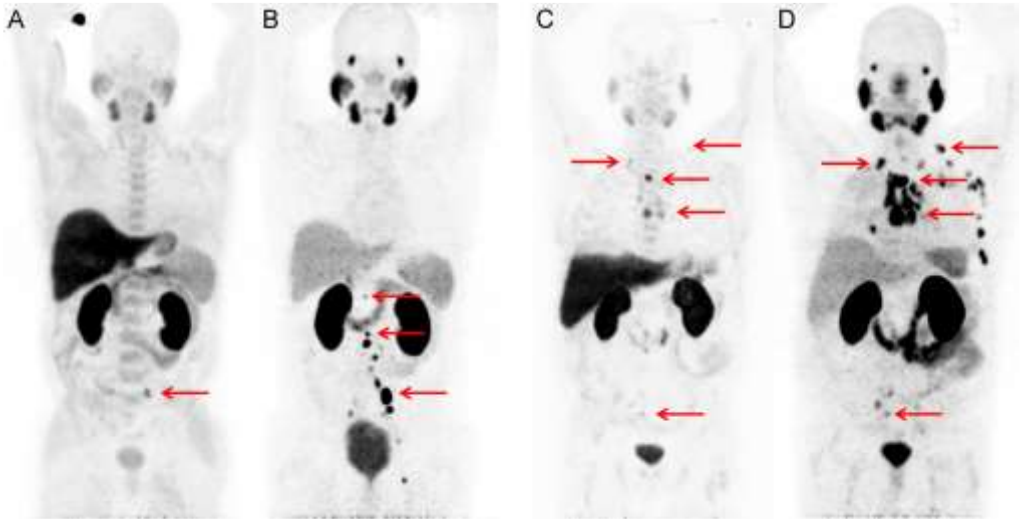
Nuklearmedizin: Theranostik und personalisierte Medizin

– was kann das Fach heute und morgen leisten?



Univ.-Prof. Dr. Frederik L. Giesel

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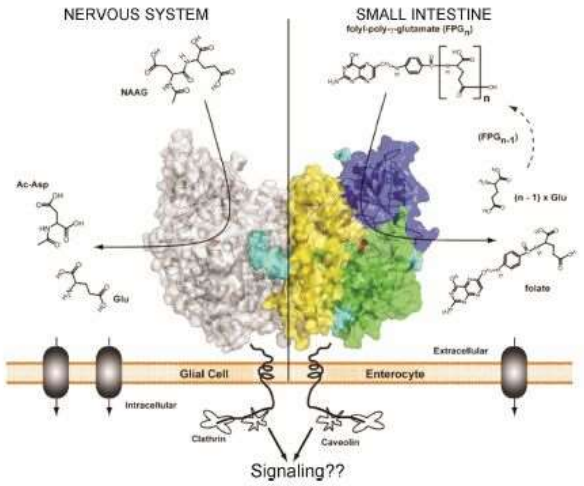
Disclosure

- Advisor: ABX, SOFIE, Telix, Alpha-Fusion
- Co-Founder/ Patentapplikations: PSMA-1007, FAP-ligands

Overview

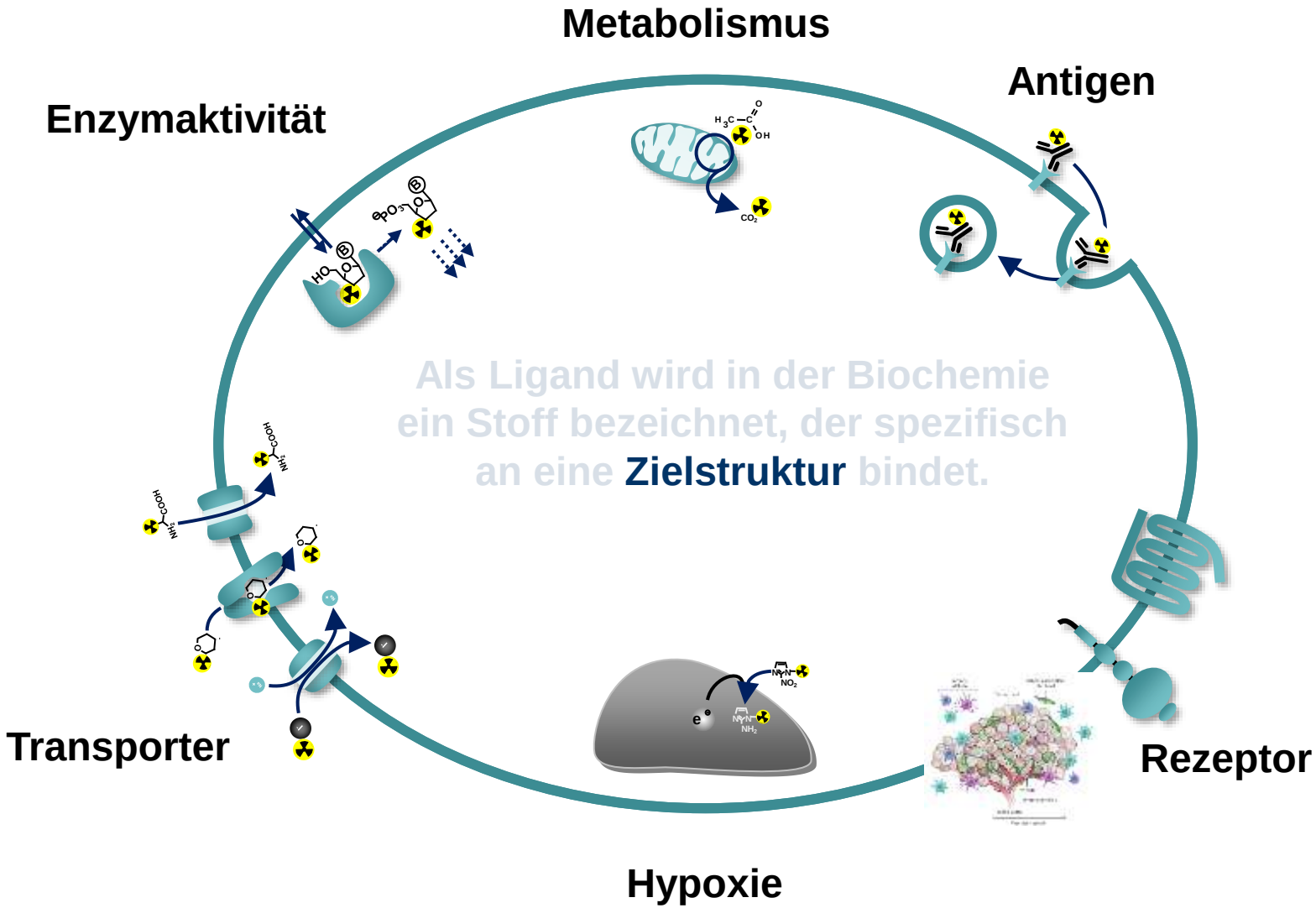
- Background / General Introduction
- Recurrent prostate cancer
- Primary staging and detection
- PSMA-ligand therapy



Molekulare Diagnostik: spez. Liganden

Als Ligand wird in der Biochemie ein Stoff bezeichnet, der spezifisch an eine Zielstruktur bindet.

Molekulare Diagnostik: spez. Liganden

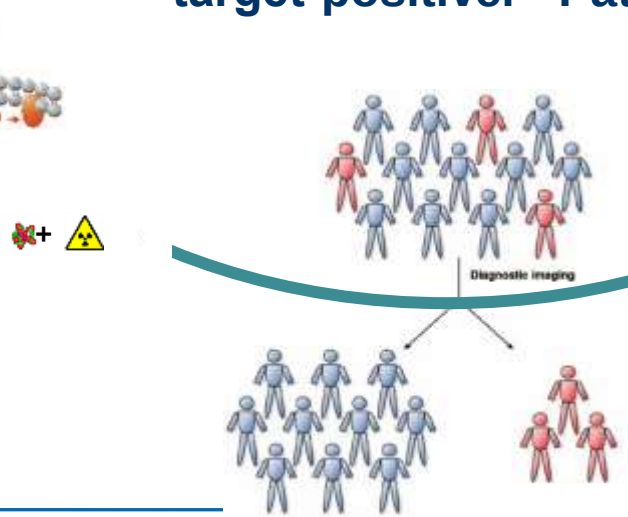


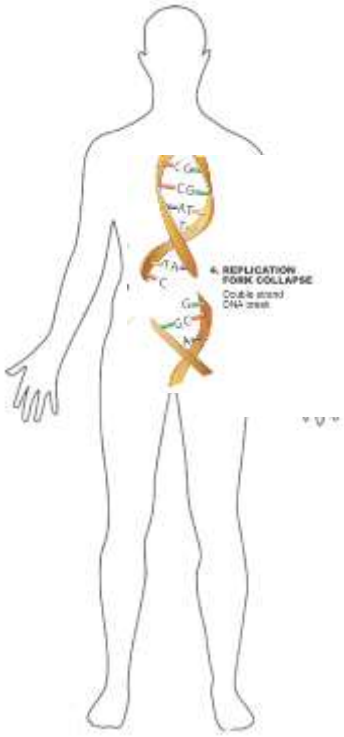
Definition: Theranostik (Therapie + Diagnostik)

Bildgebende Diagnostik

Gleiches Trägermolekül für diagnostische (z.B. PET/CT) und therapeutische (Radioliganden-Tx) Zwecke

Diagnostik ermöglicht Vorselektion “target-positiver” Patienten





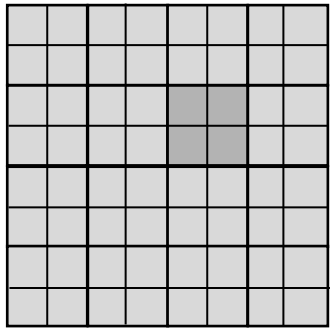
Systemische Strahlentherapie

Grundlagen: Radiologie vs. Nuklearmedizin

Signal/Hintergrund

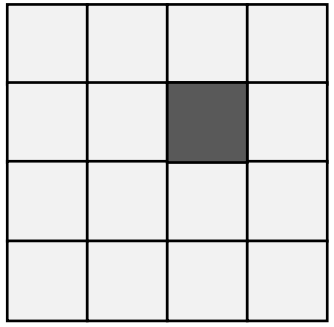
Radiologie (CT/MRT)

Detektion und Erfassung
strukturelle Veränderungen

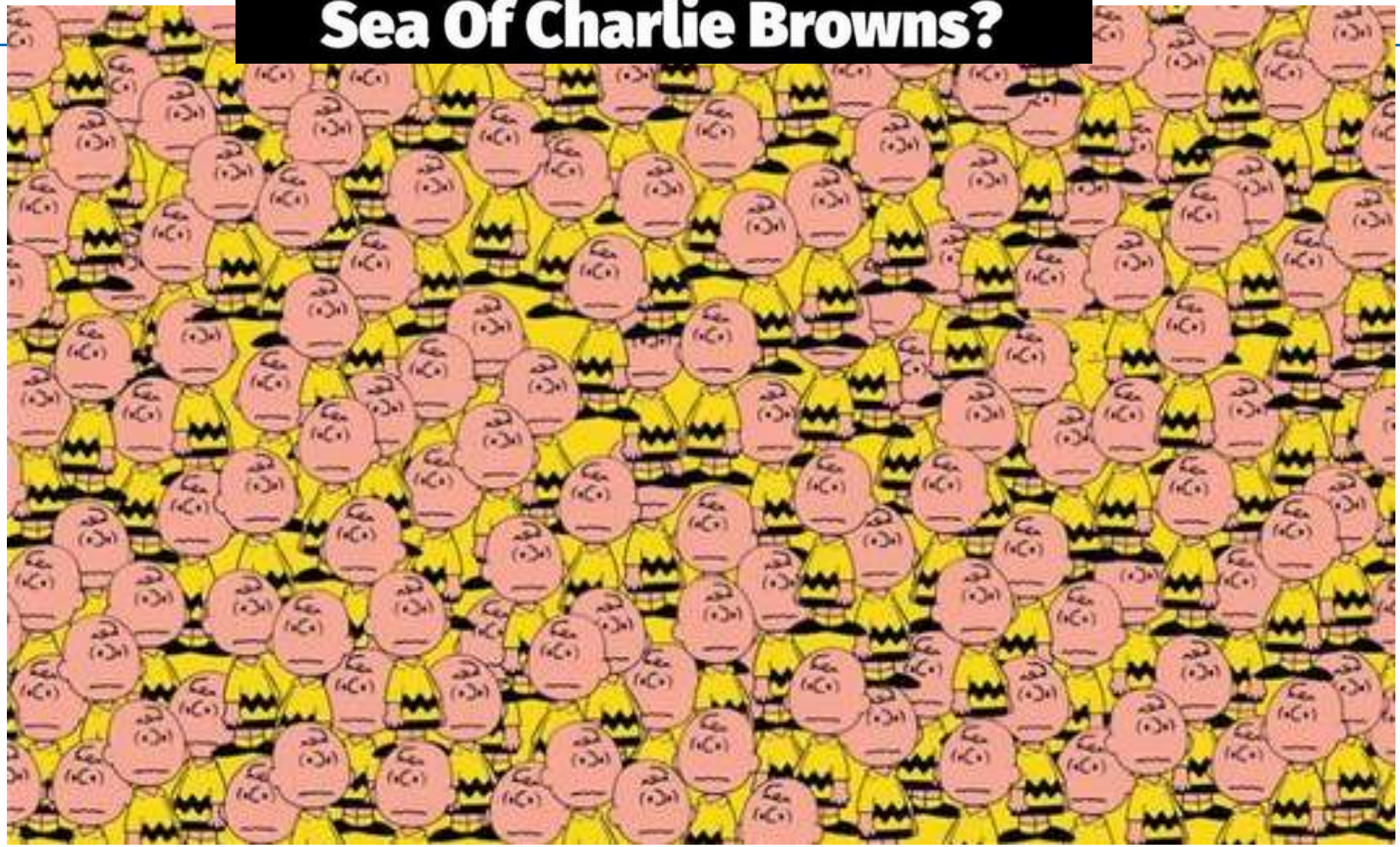


Nuklearmedizin (Gammakamera/SPECT/PET)

Detektion und Erfassung
funktioneller und metabolischer
Prozesse



Can You Find Pikachu In This Sea Of Charlie Browns?



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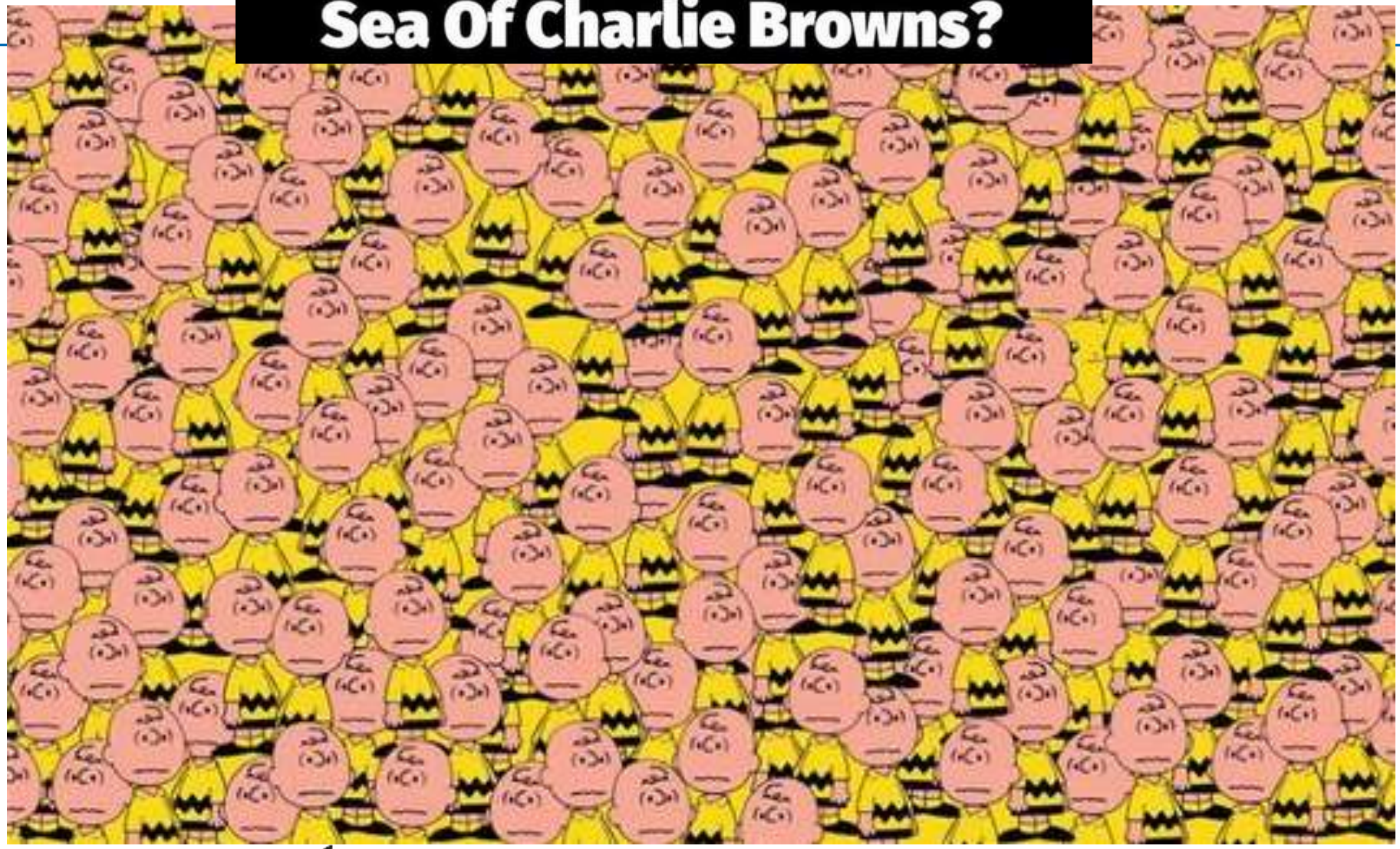
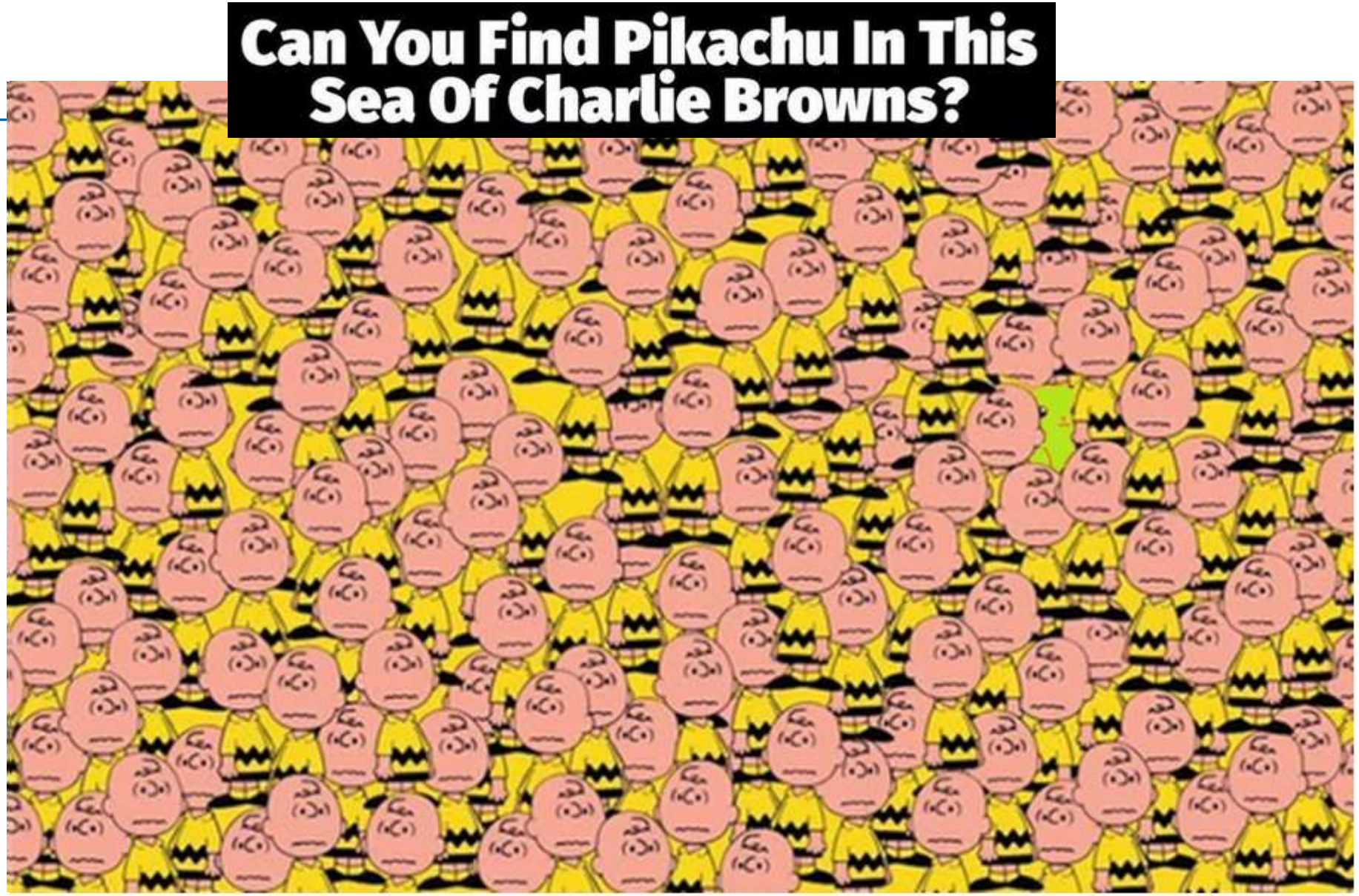


Pikachu

Can You Find Pikachu In This Sea Of Charlie Browns?

Pikachu

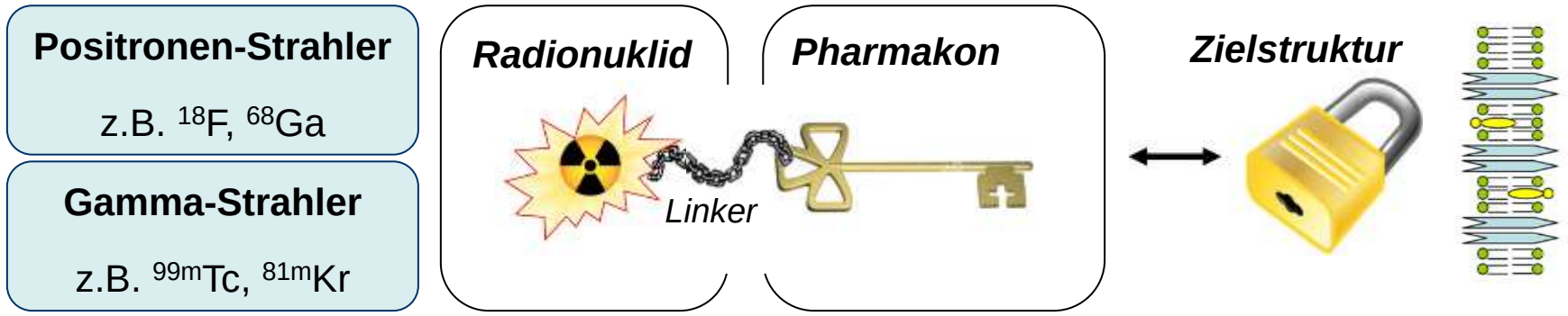


Fusionierung Struktur + Funktion = Hybridbildgebung

Grundlagen: Radiopharmakon

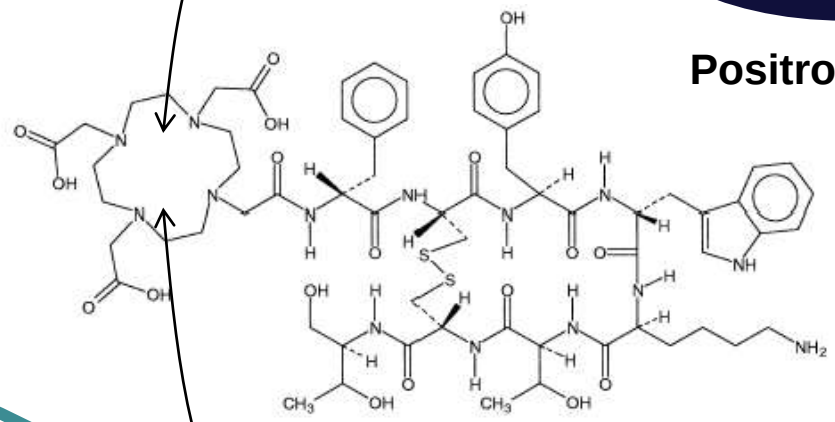
Besteht aus **zwei Komponenten**

- Radioaktives Isotop (***Radionuklid***)
- Shuttle-Molekül (***Pharmakon***)



Nuclear Medicine: Theranostics (Dx+Tx)

Besteht aus **zwei Komponenten**



Diagnostik
^{68}Ga

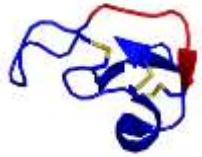
Positronen-Strahler

Therapie
^{90}Y, ^{177}Lu, ^{213}Bi, ^{225}Ac

Beta-/Alpha-Strahler

Nuclear Medicine: Theranostics (Dx+Tx)

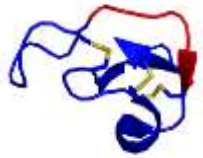
small molecules



specific intra-cellular accumulation
(endocytosis)

Nuclear Medicine: Theranostics (Dx+Tx)

small molecules



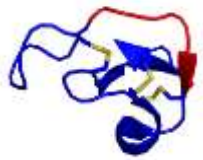
Thyroid

Iodine

specific intra-cellular accumulation
(endocytosis)

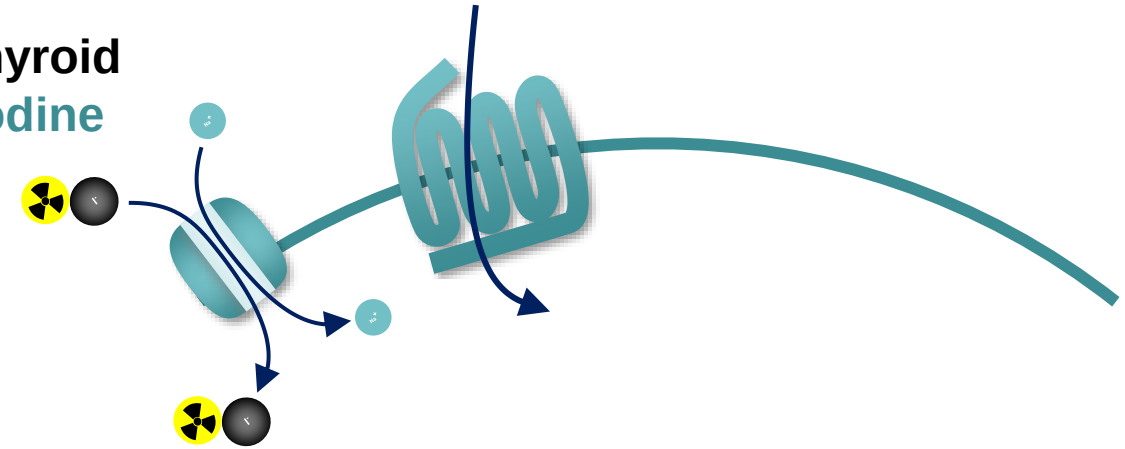
Nuclear Medicine: Theranostics (Dx+Tx)

small molecules



NET
DOTATOC

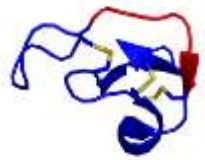
Thyroid
Iodine



specific intra-cellular accumulation
(endocytosis)

Nuclear Medicine: Theranostics (Dx+Tx)

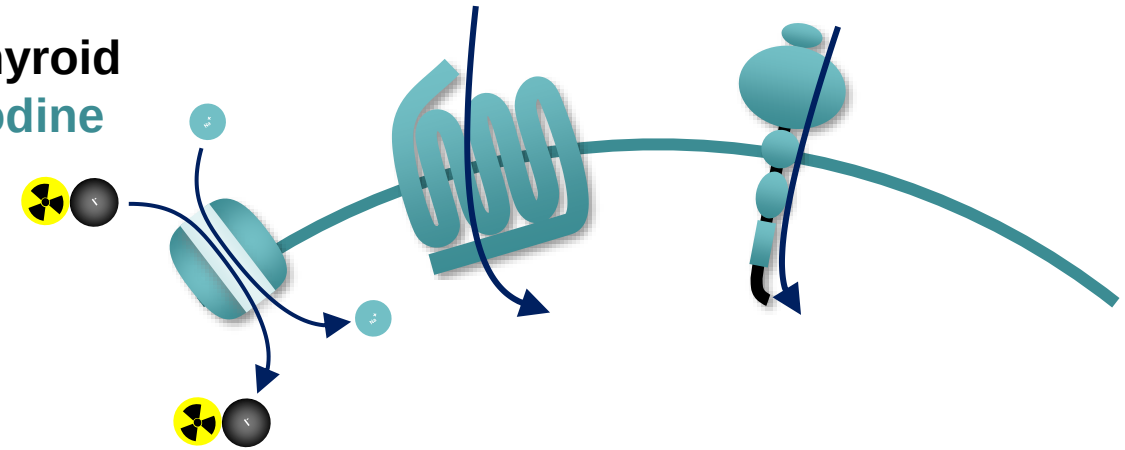
small molecules



NET
DOTATOC

Prostate-Ca
PSMA

Thyroid
Iodine



specific intra-cellular accumulation
(endocytosis)

Nuclear Medicine: Theranostics (Dx+Tx)

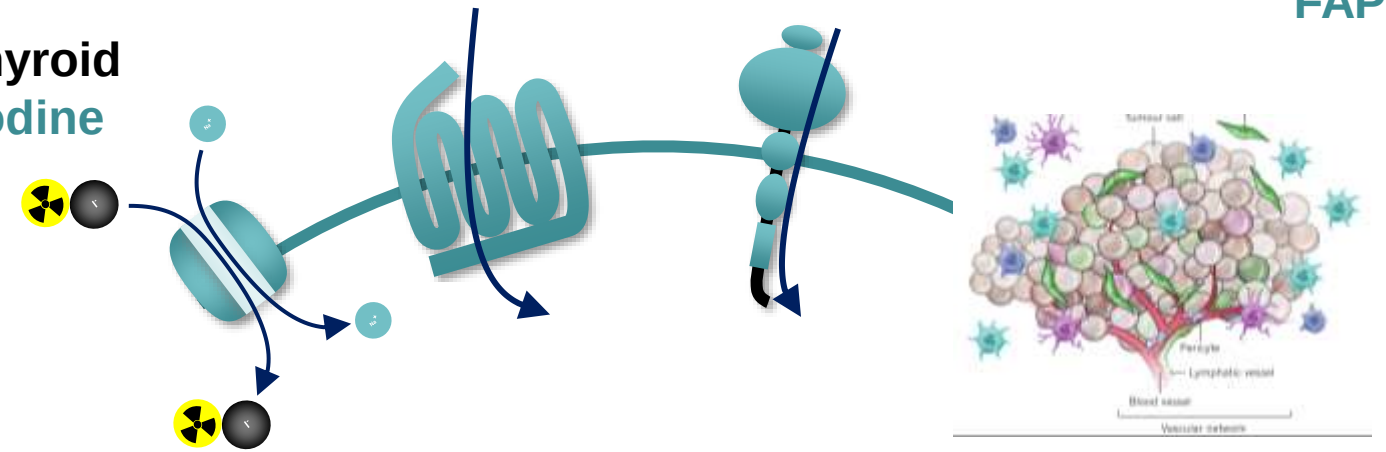
small molecules

NET
DOTATOC

Prostate-Ca
PSMA

Pan-Tracer
FAPI

Thyroid
Iodine



specific intra-cellular accumulation
(endocytosis)

Overview

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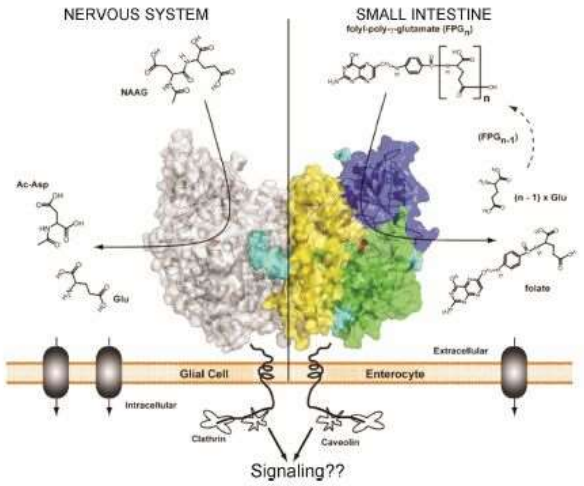
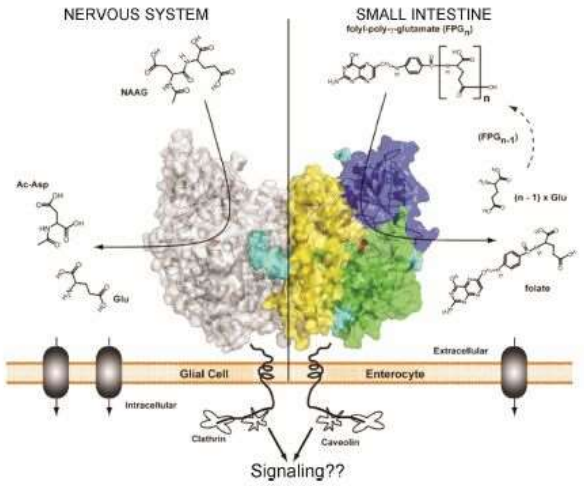
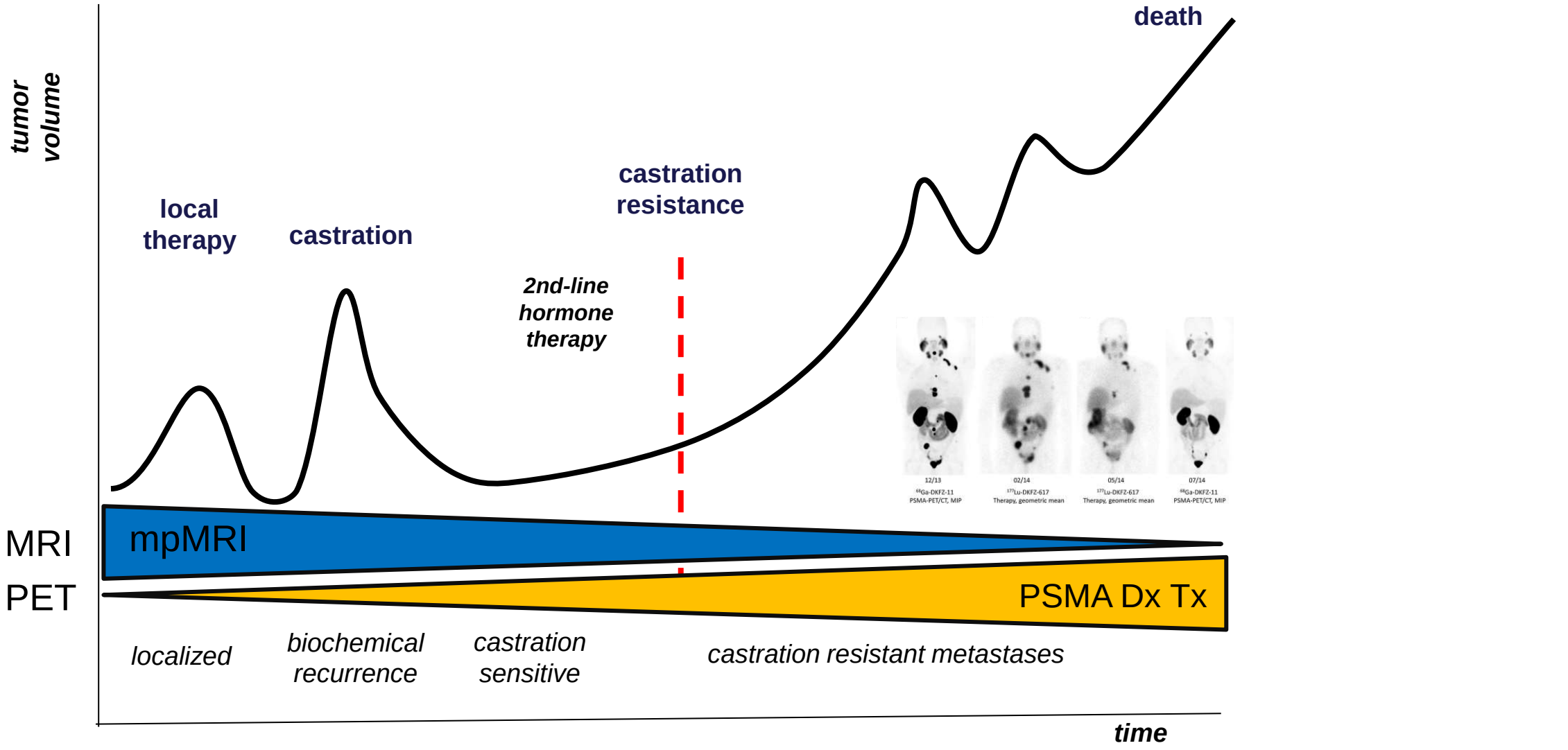


Overview

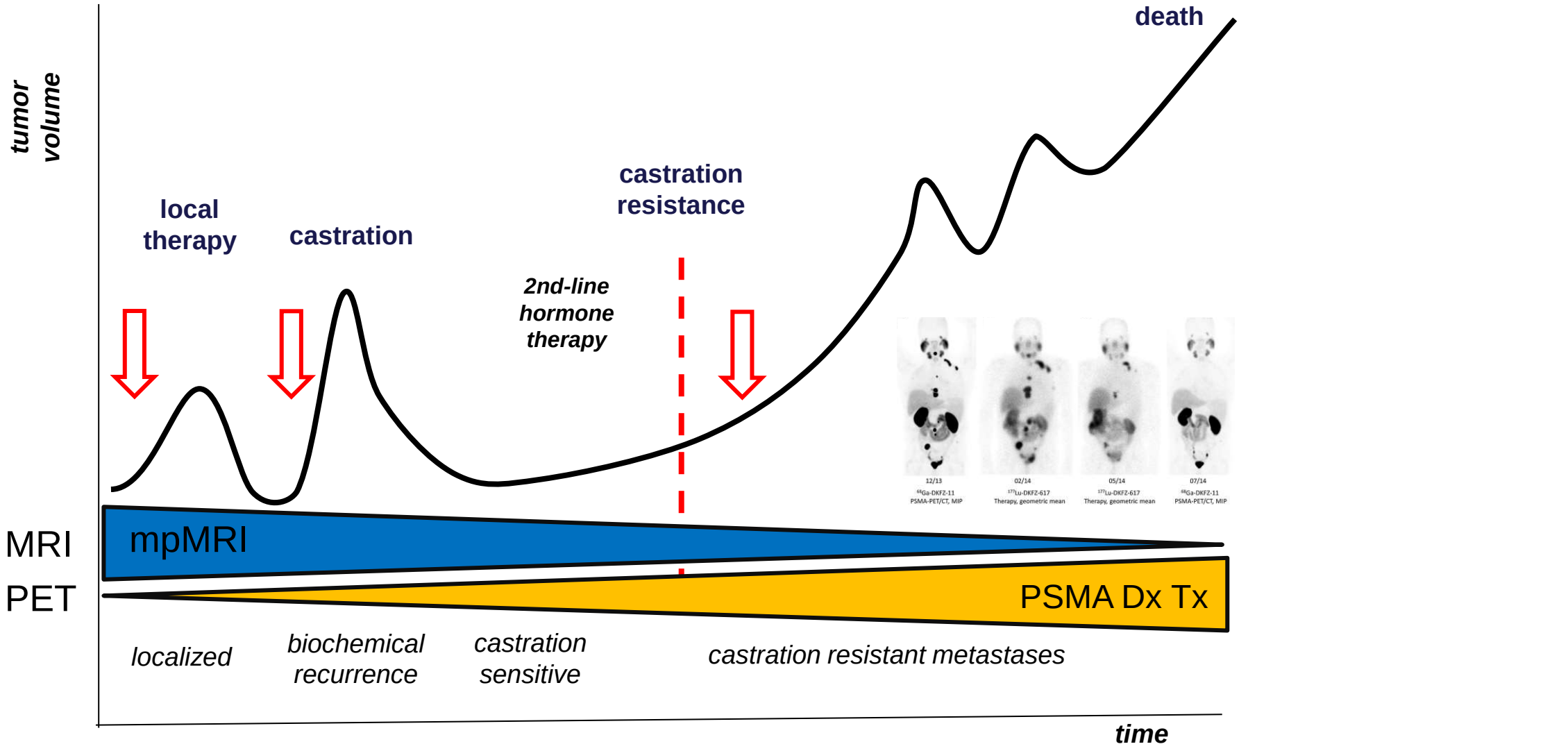
- **Background + biology and different PSMA-ligands**
- Recurrent prostate cancer
- Primary staging and detection
- PSMA-ligand therapy



Background


tumor volume
death
local therapy
castration
castration resistance
2nd-line hormone therapy
MRI
mpMRI
PET
PSMA Dx Tx
localized
biochemical recurrence
castration sensitive
castration resistant metastases
time

Background


tumor volume
death
local therapy
castration
castration resistance
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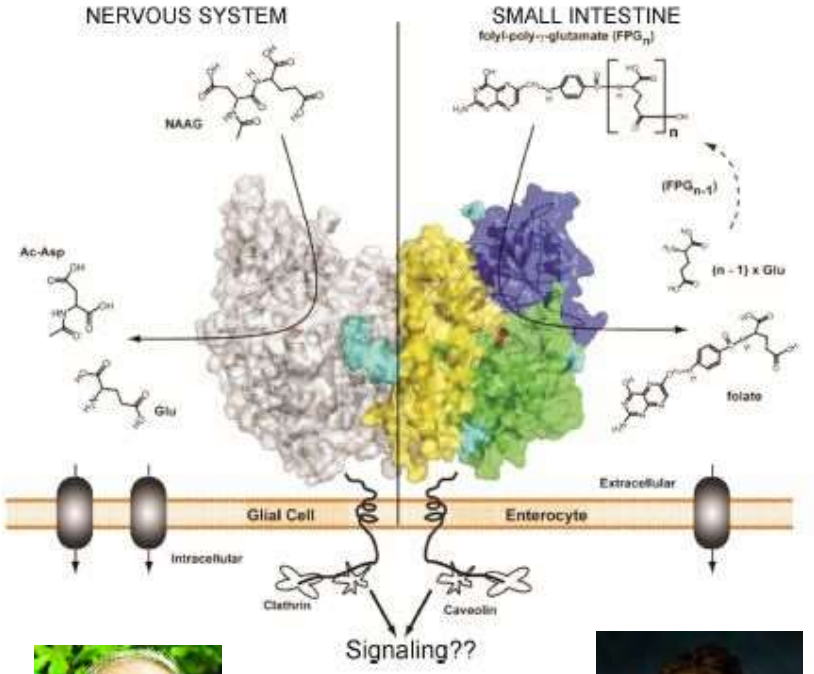
MRI
mpMRI
PET
PSMA Dx Tx
localized
biochemical recurrence
castration sensitive
castration resistant metastases
time

Background + Biology

- **Prostate-specific membran antigen**
- [syn. **Glutamate carboxyeptidase II (GCP-II)**]

- Cell surface protein with overexpression in prostate cancer (750 AS, 84 kDa)

- **PSMA expression increases progressively** in:
  - Higher graded tumors
  - Under androgen deprivation
  - Metastastic disease
  - Hormone-refractory prostate cancer
  - Also in tumor neovasculature



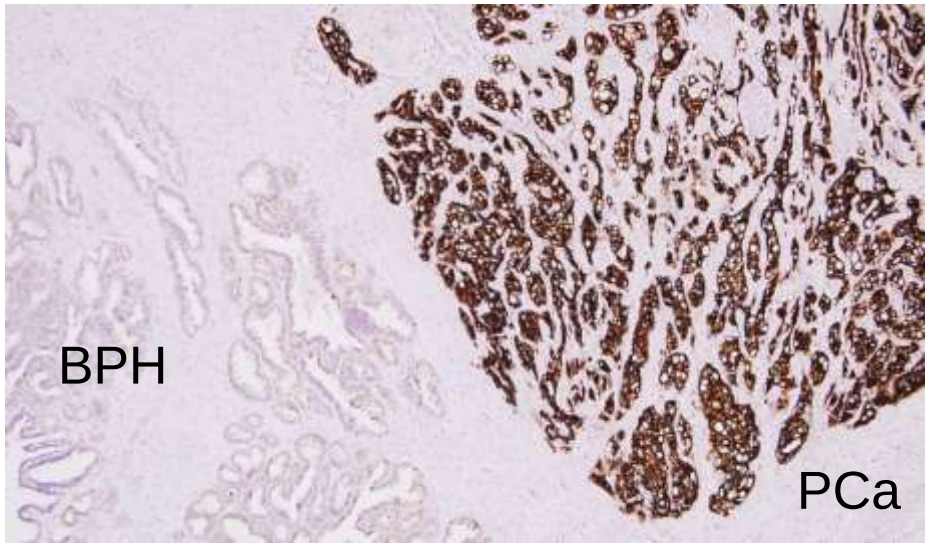
A. Kozikowski

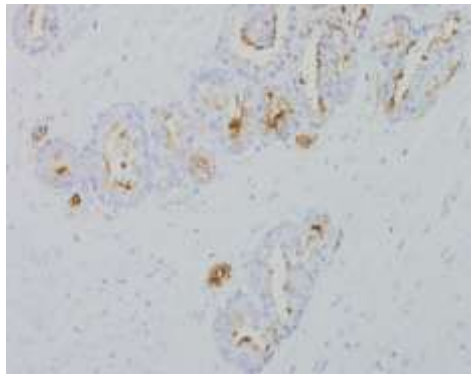
M. Pomper

Kozikowski AP et al., J Med Chem 2004

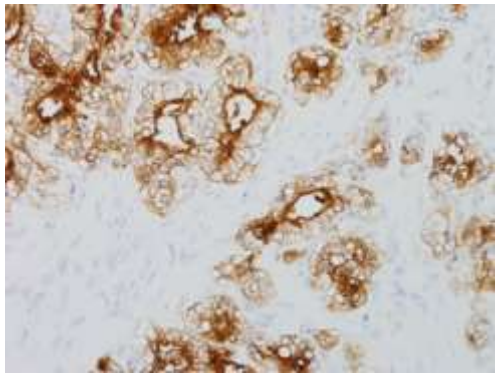
Biology + PSMA-Expression

# Cases Studied	% Cases Reported to be PSMA Positive	Reference
251	94%	Wright et al
184	100%	Bostwick et al
51	84%	Mannweiler, et al
42	88%	Kusumi, et al
21	100%	Ananias, et al
905	99.9%	Loda, et al

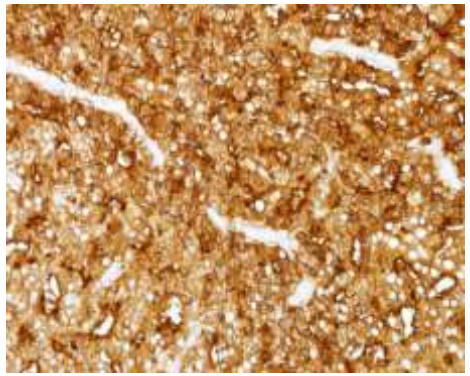




Gleason 3



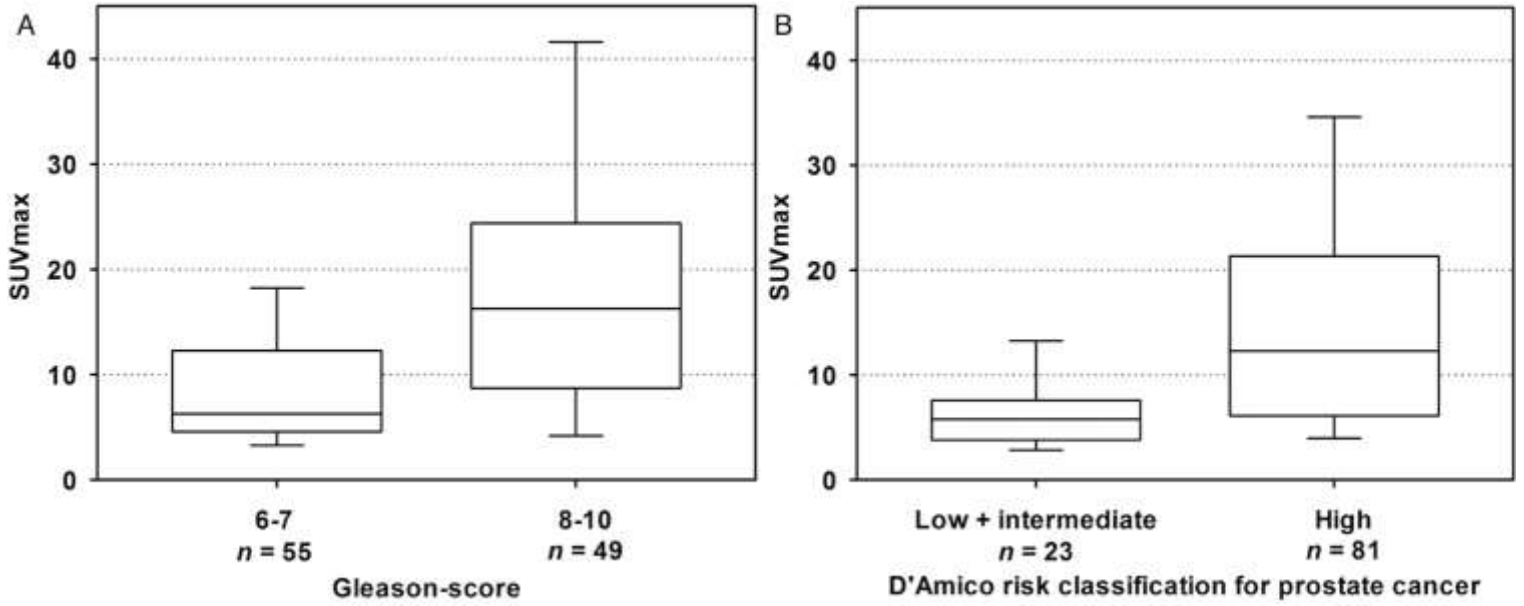
Gleason 4

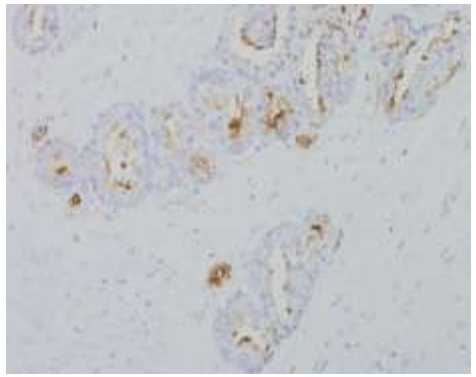


Gleason 5

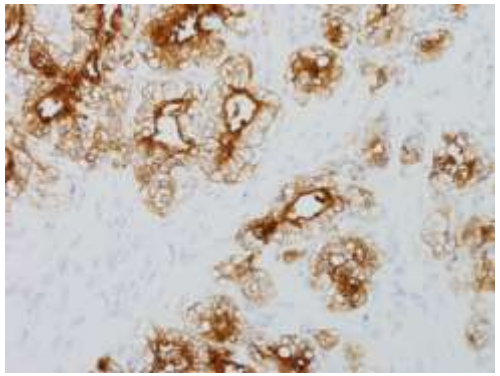
Courtesy of Dr. Neil Bander New York-Presbyterian Hospital

Biology + PSMA-Expression

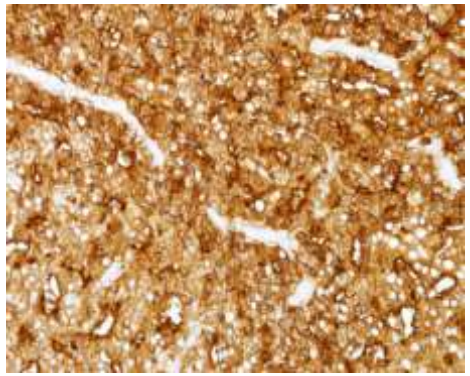




Gleason 3



Gleason 4



Gleason 5

Körber et al., JNM 2017, in print and Uprimy et al, EJNMMI 2017

PSMA-Expression + Histopathology

Results After Comparison Between PET/CT and Histopathology

Tracer	Study	Number of patients	Sensitivity	Specificity	PPV	NPV
^{68}Ga-PSMA-11	Hope, 2019 (*17*)	266 patients, 29 articles	74%	96%	93%	85%
	Perera, 2016 (*4*)	239 patients, 5 studies	80%	97%	—	—
	Afshar-Oromieh, 2015 (*3*)	42 patients	76.6%	100%	100%	91.4%
	Kuten, 2020 (*18*)	16 patients	85.7%	98.2%	96.8%	91.5%
^{18}F-PSMA-1007	Kuten, 2020 (*18*)	16 patients	100%	90.9%	87.5%	100%
	Giesel, 2017 (*8*)	8 patients	94.7%	—	—	—
	Kesch, 2017 (*9*)	10 patients	71%	81%	83%	68%
	Sprute et al. (this work)	96 patients, overall	71.2%	99.5%	91.3%	97.9%
		96 patients, lymph nodes >3mm	81.7%	99.6%	92.4%	98.9%

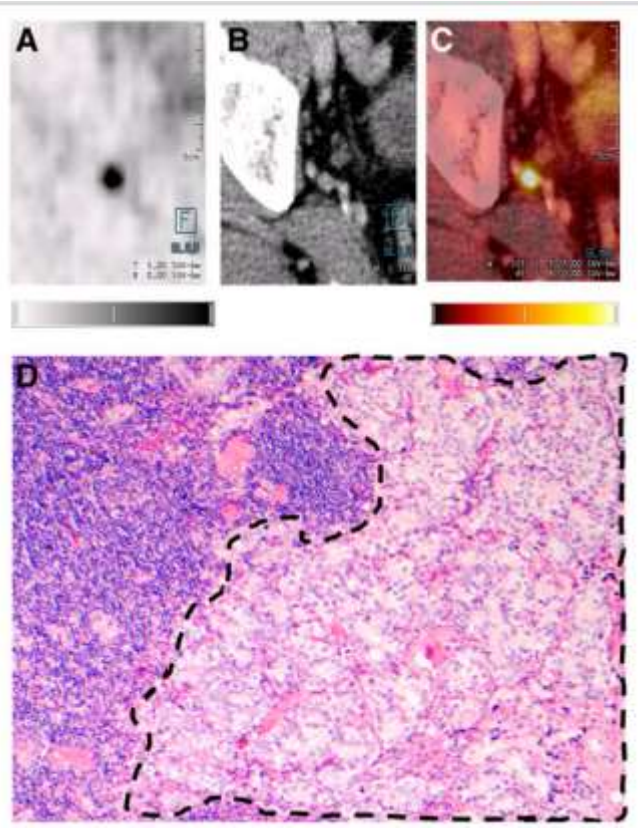
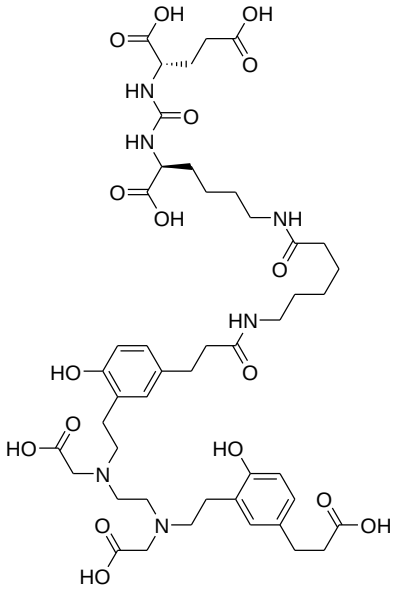


FIGURE 1. (A–C) Axial ^{18}F-PSMA-1007 PET (A), CT (B), and ^{18}F-PSMA-1007 PET/CT (C) images of 73-y-old patient with prostate adenocarcinoma (Gleason score, 4 + 3; T3bN1M0; correlation between PET/CT and histopathology for exemplary LN). (D) Confirmed histopathologic staining (hematoxylin and eosin, ×10) of acinar structures of prostate adenocarcinoma (dashed outline) adjacent to normal LN structures. Quantitative gray scale and color scale represent SUV from 0.00 to 5.00.

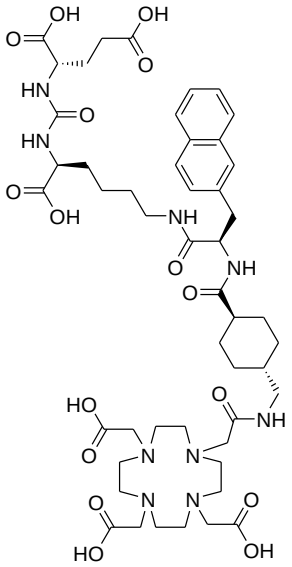
Sprute et al., JNM 2021

PSMA-ligands in PET imaging



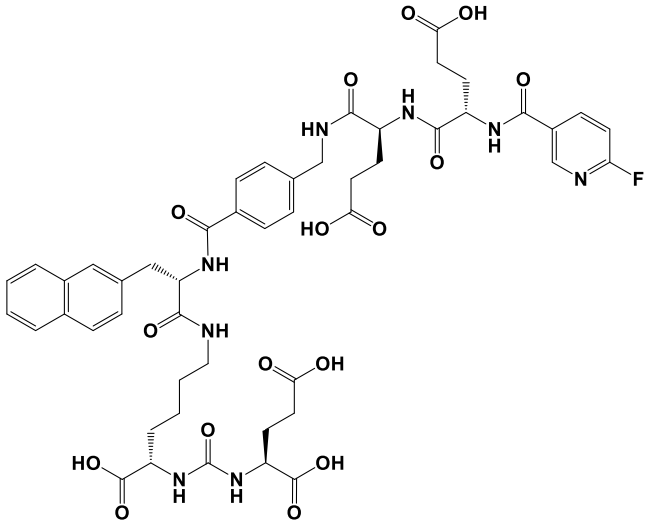
^{68}Ga-PSMA-11

Eder et al.
Bioconjugate Chem 2012



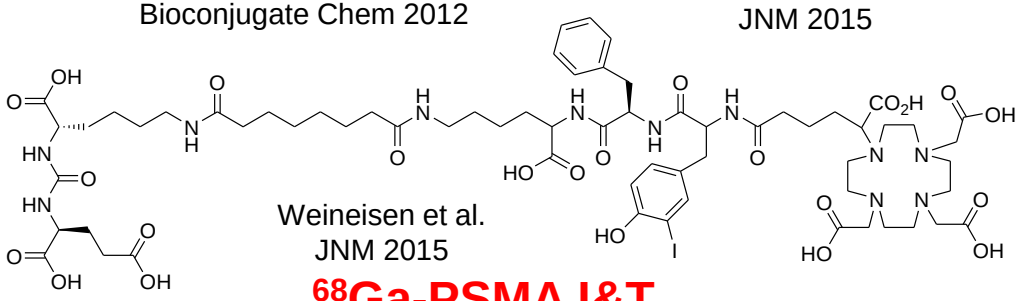
^{68}Ga-/^{177}Lu-PSMA-617 (Pluvicto®)

Benesova et al.,
JNM 2015



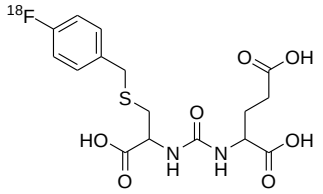
^{18}F-PSMA1007

Giesel et al.
EJNMMI 2016



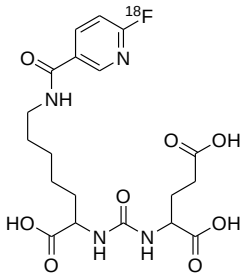
Weineisen et al.
JNM 2015

^{68}Ga-PSMA I&T



^{18}F-DCFBC

Cho et al.
JNM 2012



^{18}F-DCFPyL (Pylarify®)

Szabo et al.
Mol Im Biol 2015

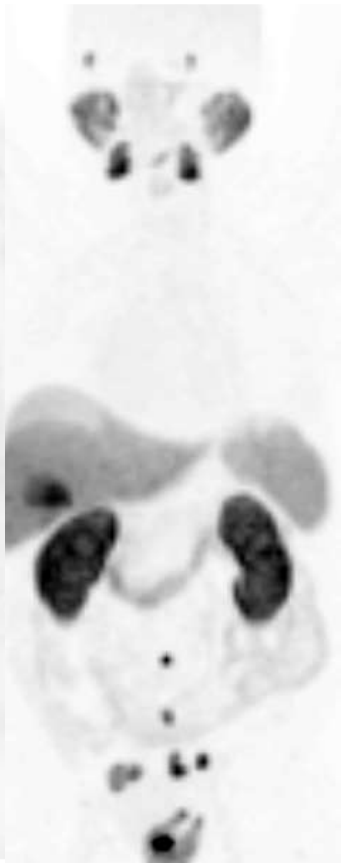
PSMA-ligands in PET imaging

^{68}Ga-PSMA-11 (PSMA HBED-CC)	^{68}Ga-PSMA-I&T	^{68}Ga-PSMA-617
		
Afshar-Oromieh A al. EJNMMI 2013	Weineisen M et al. JNM 2015	Afshar-Oromieh A al. EJNMMI 2015

^{68}Ga-PSMA ligands

^{18}F-PSMA ligands

PSMA-ligands in PET imaging

^{68}Ga-PSMA-11 (PSMA HBED-CC)	^{68}Ga-PSMA-I&T	^{68}Ga-PSMA-617	^{18}F-DCFBC	^{18}F-DCFPyL	^{18}F-PSMA1007
					
Afshar-Oromieh A al. EJNMMI 2013	Weineisen M et al. JNM 2015	Afshar-Oromieh A al. EJNMMI 2015	Cho S et al. JNM 2012	Szabo Z et al. Mol Im Biol 2015	Giesel et al. EJNMMI 2016
		^{68}Ga-PSMA ligands		^{18}F-PSMA ligands	

PSMA-Ligands + drug approval

PSMA Imaging

US/EU Market / FDA/EMA drug approval

Lantheus Medical Imaging

(Pylarify®)

PyL (^{18}F-PSMA)
BCR patients

06/2021

TELIX PHARMACEUTICALS

TLX591 (^{68}Ga-PSMA)
BCR patients

12/2021

ABX

^{18}F-PSMA-1007
BCR patients

PSMA-Ligands + drug approval

PSMA Imaging

US/EU Market / FDA/EMA drug approval

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06/2021

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BCR patients

12/2021

ABX

^{18}F-PSMA-1007
BCR patients

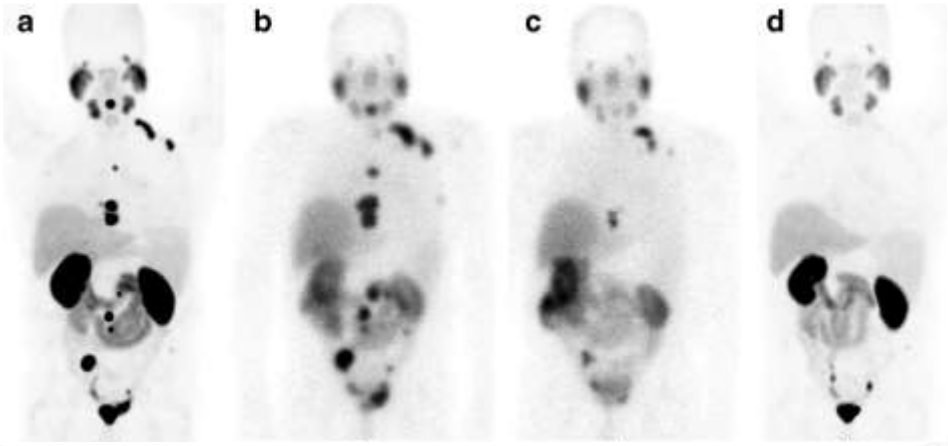
PSMA Therapy

US/EU Market / FDA/EMA drug approval

NOVARTIS

^{177}Lu-PSMA-617 /**Pluvicto®**

03/2022



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- **Recurrent prostate cancer**
- Primary staging and detection
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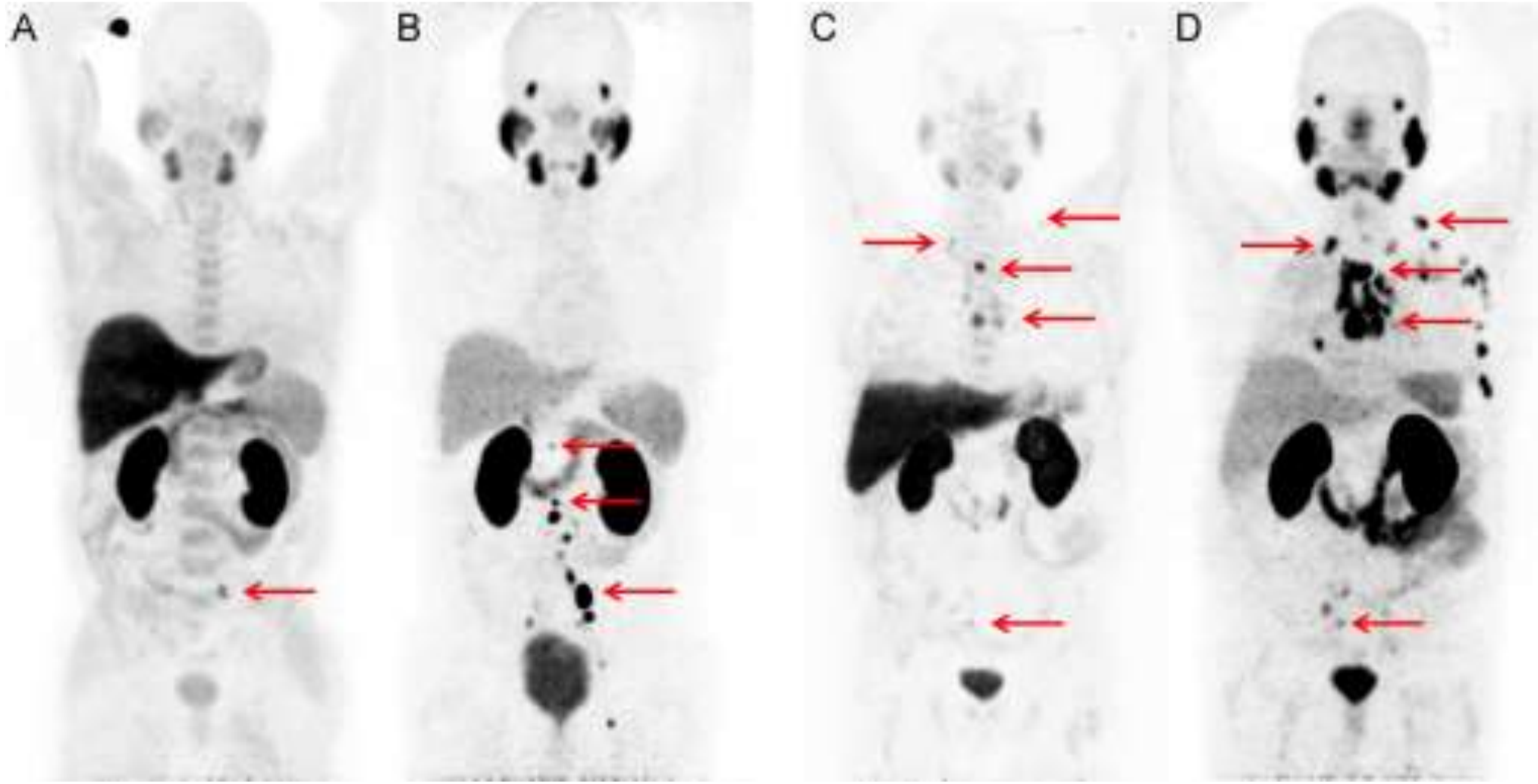
Recurrent prostate cancer (Choline vs. PSMA)

^{18}FECh-PET/CT

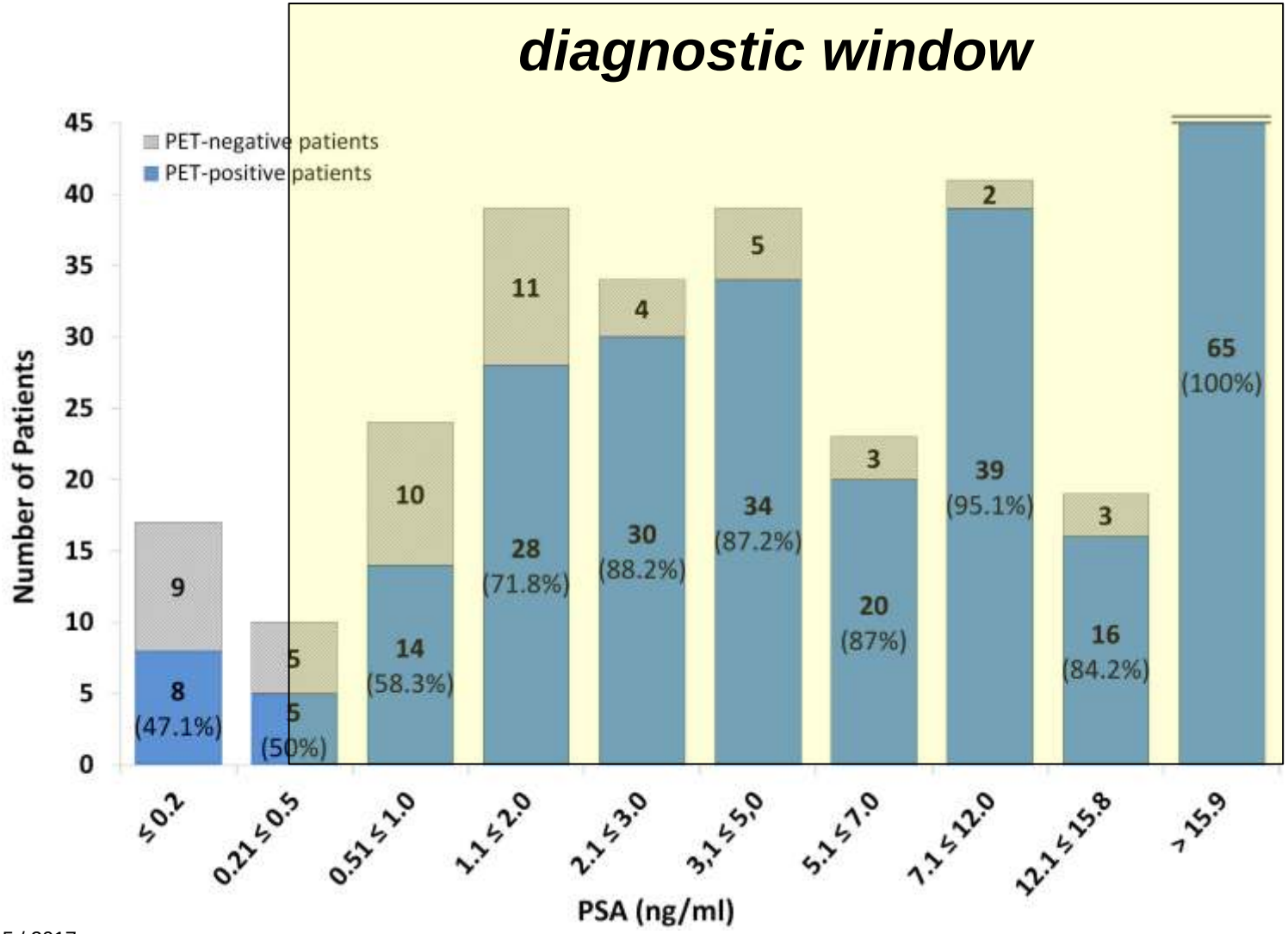
^{18}FECh-PET/CT

Recurrent prostate cancer (Choline vs. PSMA)



^{18}FECh-PET/CT ^{68}Ga-PSMA-PET/CT ^{18}FECh-PET/CT ^{68}Ga-PSMA-PET/CT

Recurrent prostate cancer (Detection efficacy)

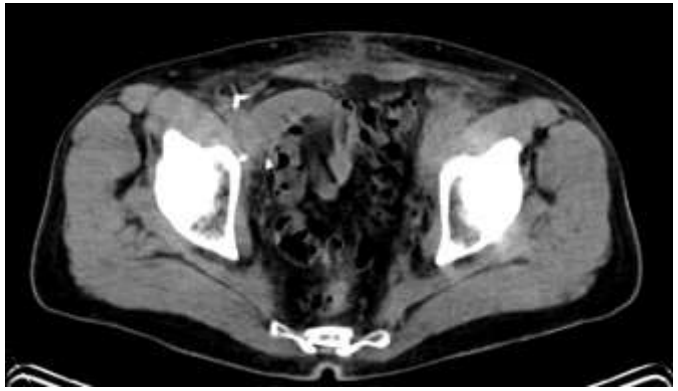


Afshar-Oromieh et al. EJNMMI 2015 / 2017

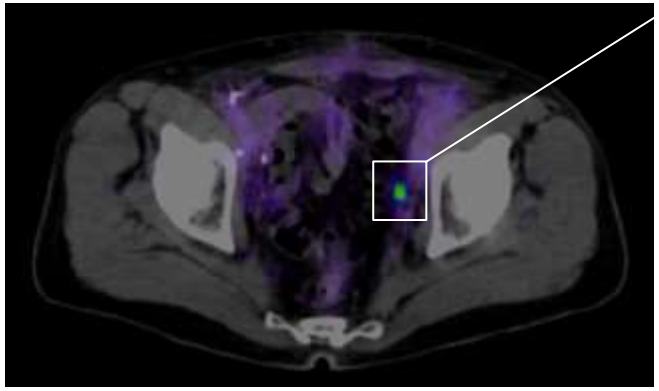
Recurrent prostate cancer

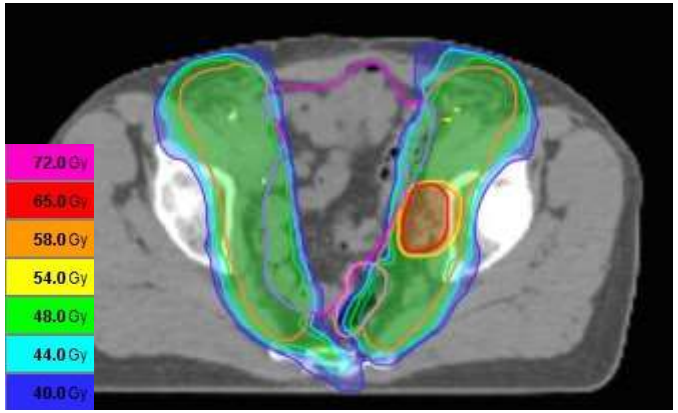
Impact Patient Management

$T_3N_0M_0$



$T_3N_1M_0$



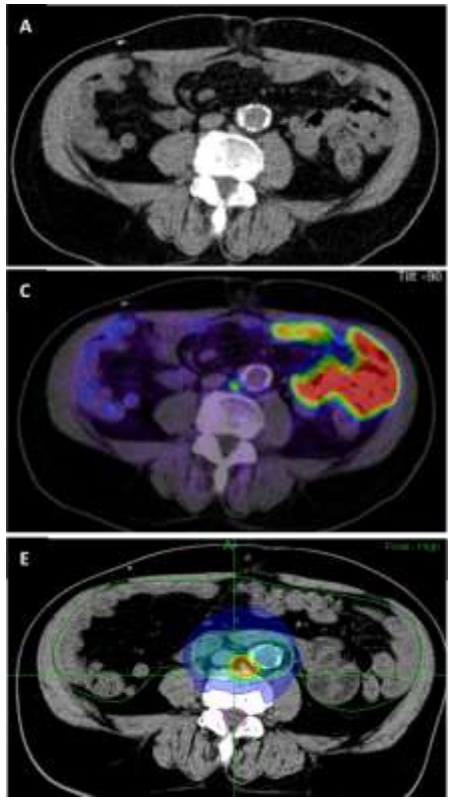


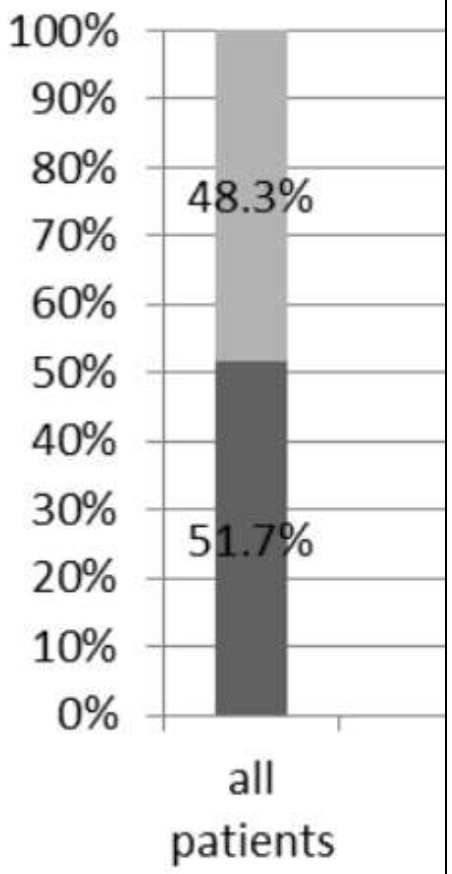
- conventional staging was $T_3N_0M_0$, ^{68}Ga-PSMA PET revealed inguinal and iliac metastases
- IMRT Plan was modified according to these findings with groins and simultaneous integrated boost (SIB)

Sterzing et al. EJNMMI 2015 / 2017

Recurrent prostate cancer

Impact Patient Management in RadioOncology





Sterzing et al, EJNMMI 2016

Dewes *et al. Radiation Oncology* (2016) 11:73
DOI 10.1186/s13014-016-0646-2

Radiation Oncology

RESEA

Integ
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Sabrina De
Jürgen E.

Abstract

Backgrou
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Conclusi

Shakespeare *Radiation Oncology* (2015) 10:233
DOI 10.1186/s13014-015-0548-8

Radiation Oncology

SHORT REPORT

Open Access

CrossMark

Effect of prostate-specific membrane antigen positron emission tomography on the decision-making of radiation oncologists

Thomas P. Shakespeare[1,2]

Abstract

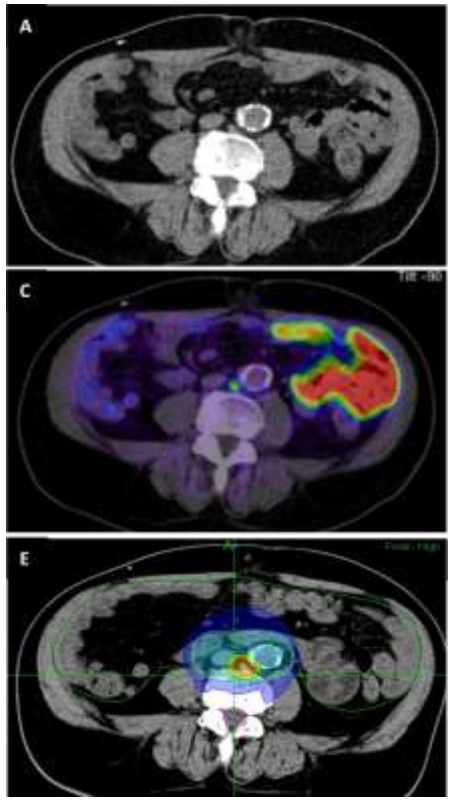
Background: Positron emission tomography (PET) imaging is routinely used in many cancer types, although is not yet a standard modality for prostate carcinoma. Prostate-specific membrane antigen (PSMA) PET is a promising new modality for staging prostate cancer, with recent studies showing potential advantages over traditional computed tomography (CT), magnetic resonance imaging (MRI) and nuclear medicine bone scan imaging. However, the impact of PSMA PET on the decision-making of radiation oncologists and outcomes after radiotherapy is yet to be determined. Our aim was to determine the impact of PSMA PET on a radiation oncologist's clinical practice.

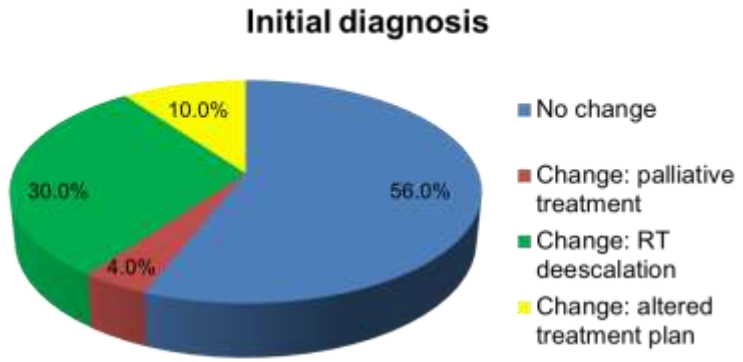
Findings: Patients in a radiation oncology clinic who underwent PSMA PET were prospectively recorded in an electronic oncology record. Patient demographics, outcomes of imaging, and impact on decision-making were evaluated.

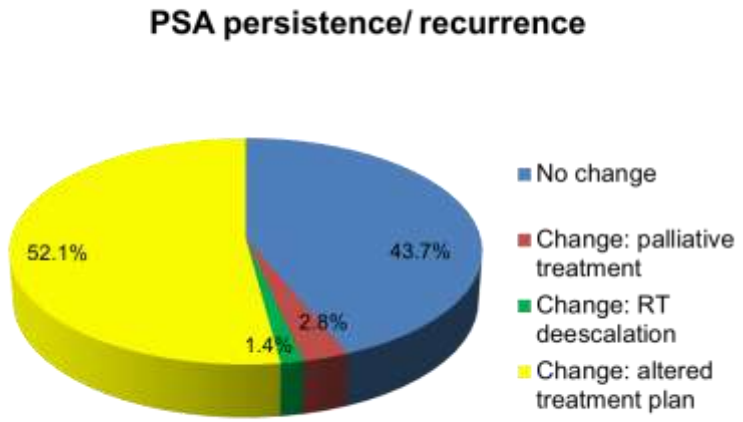
Fifty-four patients underwent PSMA PET between January and May 2015. The major reasons for undergoing PET included staging before definitive (14.8 %) or post-prostatectomy (33.3 %) radiotherapy, and investigation of PSA failures following definitive (16.7 %) or post-prostatectomy (33.3 %) radiotherapy. In 46.3 % of patients PSMA was

Recurrent prostate cancer

Impact Patient Management in RadioOncology

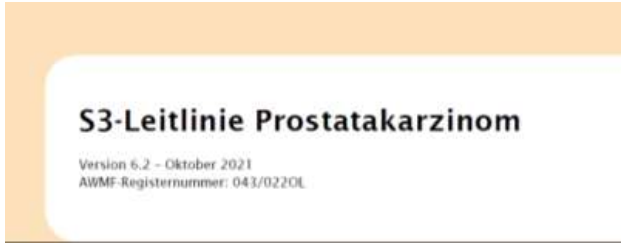






Körber et al., JNM 2018; n=212

Recurrent prostate cancer (Leitlinien): BCR

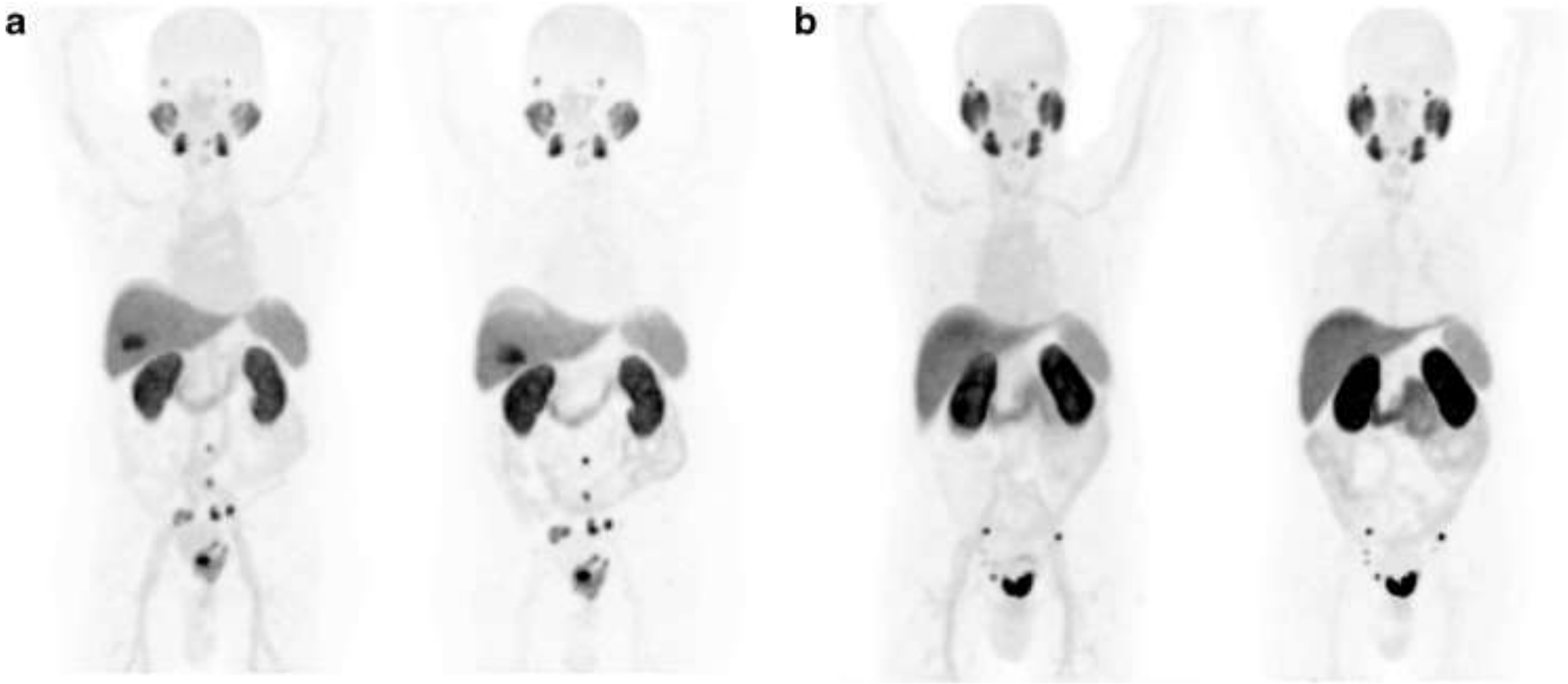


5.29	Evidenzbasierte Empfehlung	geprüft 2018
Empfehlungsgrad **0**	a. Im Rahmen einer Rezidivdiagnostik (nach primär kurativer Therapie, s. Empfehlung 7.2 und 7.3) kann primär eine PET Hybrid-Bildgebung mit radioaktiv markierten PSMA-Liganden zur Beurteilung der Tumorausdehnung erfolgen, falls sich aus dem Befund eine therapeutische Konsequenz ergibt.	
Empfehlungsgrad **A**	b. Ein negatives PSMA-PET soll eine frühe Salvage-Therapie nicht verzögern.	

Overview

- Background + biology and different PSMA-ligands
- Recurrent prostate cancer
- **Primary staging and detection**
- PSMA-ligand therapy

Primary staging and detection



Primary staging and detection

2011

2022

Primary staging and detection

Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multi-centre study

*Michael S Hofman, Nathan Lawrentschuk, Roslyn J Francis, Colin Tang, Ian Vela, Paul Thomas, Natalie Rutherford, Jarad M Martin, Mark Frydenberg, Ramdave Shakher, Lih-Ming Wong, Kim Taubman, Sze Ting Lee, Edward Hsiao, Paul Roach, Michelle Nottage, Ian Kirkwood, Dickon Hayne, Emma Link, Petra Marusic, Anetta Matera, Alan Herschtal, Amir Iravani, Rodney J Hicks, Scott Williams, Declan G Murphy, for the proPSMA Study Group Collaborators**

Summary

Background Conventional imaging using CT and bone scan has insufficient sensitivity when staging men with high-risk localised prostate cancer. We aimed to investigate whether novel imaging using prostate-specific membrane antigen (PSMA) PET-CT might improve accuracy and affect management.

Methods In this multicentre, two-arm, randomised study, we recruited men with biopsy-proven prostate cancer and high-risk features at ten hospitals in Australia. Patients were randomly assigned to conventional imaging with CT and bone scanning or gallium-68 PSMA-11 PET-CT. First-line imaging was done within 21 days following randomisation. Patients crossed over unless three or more distant metastases were identified. The primary outcome was accuracy of first-line imaging for identifying either pelvic nodal or distant-metastatic disease defined by the receiver-operating curve using a predefined reference-standard including histopathology, imaging, and biochemistry at 6-month follow-up. This trial is registered with the Australian New Zealand Clinical Trials Registry, ANZCTR12617000005358.

Findings From March 22, 2017 to Nov 02, 2018, 339 men were assessed for eligibility and 302 men were randomly assigned. 152 (50%) men were randomly assigned to conventional imaging and 150 (50%) to PSMA PET-CT. Of 295 (98%) men with follow-up, 87 (30%) had pelvic nodal or distant metastatic disease. PSMA PET-CT had a 27% (95% CI 23–31) greater accuracy than that of conventional imaging (92% [88–95] *vs* 65% [60–69]; p<0·0001). We found a lower sensitivity (38% [24–52] *vs* 85% [74–96]) and specificity (91% [85–97] vs 98% [95–100]) for conventional imaging compared with PSMA PET-CT. Subgroup analyses also showed the superiority of PSMA PET-CT (area under the curve of the receiver operating characteristic curve 91% vs 59% [32% absolute difference; 28–35] for patients with pelvic nodal metastases, and 95% vs 74% [22% absolute difference; 18–26] for patients with distant metastases). First-line conventional imaging conferred management change less frequently (23 [15%] men [10–22] *vs* 41 [28%] men [21–36]; p=0·008) and had more equivocal findings (23% [17–31] *vs* 7% [4–13]) than PSMA PET-CT did.

Published Online
March 22, 2020
https://doi.org/10.1016/
S0140-6736(20)30314-7

See Online/Comment
https://doi.org/10.1016/
S0140-6736(20)30527-4

*A complete list of members is provided in the appendix

Molecular Imaging and Therapeutic Nuclear Medicine (Prof M S Hofman MBBS, P Marusic BSc, A Iravani MD, Prof R J Hicks MBBS), **Centre for Biostatistics and Clinical Trials** (E Link DPhil, A Matera MSc, A Herschtal PhD), **Division of Radiation Oncology** (Prof S Williams MBBS), **Division of Cancer Surgery** (Prof D G Murphy MBBCh), **Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Sir Peter MacCallum Department of Oncology** (Prof M S Hofman, N Lawrentschuk MBBS, E Link,

Primary staging and detection

Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multi-centre study

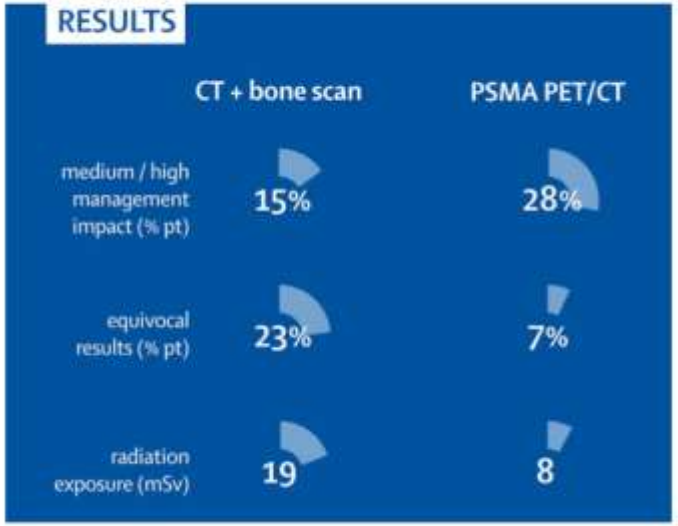
*Michael S Hofman, Nathan Lawrentschuk, Roslyn J Francis, Colin Tang, Ian Vela, Paul Thomas, Natalie Rutherford, Jarad M Martin, Mark Frydenberg, Ramdave Shakher, Lih-Ming Wong, Kim Taubman, Sze Ting Lee, Edward Hsiao, Paul Roach, Michelle Nottage, Ian Kirkwood, Dickon Hayne, Emma Link, Petra Marusic, Anetta Matera, Alan Herschtal, Amir Iravani, Rodney J Hicks, Scott Williams, Declan G Murphy, for the proPSMA Study Group Collaborators**

INTERPRETATION

PSMA PET/CT is a suitable replacement for CT and bone scanning, providing :

- superior accuracy
- management change
- lower radiation

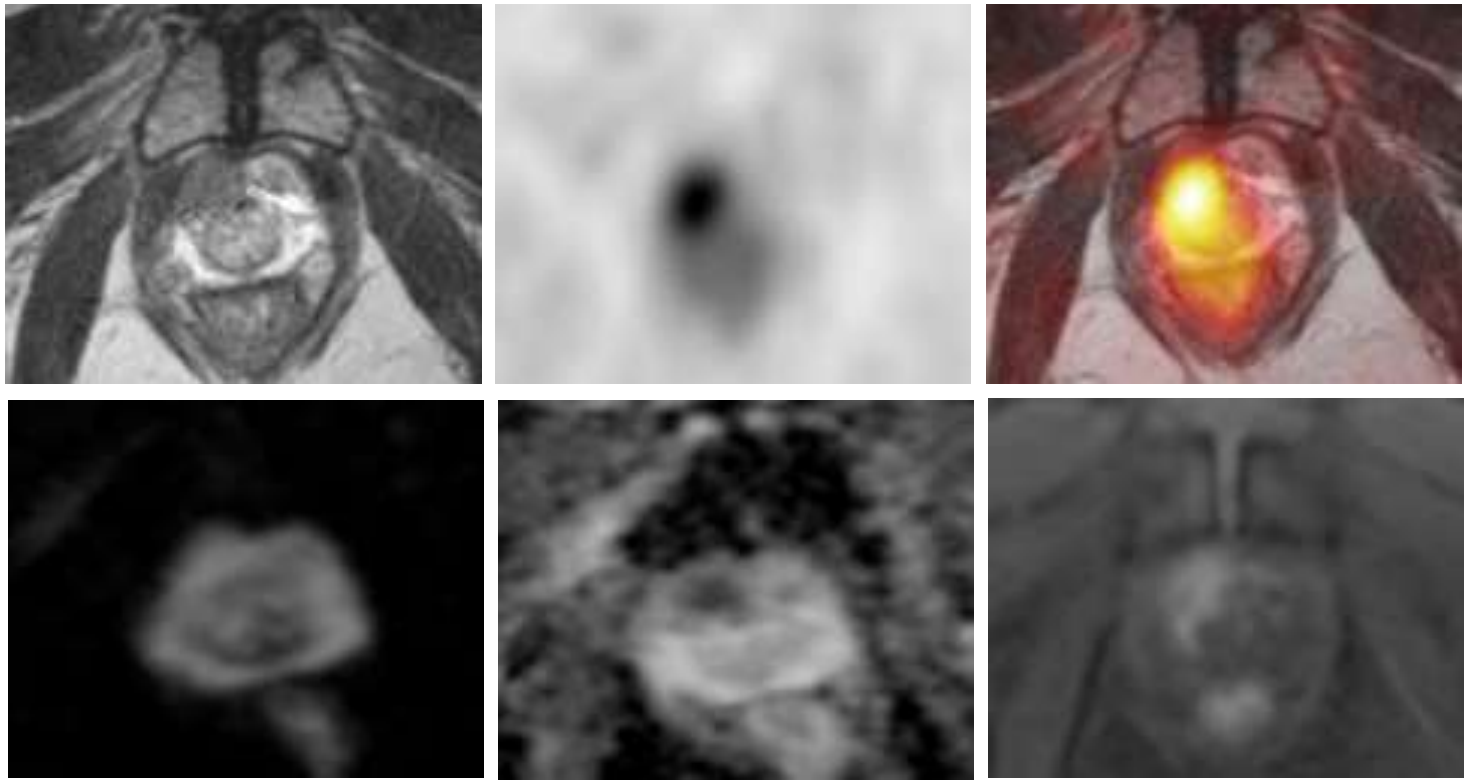
RESULTS



Primary staging and detection

T-Staging using mpMRI and PSMA-PET

68y/o pat, prior neg Bx, continious PSA-increase 10.1 ng/ml

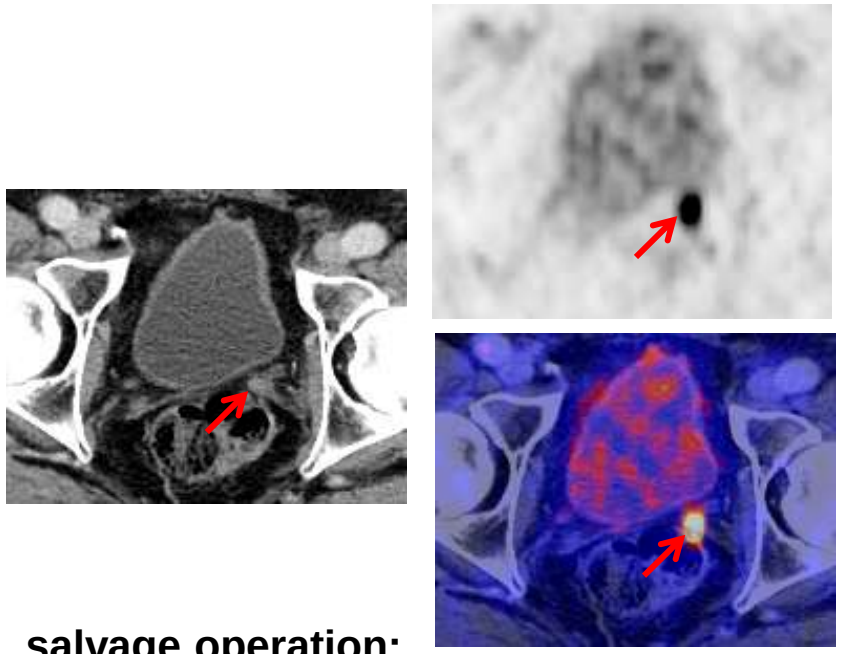


PIRDAS 5
⇒ Gleason 7b (4+3) at targeted biopsy

Local recurrence

Local recurrence

74y/o patient, s/p. RPE 2004 pT2a pN0 Gleason 7, s/p salvage RTx 2010, *PSA-value 05/15: 1.76 ng/ml*



salvage operation:
soft-tissue including seminal vesicle with a cribriforme, poorly differentiated adenocarcinoma of the prostate (Gleason 7)

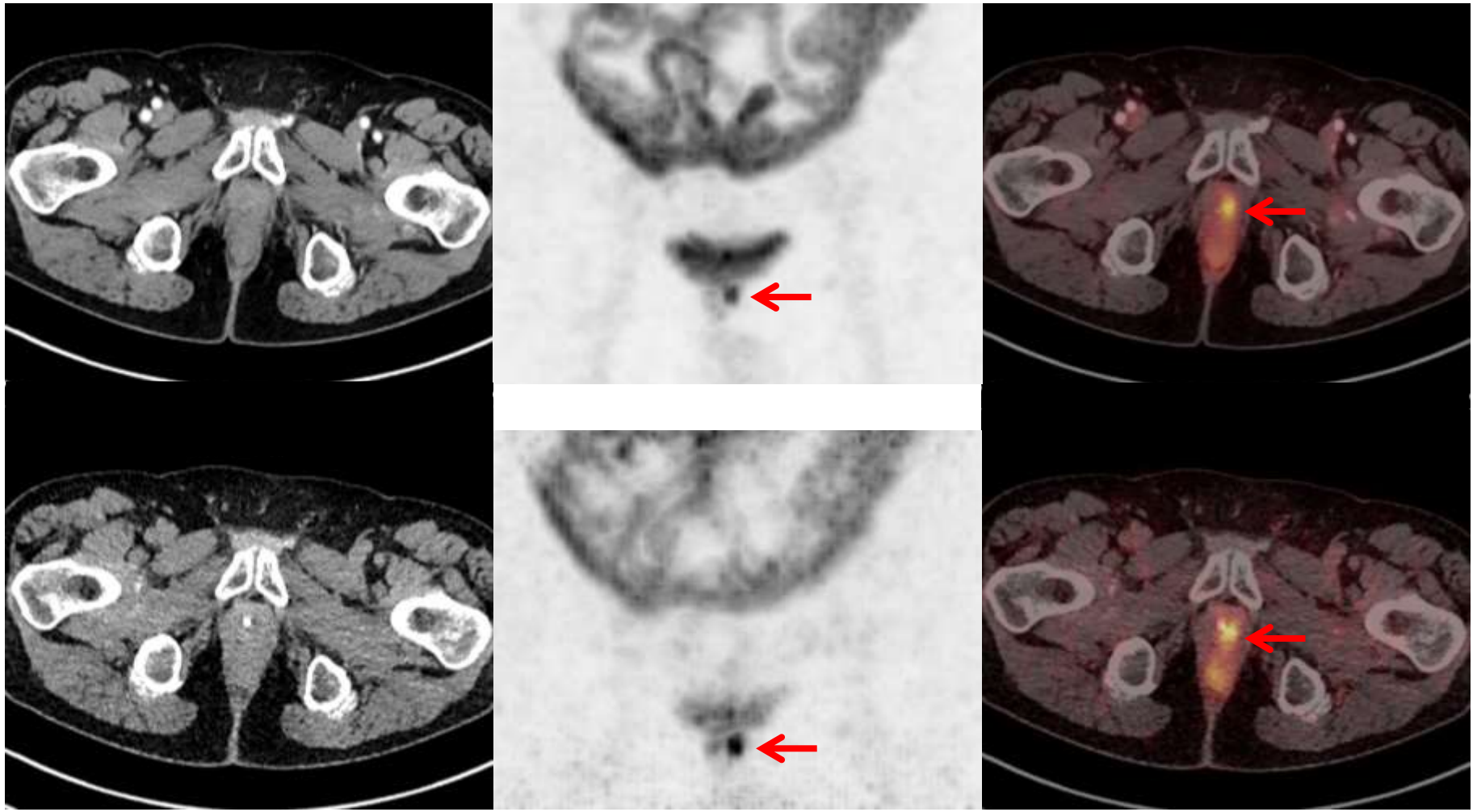
Maurer T et al, Nat Rev Uro 2016

Local Recurrence

71 y.o.
PSAnadir: 0,04
GSC 7 b, RPE 09/2013
Monate nach RPE: 111
Z.n. Radiatio

Mamlins E., Giesel F.L., Schimmöller L. / MS in preparation

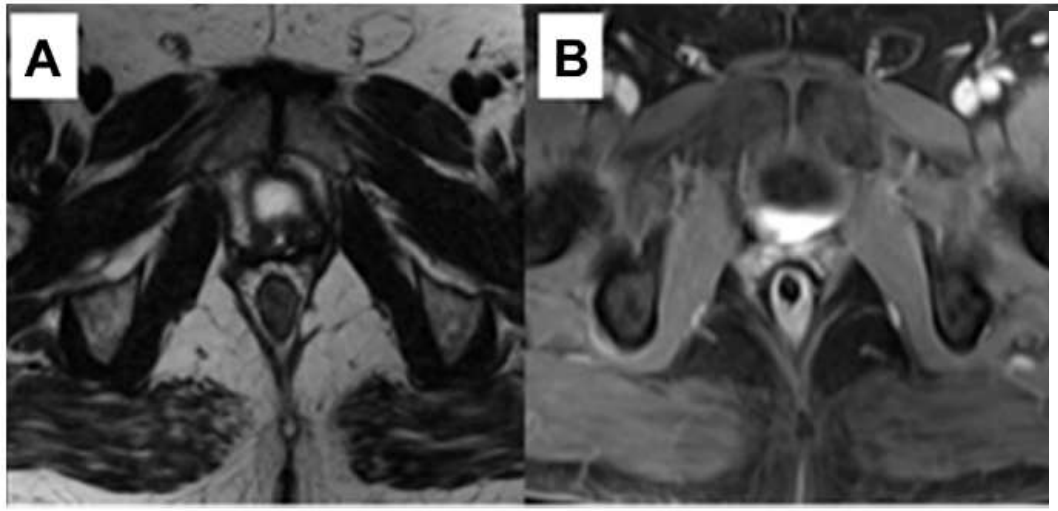
Local Recurrence

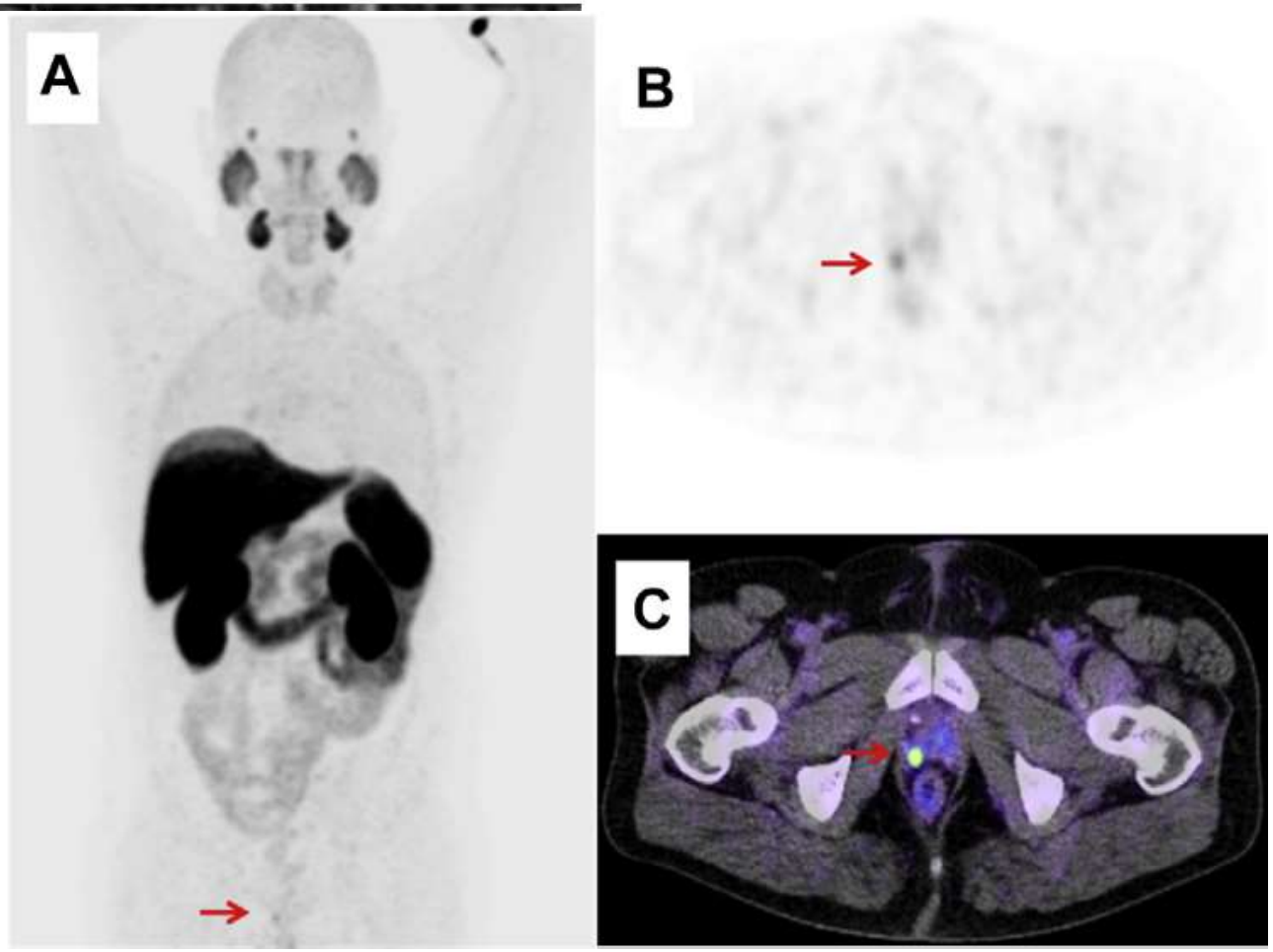


71 y.o.
PSAnadir: 0,04
GSC 7 b, RPE 09/2013
Monate nach RPE: 111
Z.n. Radiatio

E. Mamlins, F. Giesel, G. Antoch, L. Schimmöller / MS in preparation

Local recurrent



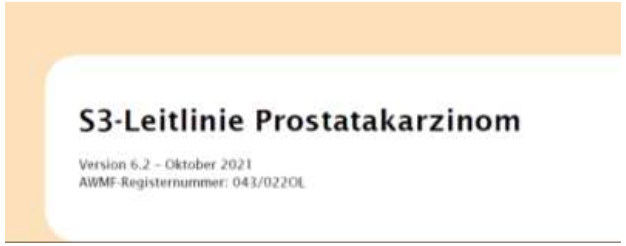


Multiparametric Magnetic Resonance Imaging Examination of a 48-Year-old Patient 6 Months After Radical Prostatectomy

Gleason Score 7, Stage pT2cN0M0

PSA elevated: 0.3 ng/mL.

Primary Staging

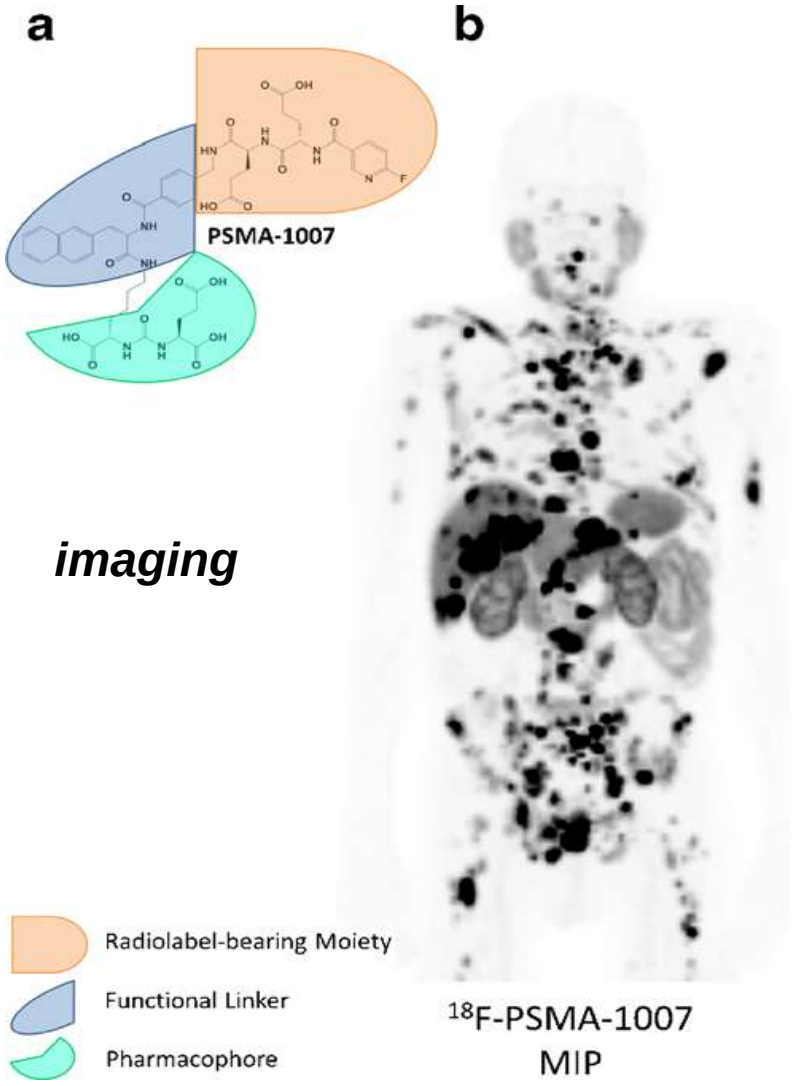


5.25	Evidenzbasierte Empfehlung / Statement	neu 2021
	a. Das PSMA-PET hat eine höhere Genauigkeit (accuracy) für den Nachweis von Prostatakarzinom-Metastasen als die Kombination aus Computertomographie und Knochenszintigraphie.	
Empfehlungsgrad **0**	b. Das PSMA-PET/CT kann beim High-Risk Prostatakarzinom (Gleason-Score 8-10 oder T-Kategorie cT3/cT4 oder PSA≥20ng/ml) zur Ausbreitungsdiagnostik eingesetzt werden.	

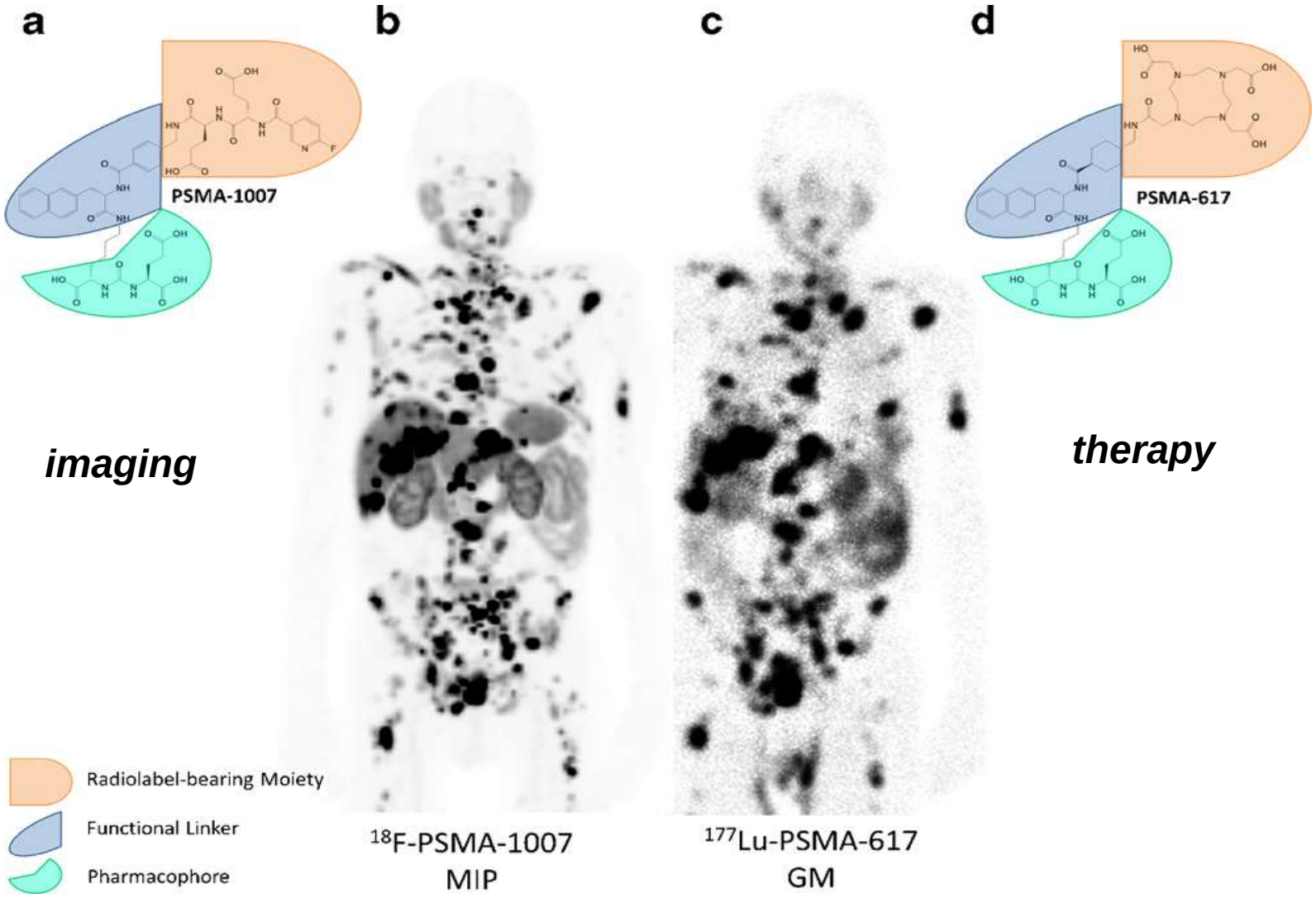
Overview

- Background + bioloy and different PSMA-ligands
- Recurrent prostate cancer
- Primary staging and detection
- **PSMA-ligand therapy**

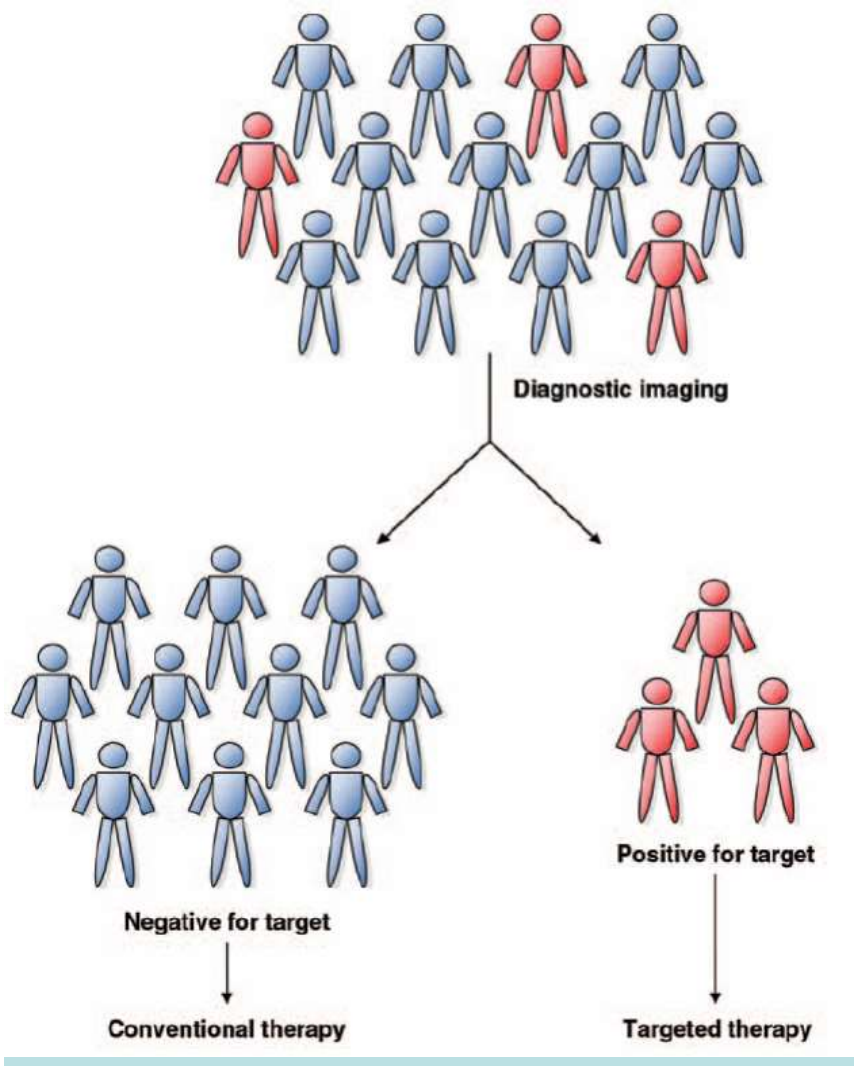
PSMA-ligand therapy



PSMA-ligand therapy

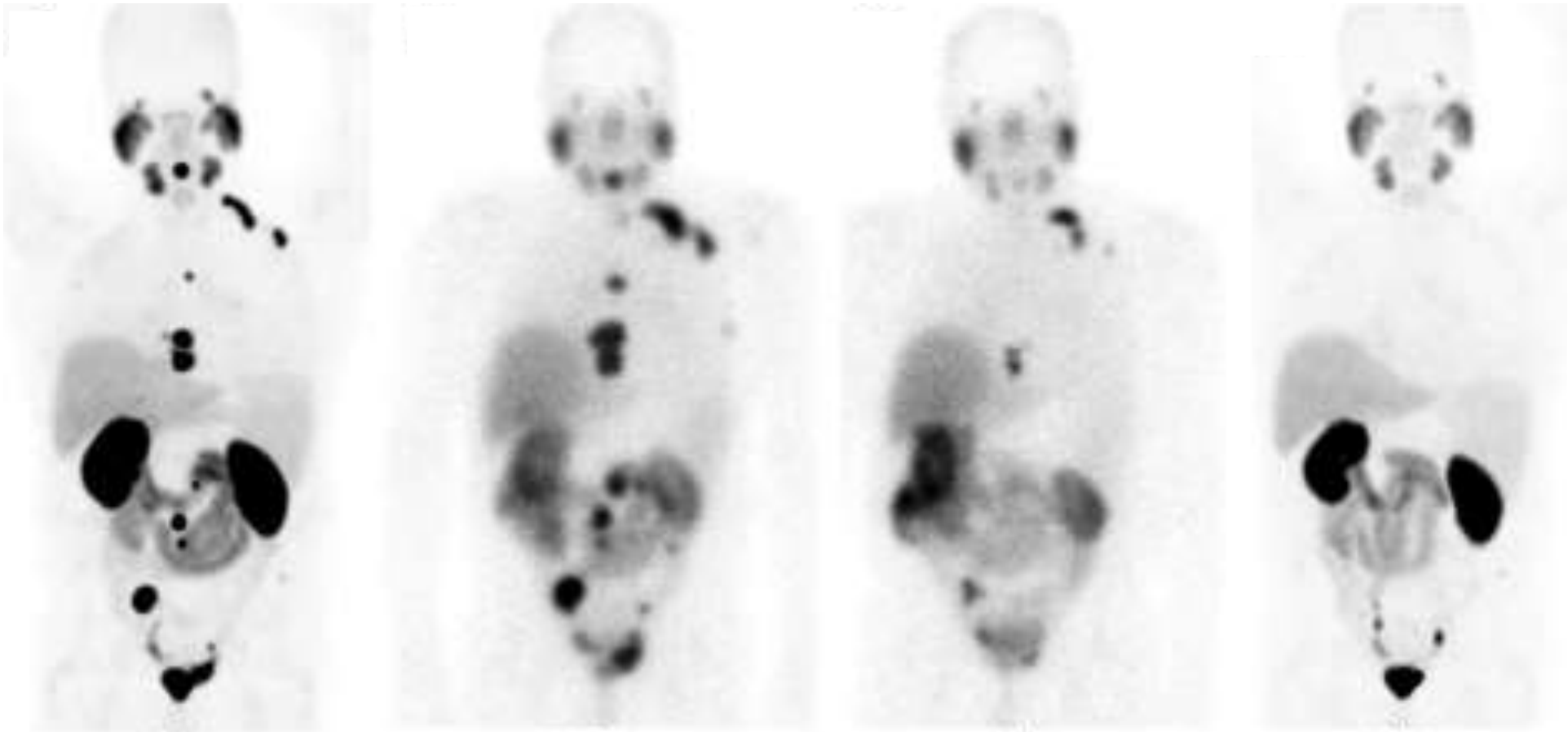


PSMA-ligand therapy

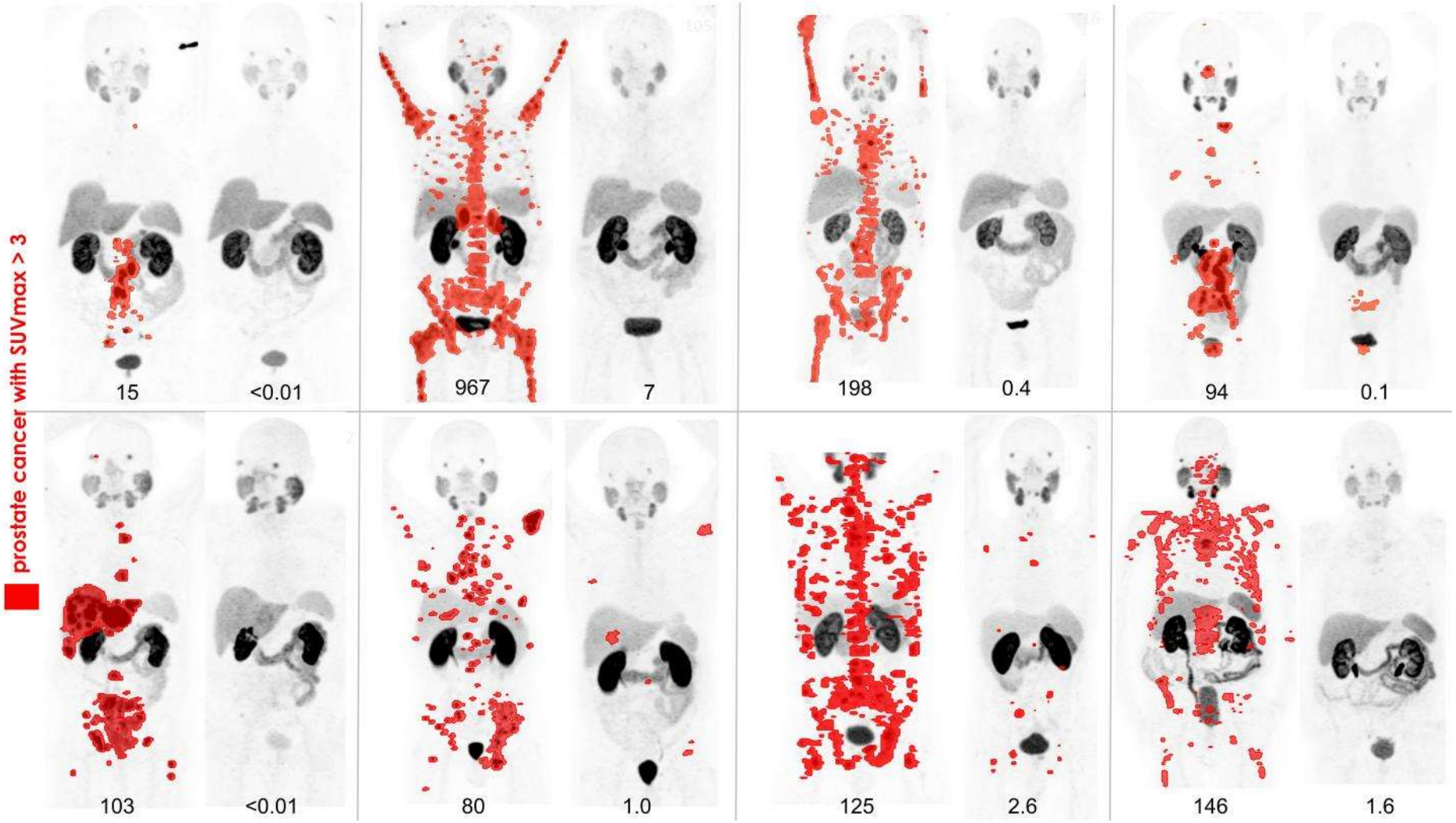


PSMA-Phenotyping

PSMA-ligand therapy

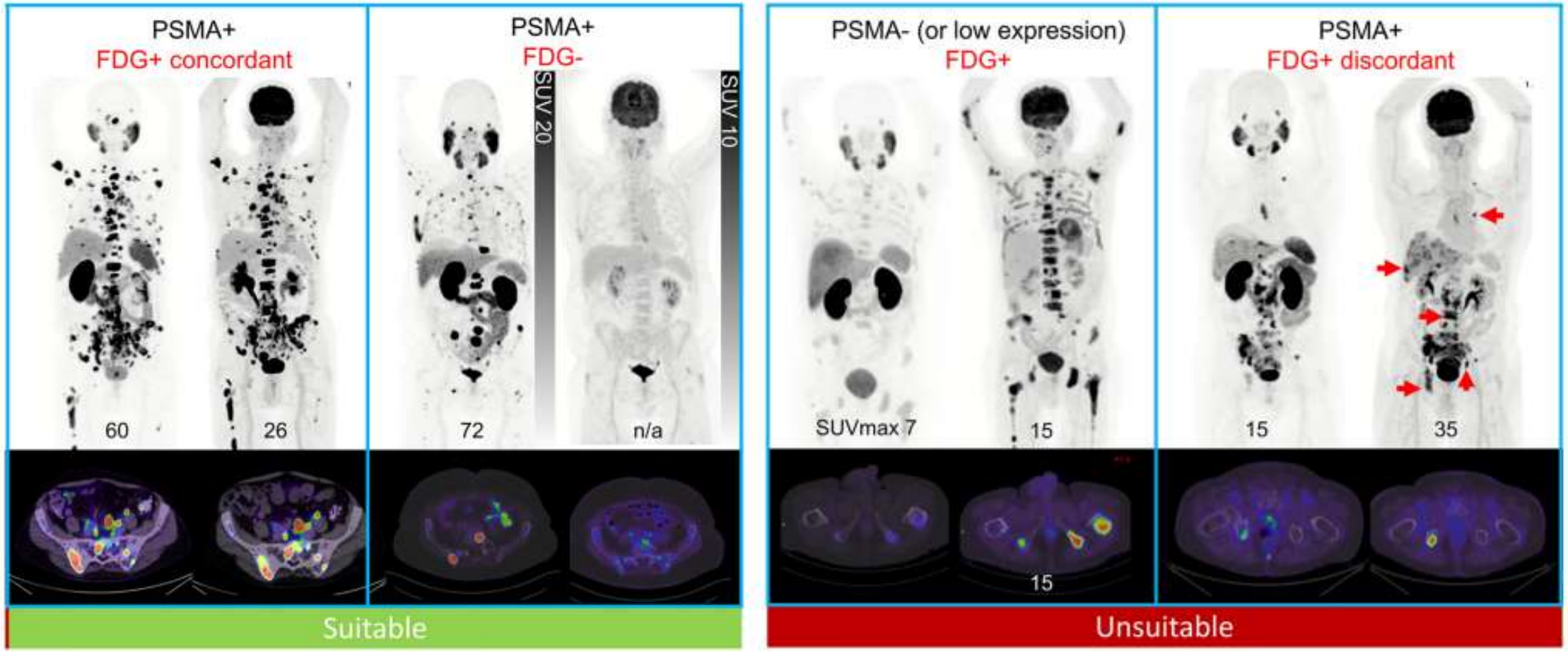


PSMA-ligand therapy



SNMMI Image-of-the-year 2018:
PSMA-Theranostik des fortgeschrittenen metastasierten Prostatakarzinoms

PSMA-ligand therapy



PSMA-ligand therapy

NOVARTIS

Search Menu

Home > News > Novartis Pluvicto™ approved by FDA as first targeted radioligand therapy for treatment of progressive, PSMA positive metastatic castration-resist ...

Novartis Pluvicto™ approved by FDA as first targeted radioligand therapy for treatment of progressive, PSMA positive metastatic castration-resistant prostate cancer

Mar 23, 2022

Ad hoc announcement pursuant to Art. 53 LR

- *FDA also approved complementary diagnostic imaging agent, Locametz®, after radiolabeling with gallium-68 for the identification of PSMA-positive lesions[2]*
- *Metastatic prostate cancer has a 5-year survival rate of less than 30%[3]; mCRPC patients who progress on multiple lines of therapy have limited treatment options*
- *FDA approval was based on pivotal Phase III VISION trial, where patients with pre-treated PSMA-positive mCRPC who received Pluvicto plus standard of care had a statistically significant reduction in risk of death[1]; both alternate primary endpoints of overall survival and radiographic progression free survival were met[1]*
- *Novartis is committed to reimagining medicine in prostate cancer with targeted radioligand therapy - a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)*

PSMA-ligand therapy

ORIGINAL ARTICLE

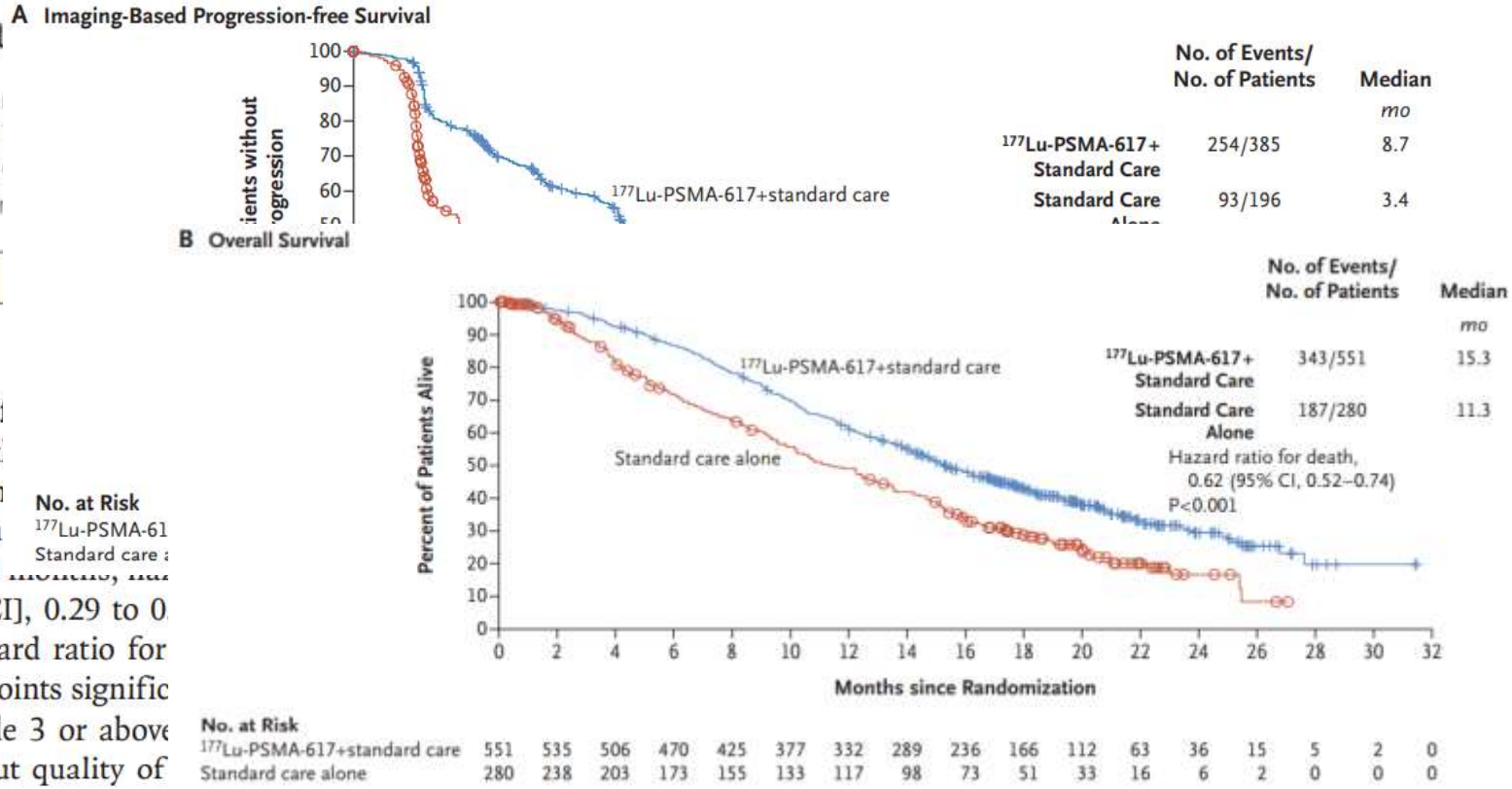
Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Ca

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahba
L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park,
A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan,
R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION I

ABSTRACT

RESULTS

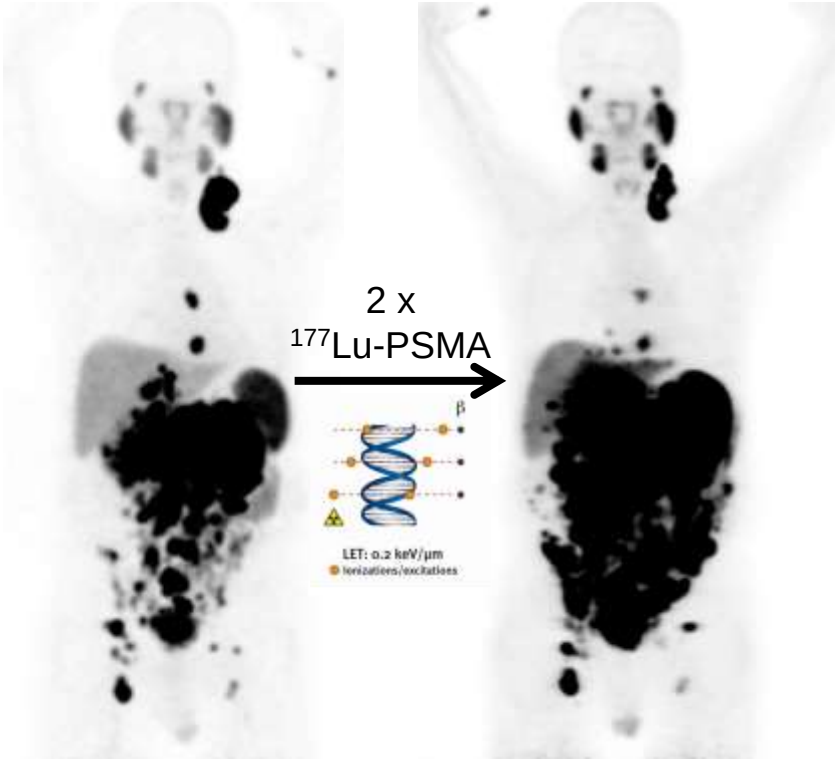
From June 2018 to mid-October 2019, a total of 831 o
underwent randomization. The baseline characteristics of t
between the groups. The median follow-up was 20.9 mon
standard care significantly prolonged, as compared with
aging-based progression-free survival (median, 8.7 vs. 3.4
progression or death, 0.40; 99.2% confidence interval [CI], 0.29 to 0
and overall survival (median, 15.3 vs. 11.3 months; hazard ratio for
95% CI, 0.52 to 0.74; P<0.001). All the key secondary end points signific
^{177}Lu-PSMA-617. The incidence of adverse events of grade 3 or above
with ^{177}Lu-PSMA-617 than without (52.7% vs. 38.0%), but quality of
adversely affected.



PSMA-Liganden Therapie

7.51	Evidenzbasierte Empfehlung	geprüft 2021
Empfehlungsgrad **0**	Für Patienten mit kastrationsresistenter, progredienter Erkrankung in gutem Allgemeinzustand kann nach Ausschöpfen der empfohlenen Therapieoptionen (siehe Empfehlung 7.46) ein Therapieversuch mit Lutetium-177-PSMA auf Basis der Empfehlung einer interdisziplinären Tumorkonferenz angeboten werden.	
Level of Evidence **3**	Literatur: [873]	
	Gesamtabstimmung: 93 %	

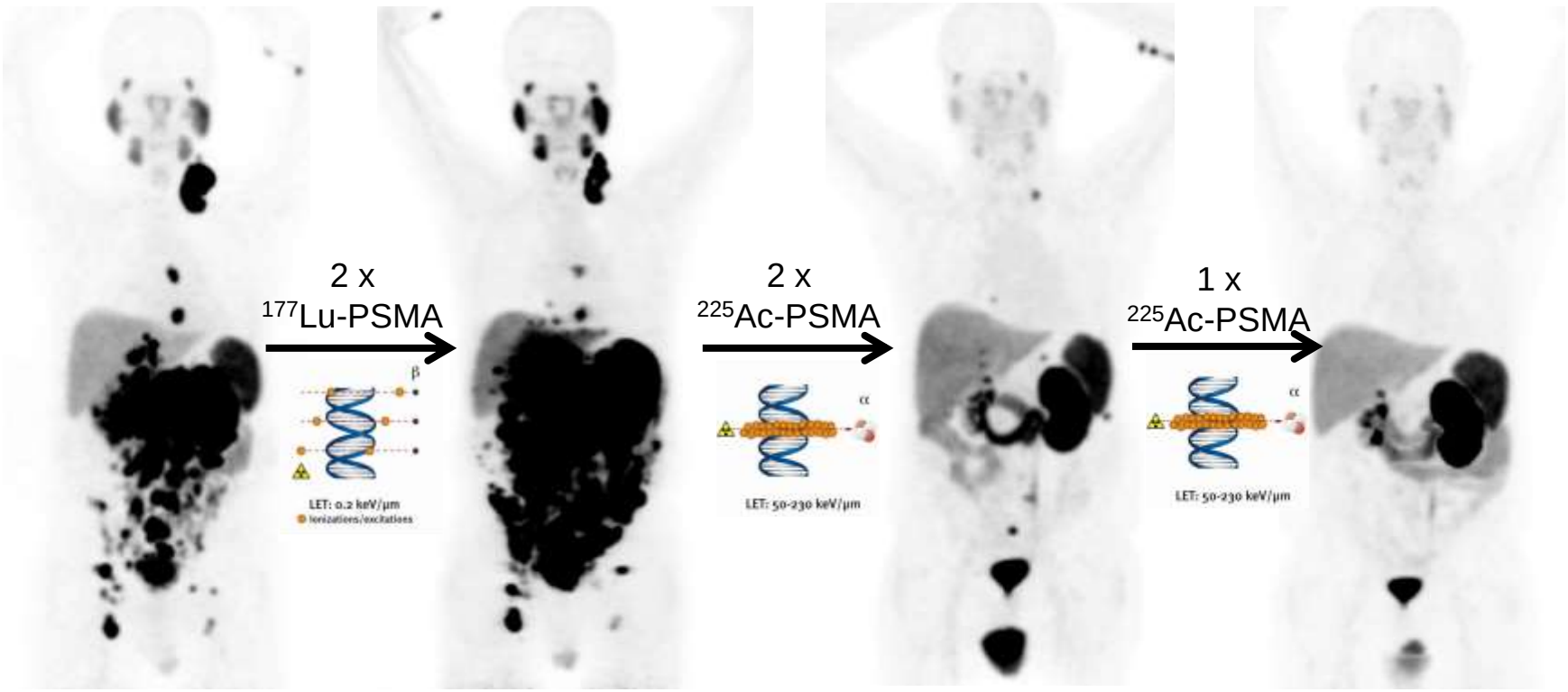
PSMA-ligand therapy (225Ac-PSMA)



6/2015
PSA = 294 ng/ml

9/2015
PSA = 419 ng/ml

PSMA-ligand therapy (225Ac-PSMA)



6/2015
PSA = 294 ng/ml

9/2015
PSA = 419 ng/ml

2/2016
PSA = 3.5 ng/ml

4/2016
PSA < 0.1 ng/ml

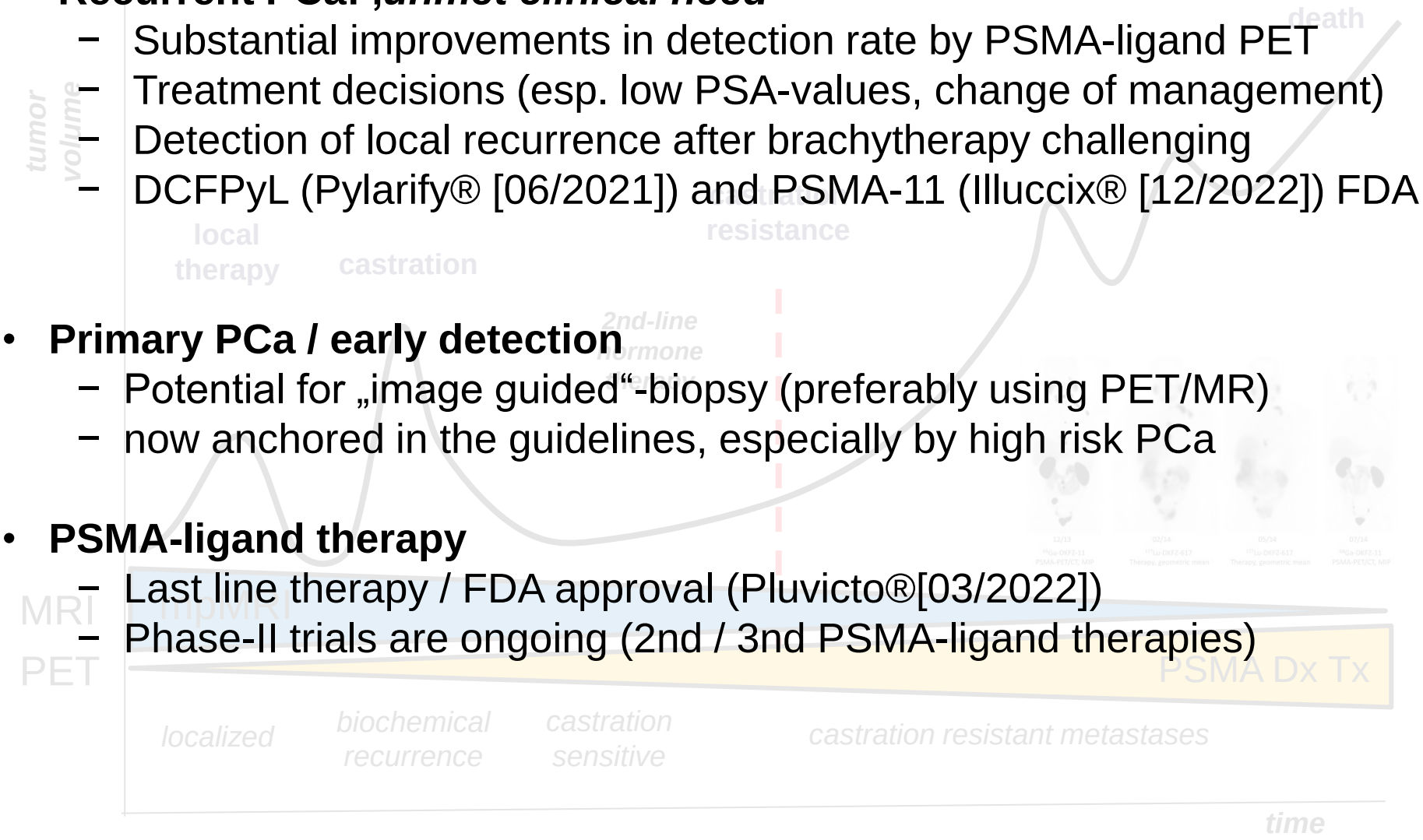
Kratochwil C et al.; JNM 2018

Summary

- **Recurrent PCa: ‚*unmet clinical need*‘**
  - Substantial improvements in detection rate by PSMA-ligand PET
  - Treatment decisions (esp. low PSA-values, change of management)
  - Detection of local recurrence after brachytherapy challenging
  - DCFPyL (Pylarify® [06/2021]) and PSMA-11 (Illuccix® [12/2022]) FDA approved

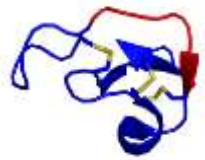
- **Primary PCa / early detection**
  - Potential for „image guided“-biopsy (preferably using PET/MR)
  - now anchored in the guidelines, especially by high risk PCa

- **PSMA-ligand therapy**
  - Last line therapy / FDA approval (Pluvicto®[03/2022])
  - Phase-II trials are ongoing (2nd / 3nd PSMA-ligand therapies)



Nuclear Medicine: Theranostics (Dx+Tx)

small molecules

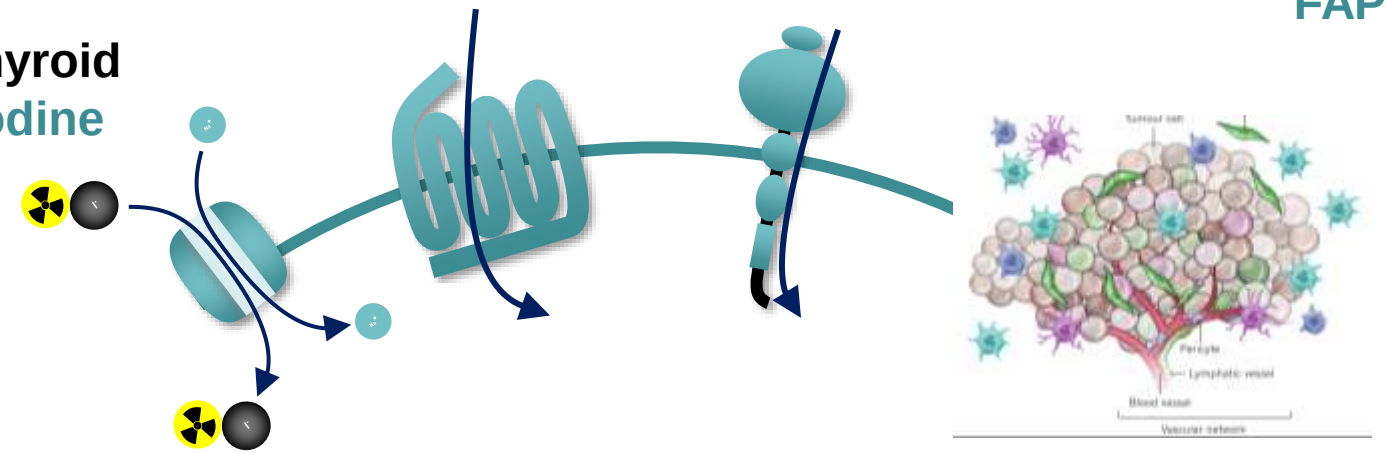


NET
DOTATOC

Prostate-Ca
PSMA

Pan-Tracer
FAPI

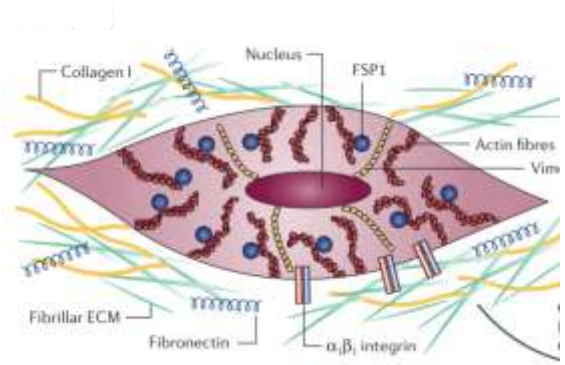
Thyroid
Iodine



specific intra-cellular accumulation
(endocytosis)

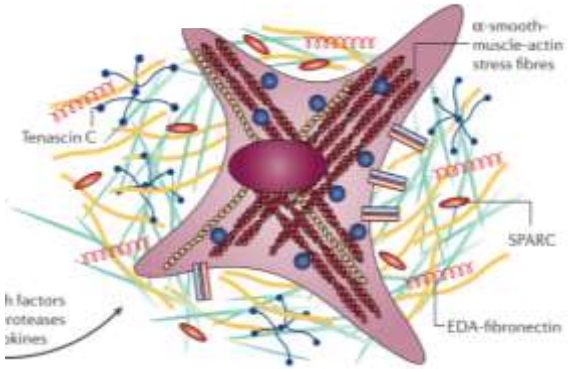
Cancer and Microenvironment

Normal Fibroblast



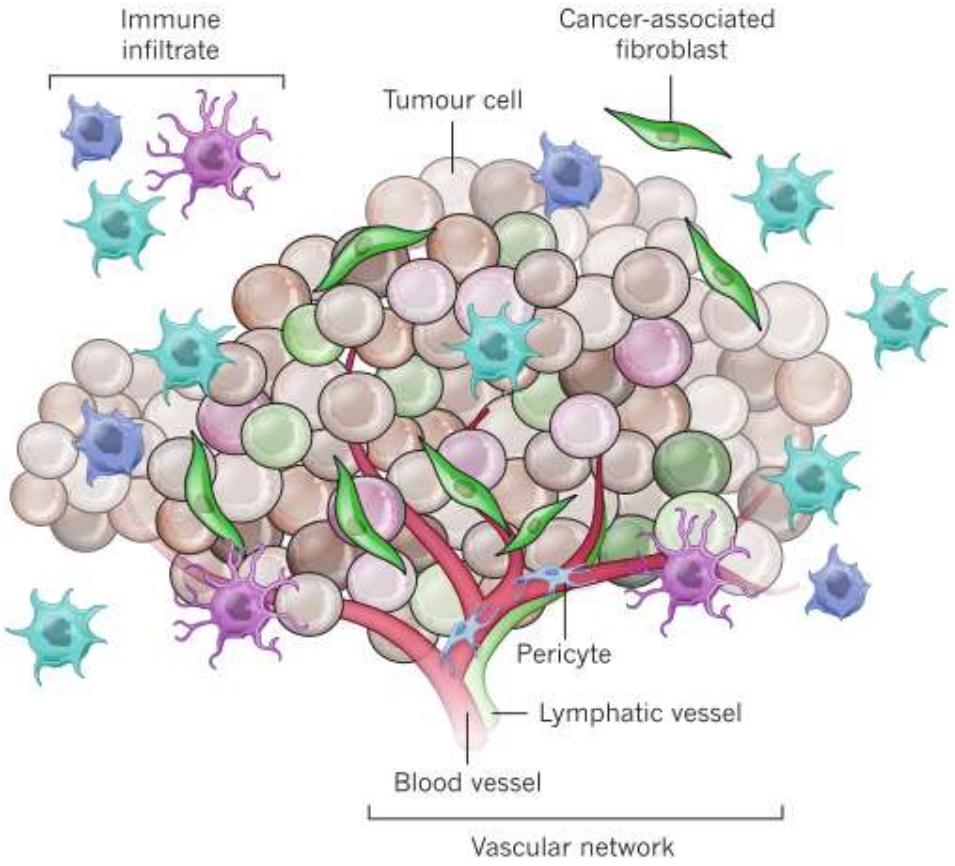
- connective tissue
- Support function by production of collagen
- wound healing

Caner associated fibroblast (CAF)



- changed structure
- increased collagen-I secretion
- support for the growth and metastasis of carcinomas

Cancer and Microenvironment
Cancer Associated Fibroblast (CAF)

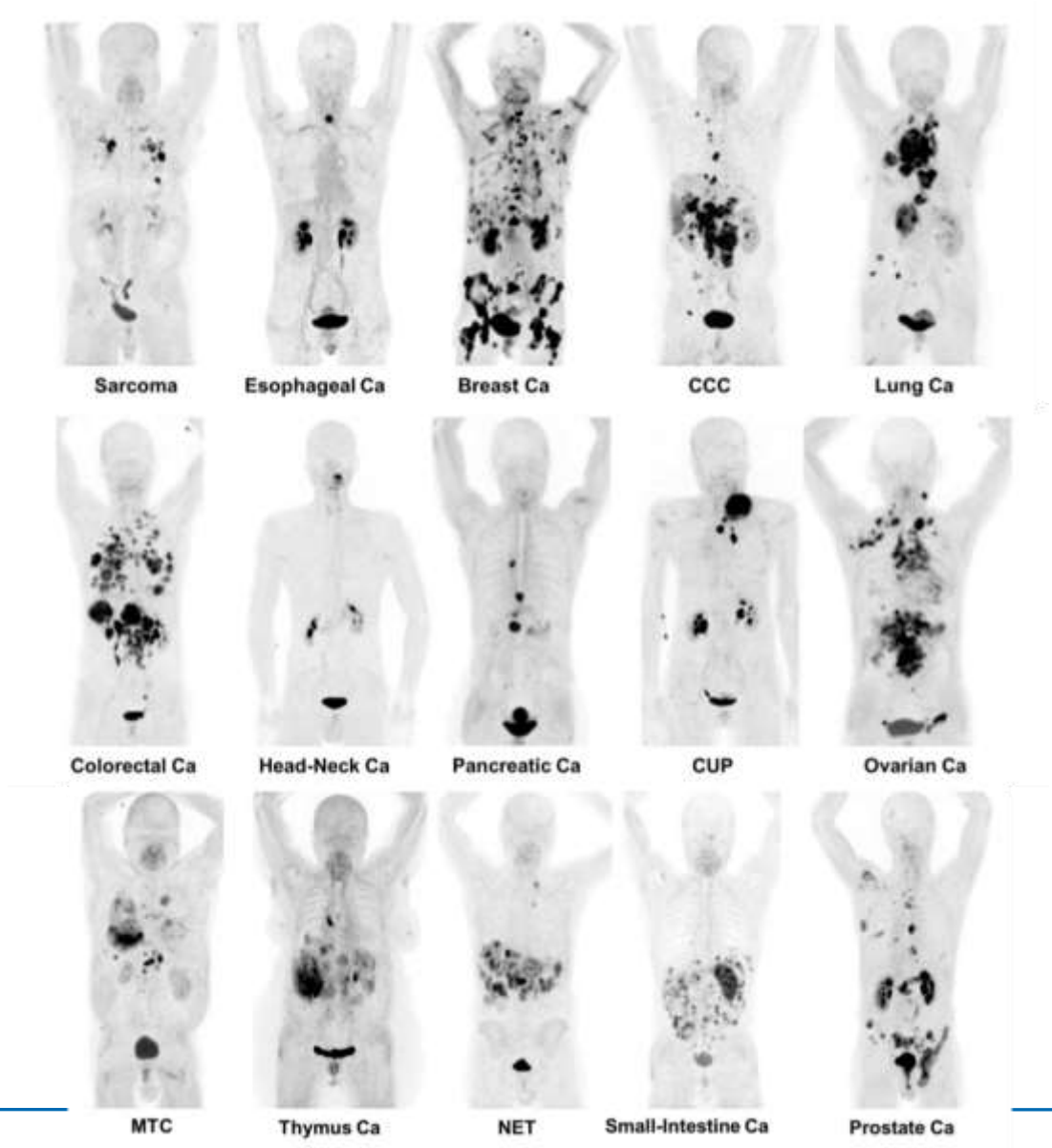


- tumor must have a certain size
- only then cancer-associated fibroblast are produced
- ~ 3 mm cell cluster

Juillerat-Jeanneret et al.; Expert Opinion on Therapeutic Targets 2017

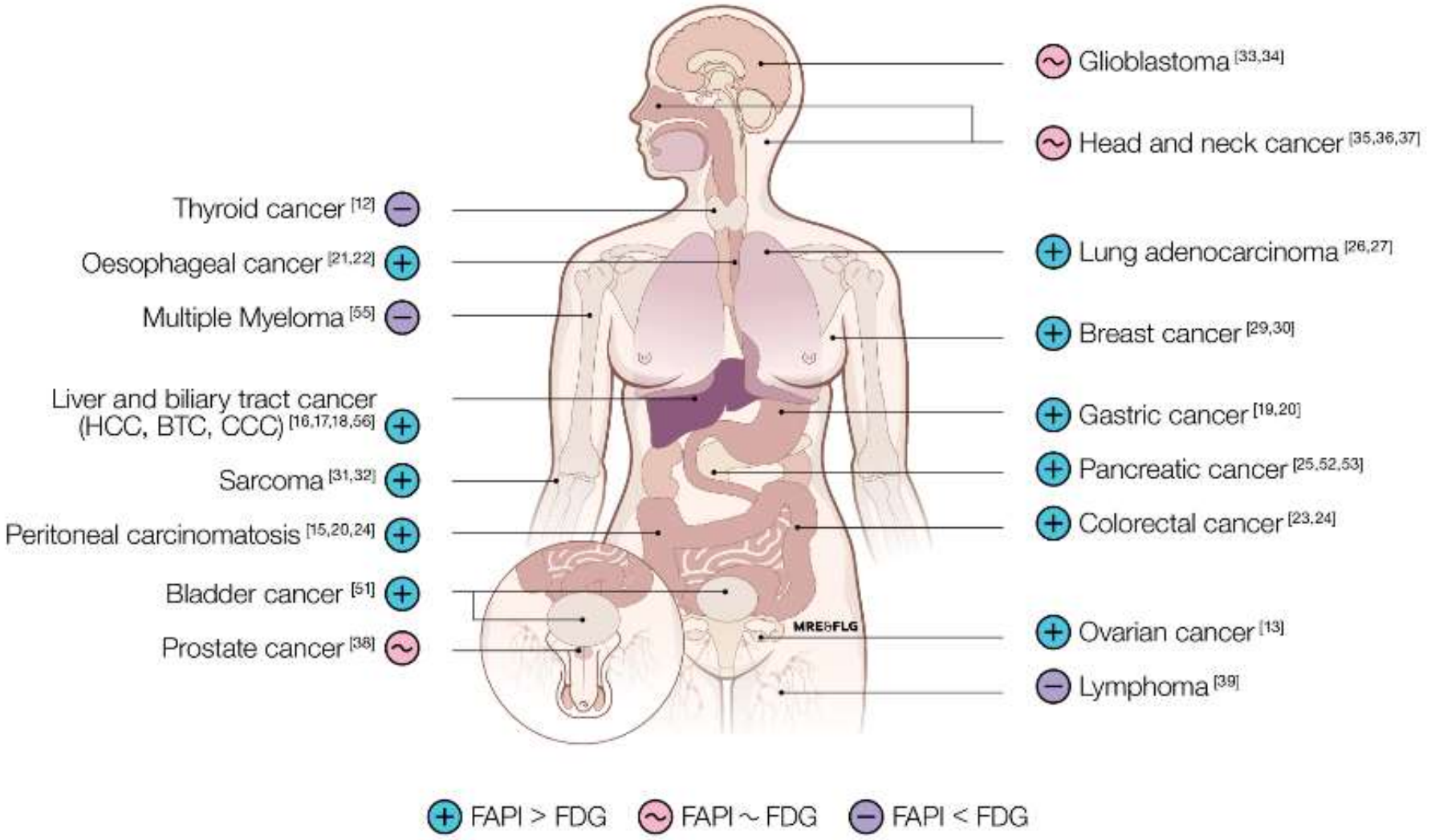
Cancer and Microenvironment

Cancer Associated Fibroblast (CAF)



FAPI- vs. FDG-PET

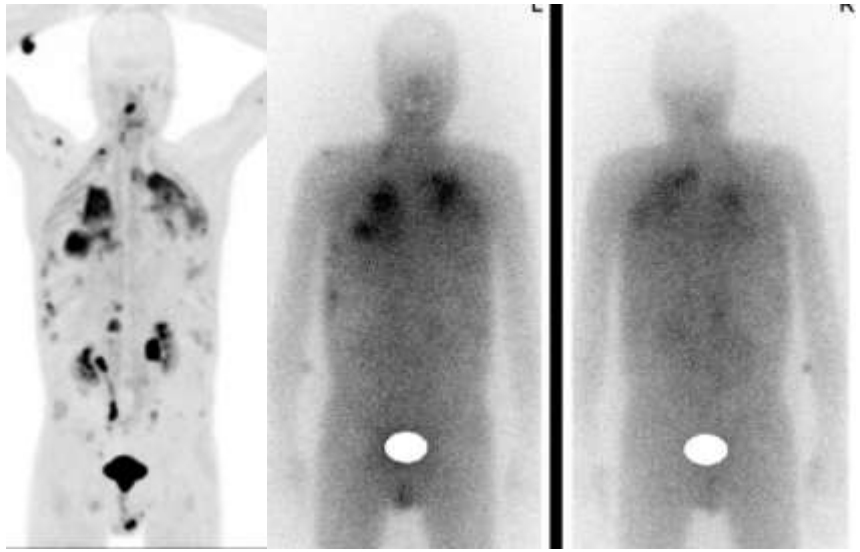
Head-to-Head comparison to FDG



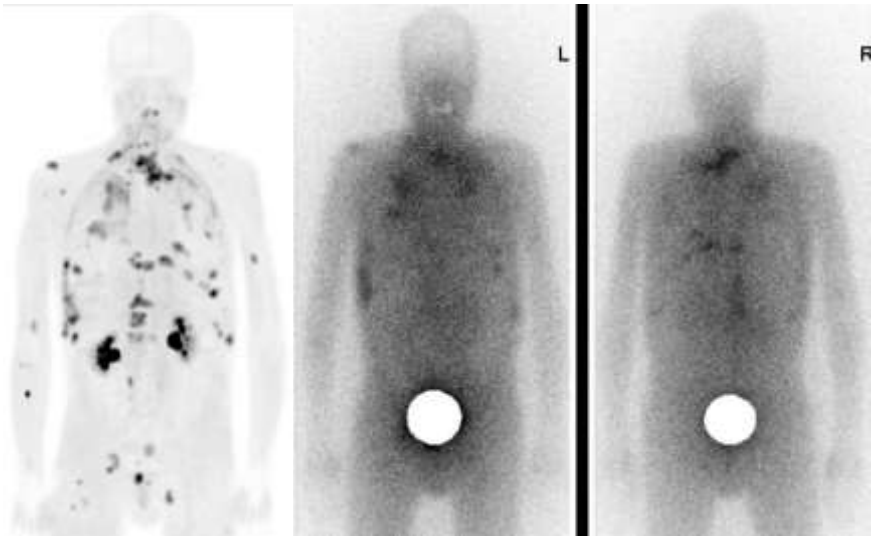
Mori et al., Radiology 2023

FAP Theranostics: FAPI-46

^{90}Y-FAPI-46 (Case HD)



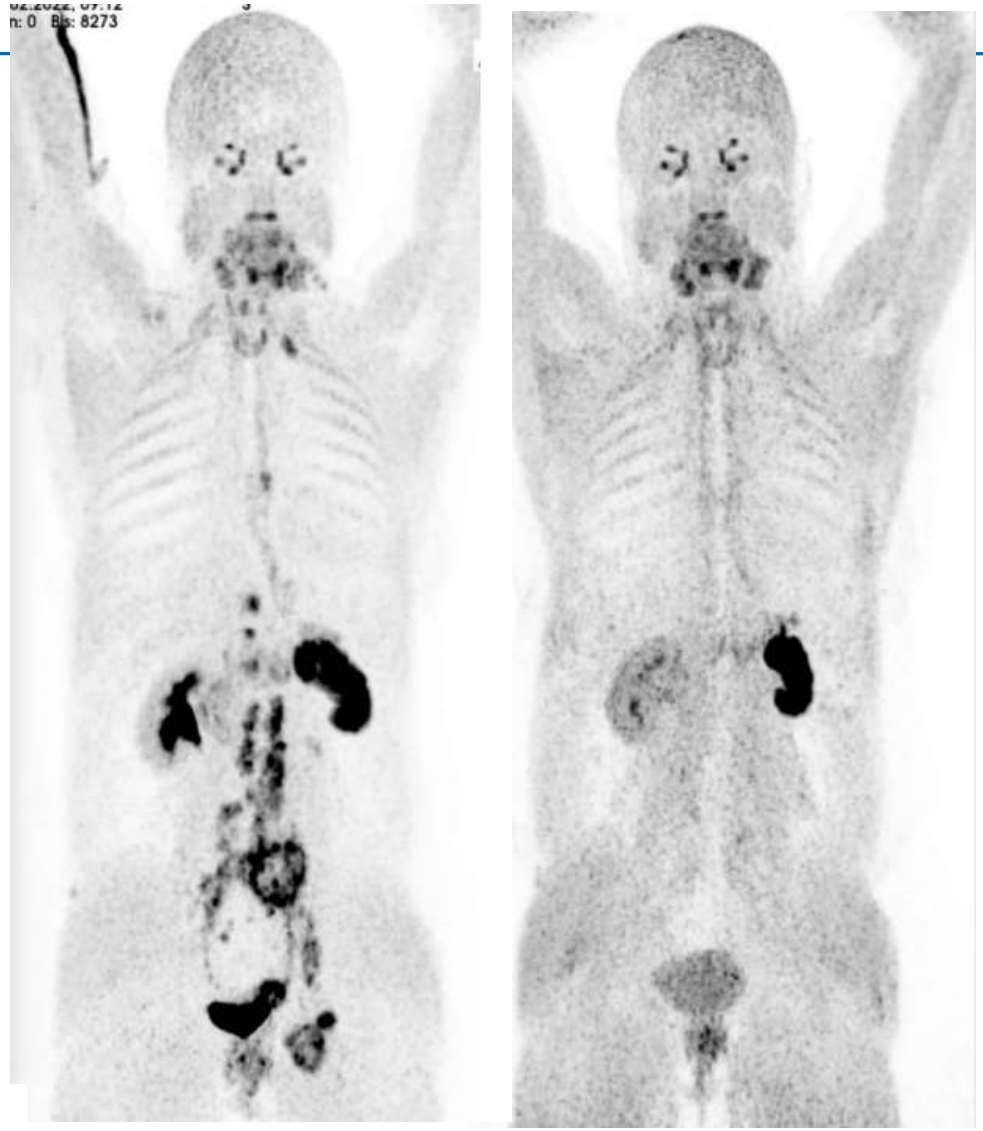
7,4 GBq ^{90}Y-FAPI-46



7,4 GBq ^{90}Y-FAPI-46

Tumor: NSCLC (Adeno-Ca)
History Tx: Carboplatin/Pemetrexed/Pembrolizumab,
Docetaxel/Pembrolizumab, FAPI/Pembrolizumab

FAP Theranostics: 3BP-3940 FAP



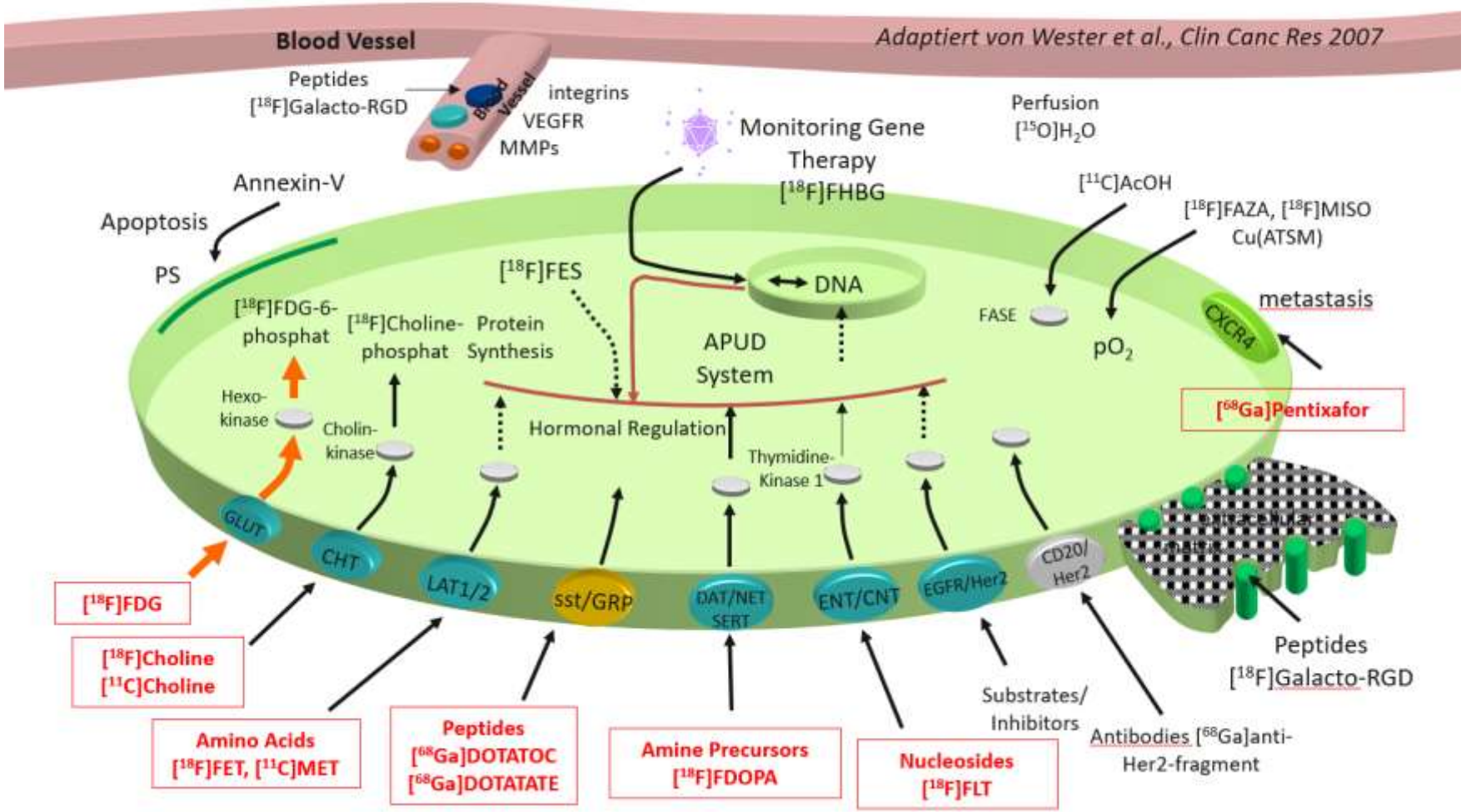
Ovarian Cancer

Baseline (right) and 8 months follow-up (left)

^{68}Ga-3BP-3940 FAP MIP images

Courtesy: R. Baum

Molecular Targets / many-to-come



DOTATOC, PSMA, CXCR4, FAPI, LAT1…



Vielen Dank für Ihre Aufmerksamkeit