in recurrent PC.



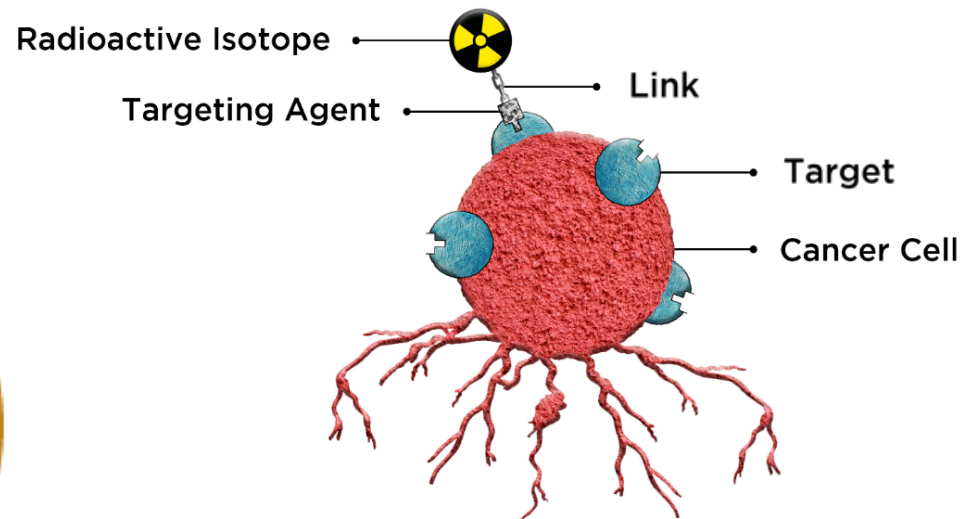
THERANOSTIC



THERANOSTIC

^{68}Ga

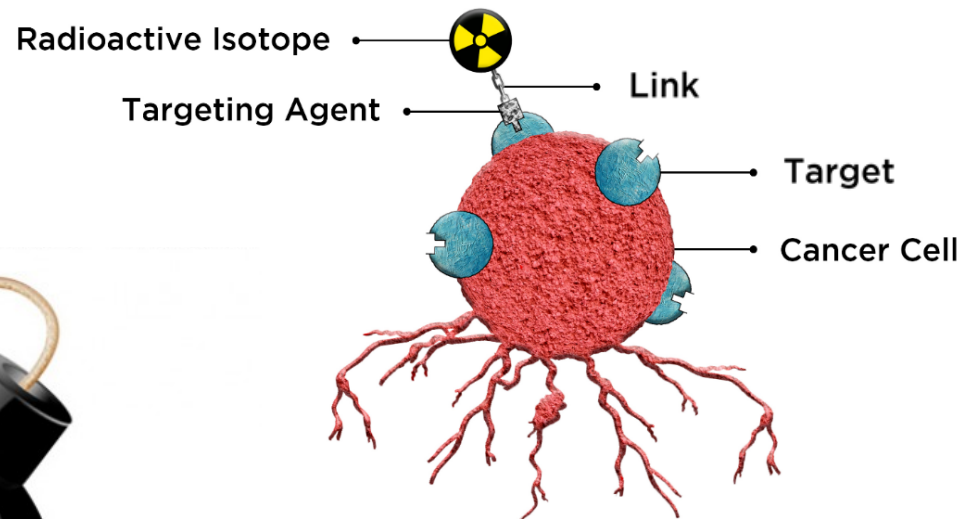
^{18}F

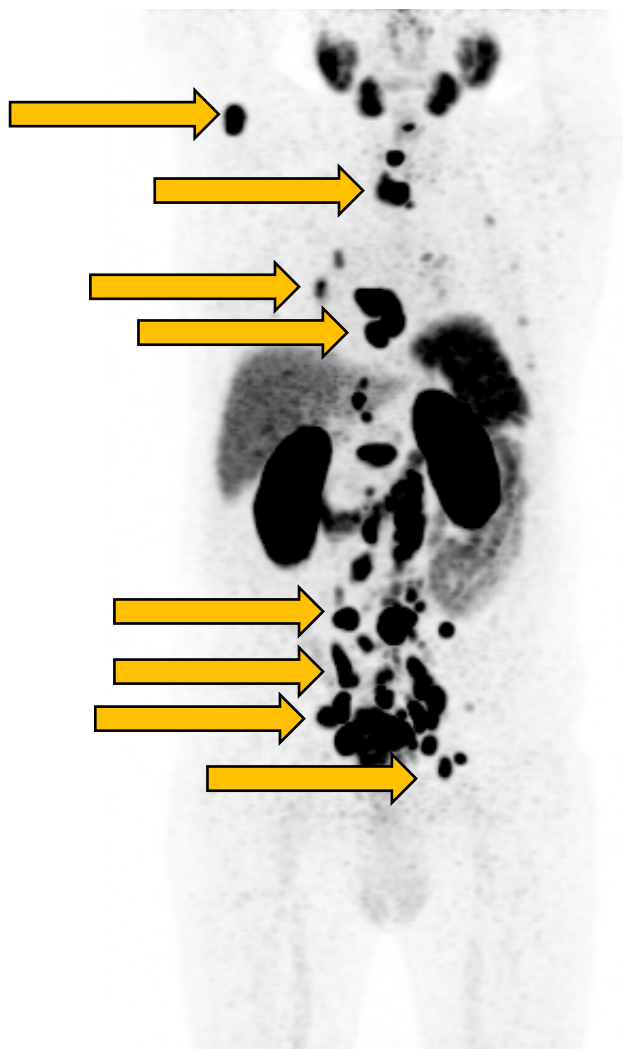


THERANOSTIC

^{177}Lu

^{225}Ac





What you See is what you Treat

Lancet Oncol 2018; 19: 825-33

[¹⁷⁷Lu]-PSMA-617 radionuclide treatment in patients with metastatic castration-resistant prostate cancer (LuPSMA trial): a single-centre, single-arm, phase 2 study

Michael S Hofman, John Violet*, Rodney J Hicks, Justin Ferdinandus, Sue Ping Thang, Tim Akhurst, Amir Iravani, Grace Kong, Aravind Ravi Kumar, Declan G Murphy, Peter Eu, Price Jackson, Mark Scalzo, Scott G Williams, Shahneen Sandhu*

Conclusion



Advantages of PSMA PET for imaging Prostate Cancer



**Non invasive, simple,
reproducible**

**Allow to study local, nodes,
bone and other**

**More sensitive than other
imaging methods**

**Rapid diffusion, easy to
implement**



ADVANCED PROSTATE CANCER
CONSENSUS CONFERENCE: APCCC 2019
29-31 August 2019, Basel/Switzerland

