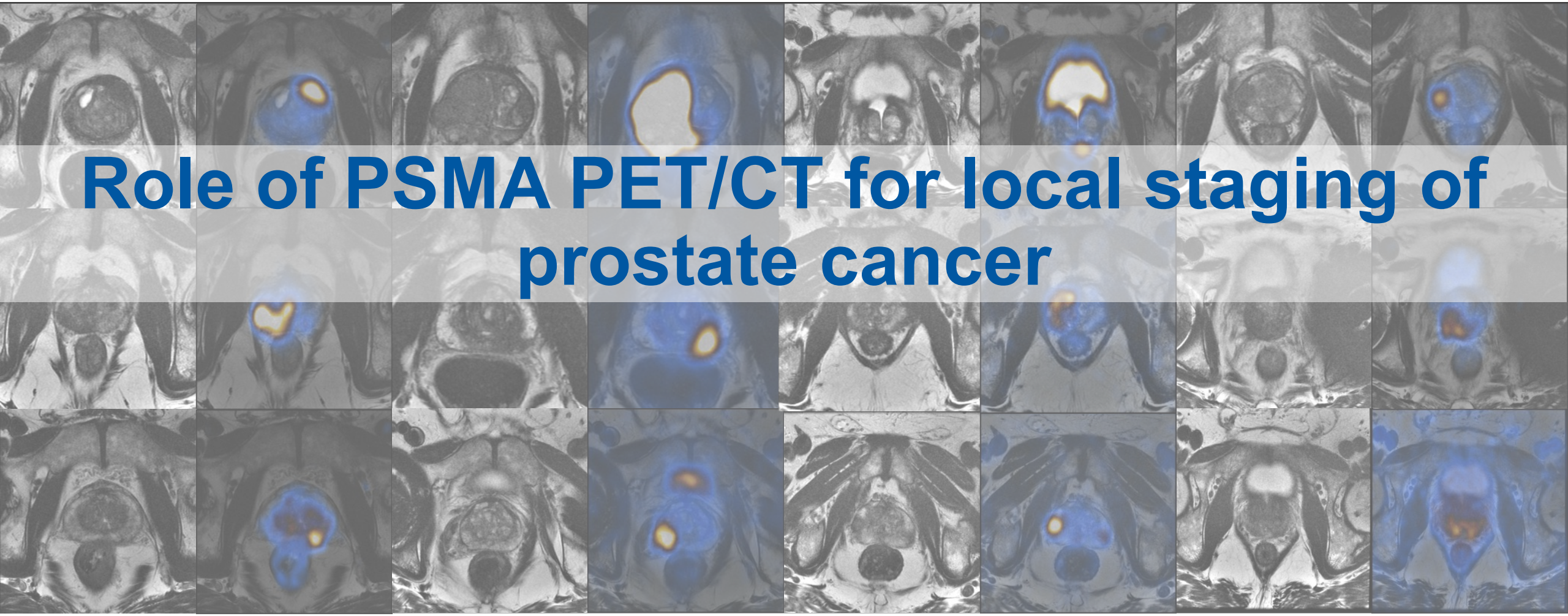
Role of PSMA PET/CT for local staging of prostate cancer



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Disclosure

Advisory role (compensated, institutional):

GE-Healthcare, AAA (Novartis), Merck & Cie, Ratio Radiotherapeutics

Research support (institutional):

GE-Healthcare, Bayer

Travel support:

GE-Healthcare, Bayer

Speakers Bureau (compensated, institutional):

GE-Healthcare, Bayer, Astellas, Janssen, AAA (Novartis)

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Agenda

1. PSMA PET for staging high risk prostate cancer
   - Indication & Accuracy:
     - Lymph node metastasis
     - Bone metastasis
2. PSMA PET tracer heterogeneity
3. PSMA and prostate cancer heterogeneity

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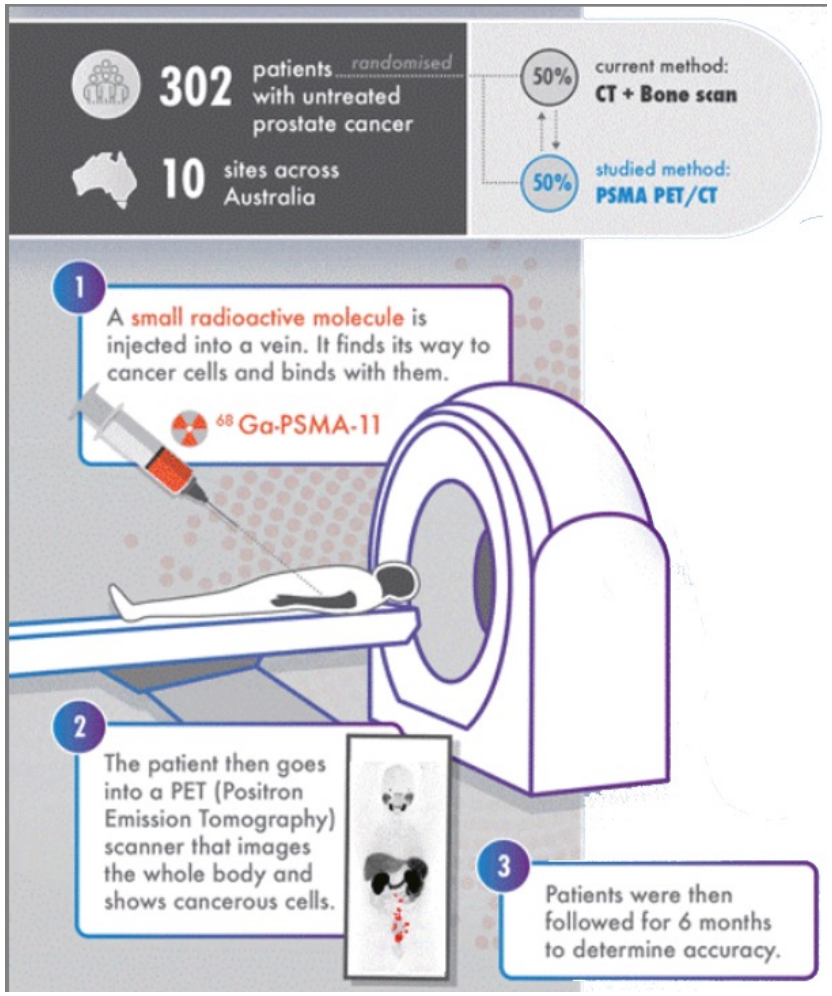
1) PSMA Staging: Indication



Positron-Emissi-onsTomographie (PET, PET/CT)	**Ja**	**f) Mittels PSMA-PET, nur bei folgenden Indikationen:**	**01.01.2019/**
		Zum primären Staging eines neudiagnostizierten nicht-metastasierten Prostatakarzinoms in den Risikokategorien: – Intermediate risk (PSA 10 – 20 ng/ml oder Gleason-Score 7 oder cT-Kategorie 2b) – High-risk (PSA > 20 ng/ml oder Gleason Score > 7 oder cT-Kategorie 2c)	**01.01.2021**
	GS 7	Zum Restaging bei biochemisch nachgewiesenem Rezidiv (PSA-Anstieg) eines Prostatakarzinoms.	

Hofman et al. Lancet. 2020 Apr 11;395(10231):1208-1216.

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1) PSMA Staging: Indication

GS 7a, PSA < 20, <cT3?

13 patients of 116 had a 5 GS 6 (0 with N+) or 8 7a (1 with N+ (PSA 15))

Lymph node Bone Soft tissue Change in Management

Article

Comparison of Multiparametric MRI, [^{68}Ga]Ga-PSMA-11 PET-CT, and Clinical Nomograms for Primary T and N Staging of Intermediate-to-High-Risk Prostate Cancer

Omar Marek Tayara [1,*], Kacper Pełka [2,3], Jolanta Kunikowska [2], Wojciech Malewski [1], Katarzyna Sklinda [4,5], Hubert Kamecki [1], Sławomir Poletajew [1], Piotr Kryst [1] and Łukasz Nyk [1]

6 of 82 patients had a GS 7a (1 with N+)

Risk

D'Amico score (n=116) PSA level (n=116) AJCC TNM staging groups (n=111)

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Ferraro DA et al. Eur J Nucl Med Mol Imaging. 2020 Mar;47(3):652-664.

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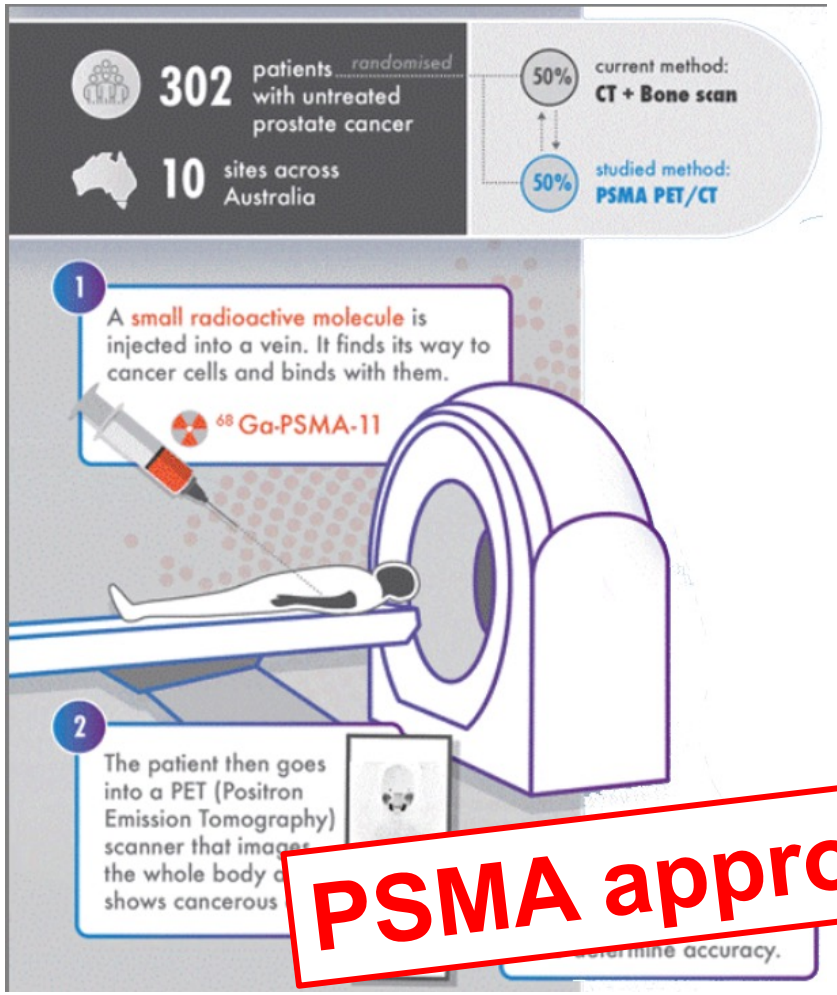
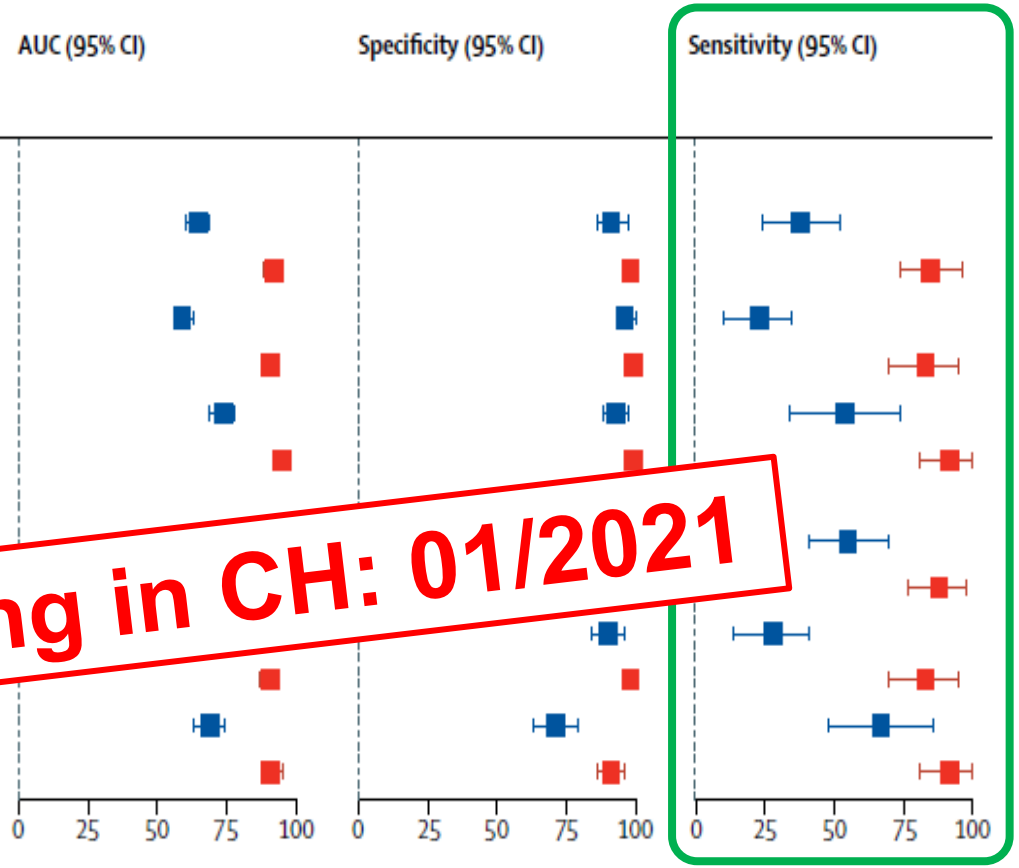
1) PSMA Staging: Indication – proPSMA



Modified D'Amico: High risk features ≥ ISUP 3 (4+3)
PSA ≥ 20 ng/ml or Local ≥ cT3

	N	Positive True/False	Negative True/False
Primary analysis			
Any metastatic disease	150	18/9	94/29
	145	34/2	103/6
Pelvic nodal	150	9/4	106/31
	145	29/1	109/6
Distant metasases	150	13/9	117/11
	145	22/1	120/2
Sensitivity analysis: equivocal lesions treated as positive			
Any metastatic disease	150	26/35	68/21
	145		
	150	16/37	89/8
	145	22/11	110/2



PSMA approved for staging in CH: 01/2021

Hofman et al. Lancet. 2020 Apr 11;395(10231):1208-1216.

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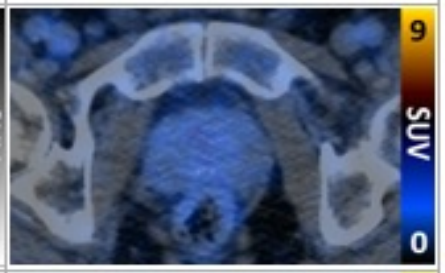
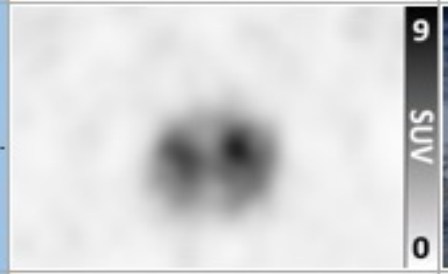
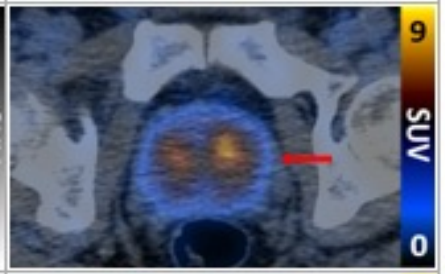
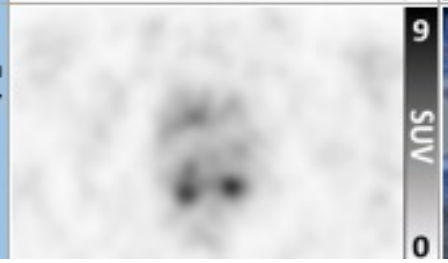
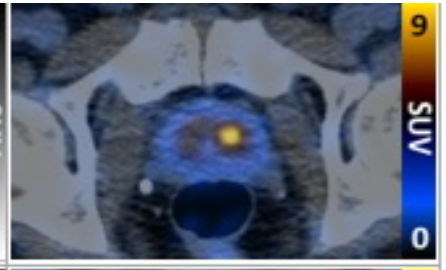
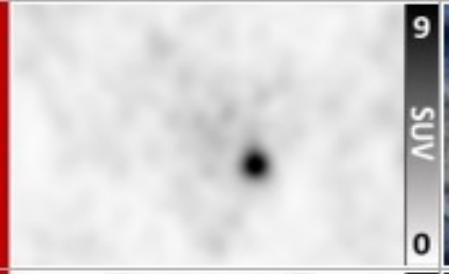
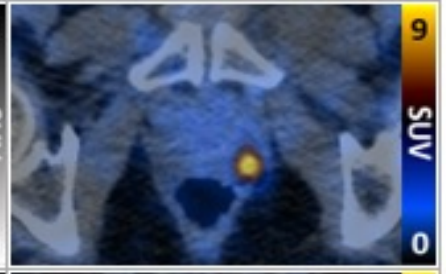
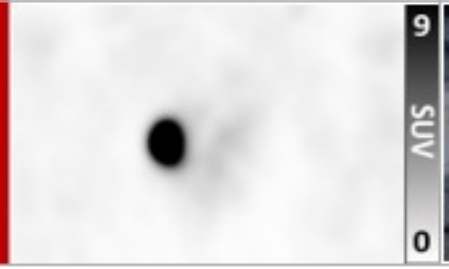
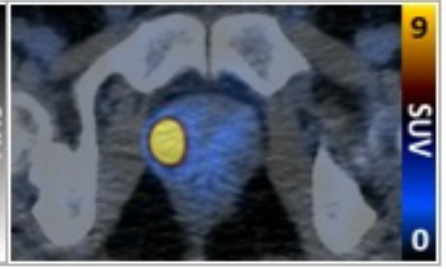
1) PSMA Staging: How to read

PRIMARY SCORE	PET	PET/CT
1: No pattern. Low grade activity only.		
2: Diffuse TZ activity, sparing the prostate peripheral margin on fused PET/CT (red arrow). This pattern can have moderate variation in TZ intensity.		
2: CZ activity. Frequently symmetrical. This pattern is classified as a PRIMARY score 4 if it extends to the prostate peripheral margin on fused PET/CT		

PRIMARY SCORE	PET	PET/CT
3: Focal TZ activity. Focal activity well above background TZ activity (at least twice background TZ).		
4 : Focal PZ activity. Any activity involving the peripheral prostate margin on fused PET/CT or apically (no minimum intensity)		
5: Intense uptake SUVmax >12		

Emmett et al. JNM (2022) 63(11):1644–1650

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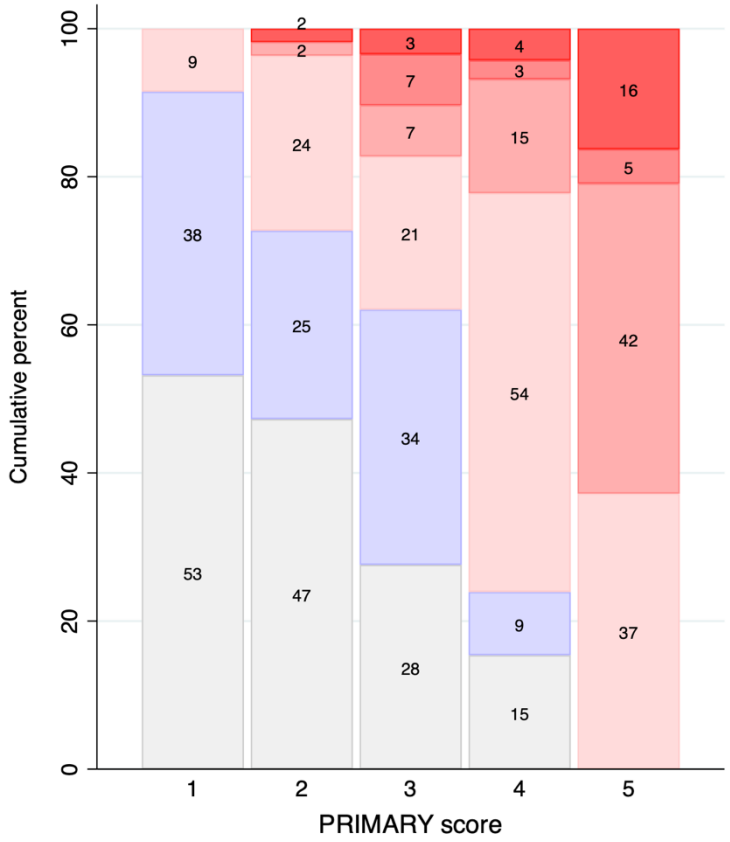
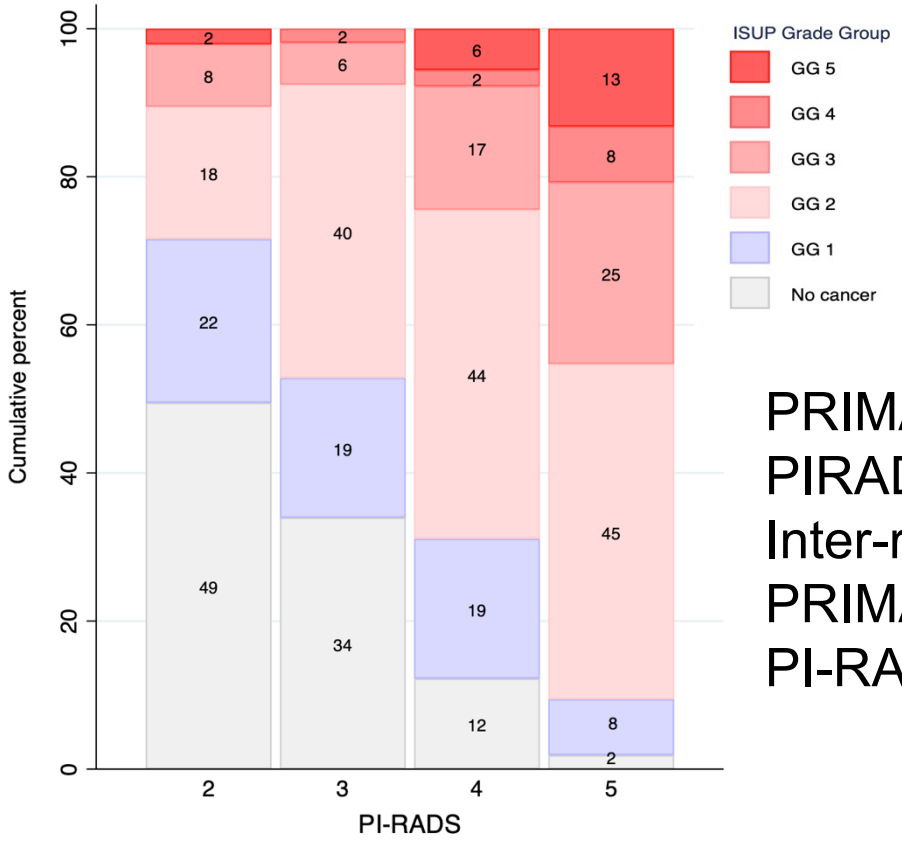
1) PSMA Staging: PCa detection – PSMA vs mpMRI

291 man with suspected PCa - biopsy naïve:

PSMA - PRIMARY



mpMRI - PIRADS



PRIMARY: Sens 88%, Spec 64%,
PIRADS: Sens 83%, Spec 53%,
Inter-rater reliability:
PRIMARY scale (κ=0.70)
PI-RADS (κ=0.58)

Emmett et al. JNM (2022) 63(11):1644–1650

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1) PSMA Staging: Accuracy lymph nodes – still not perfect

USZ: 60 pat. with RPE and PSMA PET

- 12 (20%) had nodal disease, 7 positive on PET **(58%)**
- All lymph nodes missed were smaller than 4 mm

Maurer et al., 130 patients:

- LN metastases in 30% (36/119) pts.
- 9 FN: mean size 3±1mm (range: 1-5mm)

	Patient based	LN fields based
Morphological		
% Sensitivity	43.9	28.2
% Specificity	85.4	97.1
% Accuracy	72.3	86.1
% PPV	58.1	64.7
% NPV	76.8	87.7
PSMA-PET		
% Sensitivity	**65.9**	73.5
% Specificity	98.9	99.2
% Accuracy	88.5	95.1
% PPV	96.4	94.5
% NPV	86.3	95.2

59 y.o. man.: Biopsy GS 4+3, PSA 35, => LN risk 10%

Maurer et al. The J of Urol. 2016;195:1436-1443.

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USZ

1) PSMA Staging: Accuracy lymph nodes: PSMA = classical nomograms

One-Stop-Shop Whole-Body ^{68}Ga-PSMA-11 PET/MRI Compared with Clinical Nomograms for Preoperative T and N Staging of High-Risk Prostate Cancer

Mark Thalgott[1], Charlotte Düwel[1], Isabel Rauscher[2], Matthias M. Heck[1], Bernhard Haller[3], Andrei Gafita[2], Jürgen E. Gschwend[1], Markus Schwaiger[2], Tobias Maurer[1], and Matthias Eiber[2,4]

Site	Prediction device	Sensitivity	Specificity	PPV	NPV	AUC (95% CI)	Significance P^*	Pairwise comparison (P)
LNM	^{68}Ga-PSMA-11 PET/MRI	60%	100%	100%	82.8%	0.8 (0.68–0.93)	<0.001	0.67
	MSKCC nomogram, cut-off > 48.5%	68%	83.3%	68%	83.3%	0.77 (0.66–0.89)	<0.001	0.86
	Partin tables, cut-off > 19%	60%	75%	55.6%	78.2%	0.67 (0.53–0.80)	0.022	

Maurer et al. The J of Urol. 2016;195:1436-1443.

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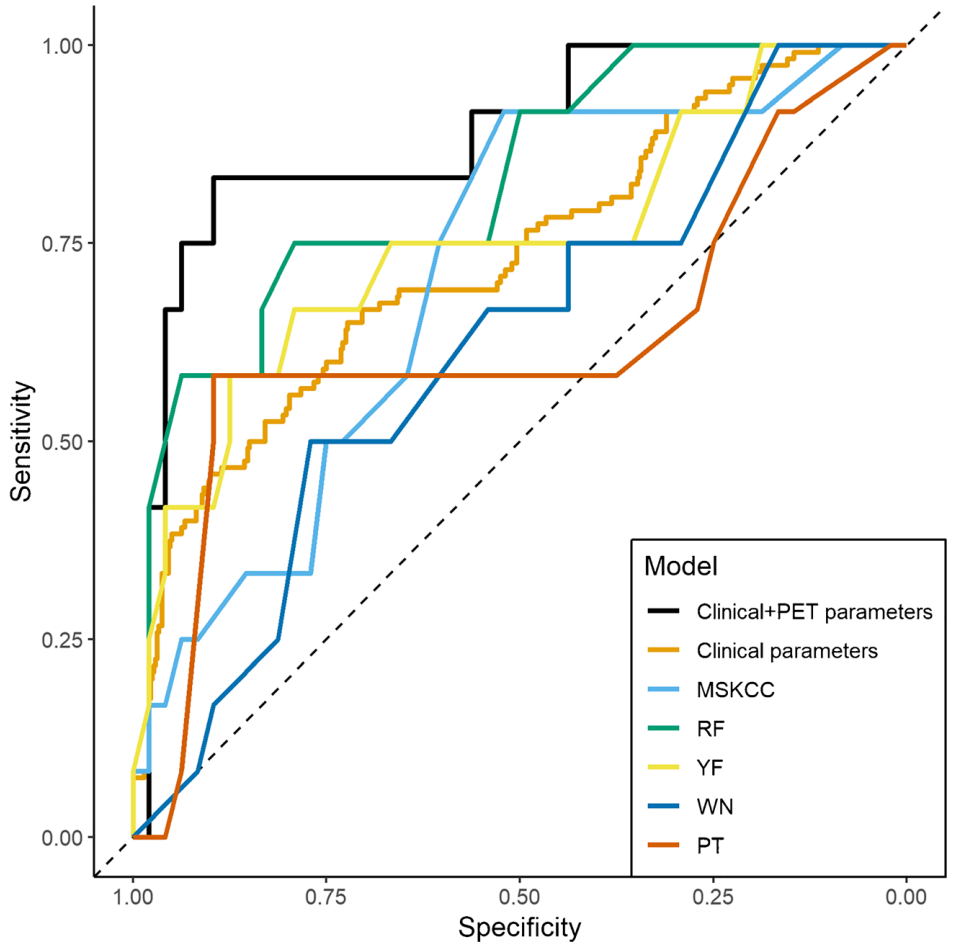
1) PSMA Staging: Lymph nodes – can PSMA improve the nomograms?

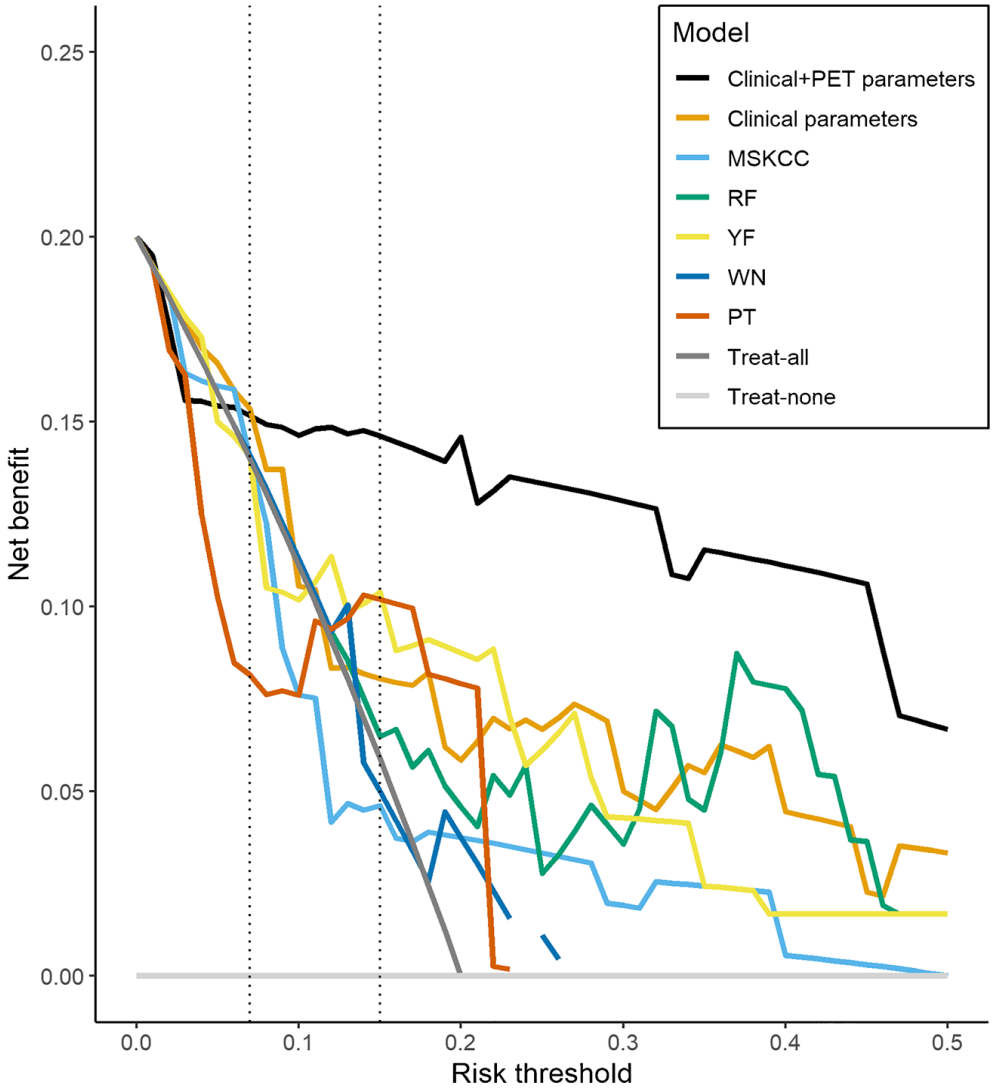
Ferraro DA et al. EJNMMI. 2020 Jan;47(1):147-159.

USZ: 60 patients with RPE and PSMA PET 04/16-08/18

- Visual analysis 7 of 12 positive on PET **(58%)**
- Best marker to predict nodal involvement: **$PSMA_{total}$**



Decision curve analysis:



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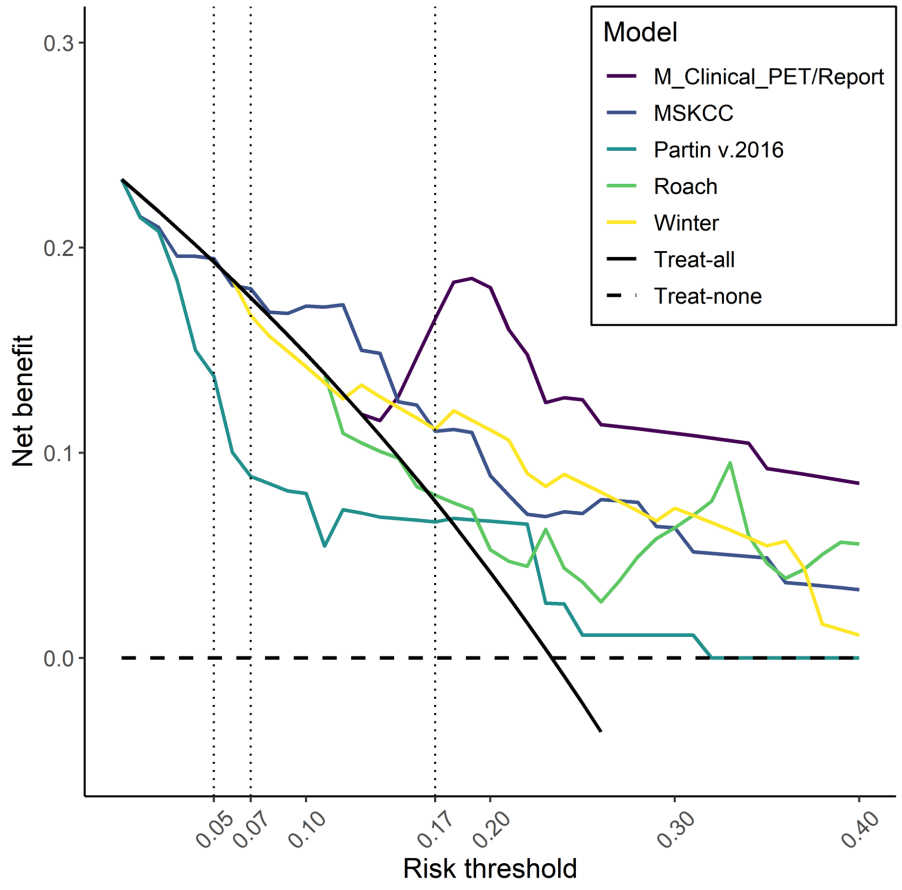
1) PSMA Staging: Lymph nodes – can PSMA improve the nomograms?

Development cohort (TUM): 159 patients with PRF and PSMA PET
Validation cohort: 90 patients with RPE and PSMA PET 04/16-07/19

An «ensamble modle» incorporating the LN read out and quant. parameters:



Model	AUC (95%-CI)
MSKCC	0.824 (0.710-0.938)
Partin	0.644 (0.505-0.783)
Roach	0.700 (0.548-0.852)
Winter	0.720 (0.590-0.851)
Model_PET/Report	**0.923 (0.863-0.984)**

Muehlematter et al. EJNMMI 2023 Aug;50(10):3137-3146.

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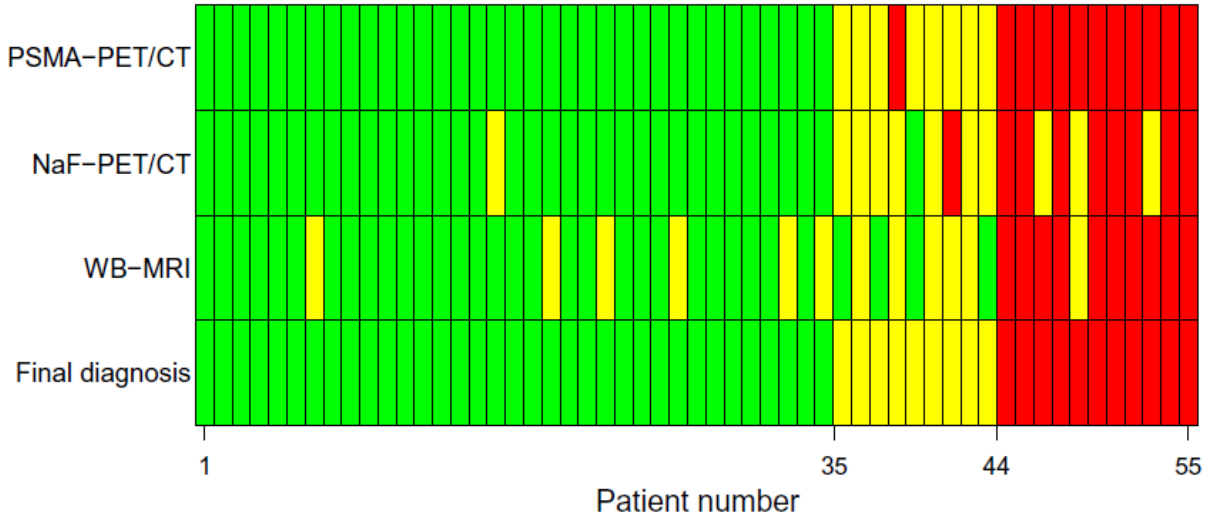
1) PSMA staging: Accuracy bone metastasis

55 patients: (mean PSA 87 ng/ml, range 5.0-1000 ng/ml)

	PSMA-PET/CT	NaF-PET/CT	WB-MRI
True positive results	20 (36%)	19 (35%)	16 (29%)
False positive results	0 (0%)	1 (2%)	6 (11%)
True negative results	35 (64%)	34 (62%)	29 (53%)
False negative results	0 (0%)	1 (2%)	4 (7%)

Green: no mets
Yellow: 1-5 mets
Red: >5 mets



Conclusion: The overall accuracy of ^{68}Ga-PSMA-11 PET/CT was significantly more advantageous compared to WB-MRI, but not to NaF-PET/CT.

Dyrbert et al. Eur Rad, March 2019, 29 (1221-1230)

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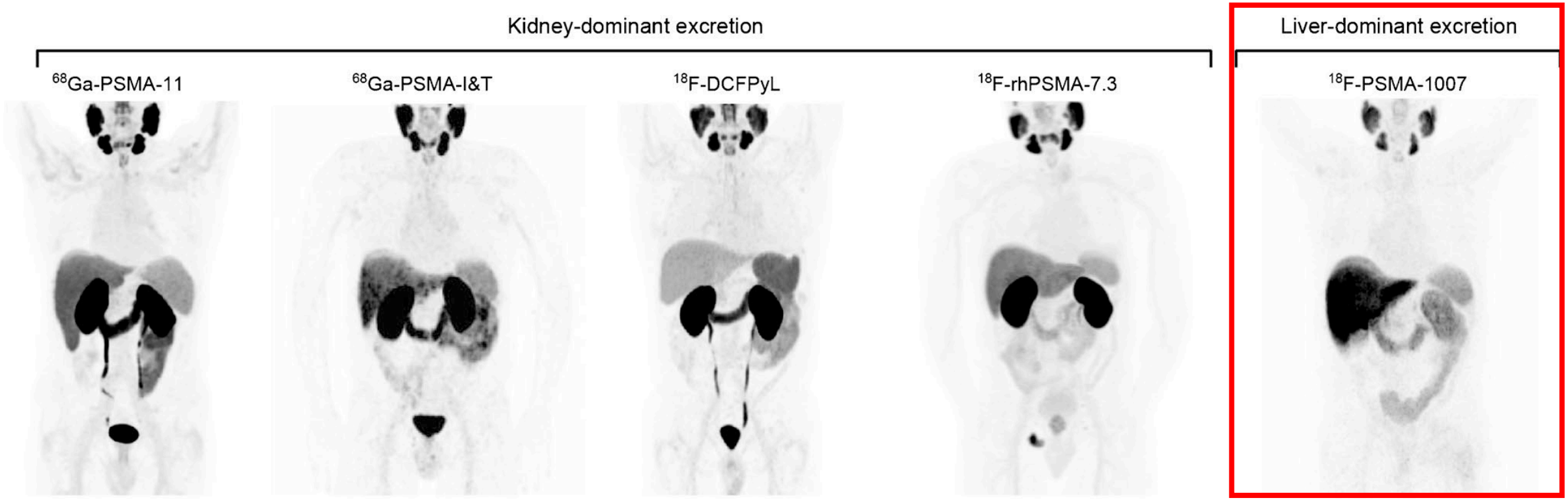
2) PSMA PET tracer heterogeneity

How to deal with different tracers?



Fendler et al. PSMA guideline 2.0 Eur J Nucl Med Mol Imaging. 2023 Jan

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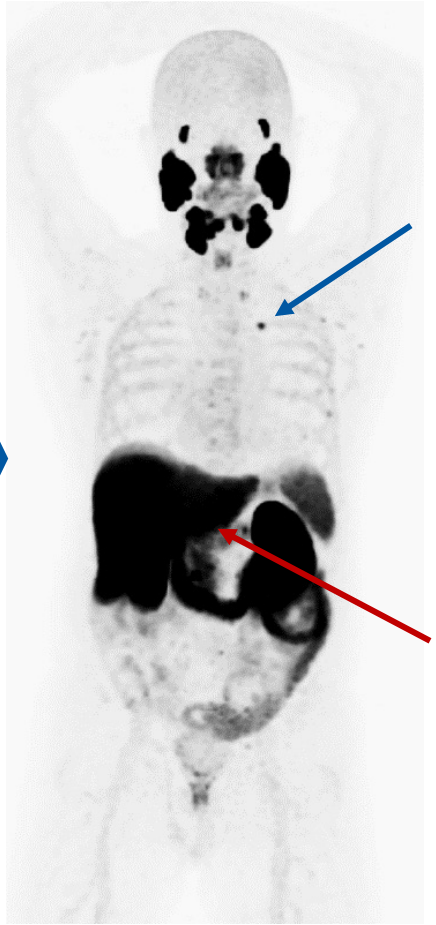
2) PSMA PET tracer heterogeneity: bone

^{68}Ga-PSMA-11

S-RT

^{18}F-PSMA-1007



2017: 70 y.o. man PSA 3.8 ng/ml with CRPCA – oligo M1 (bone)

2020: 72 y.o. man PSA 1.0 ng/ml with CRPCA – oligo M1?

PSA drop to 0.2 ng/ml for almost 2 years…

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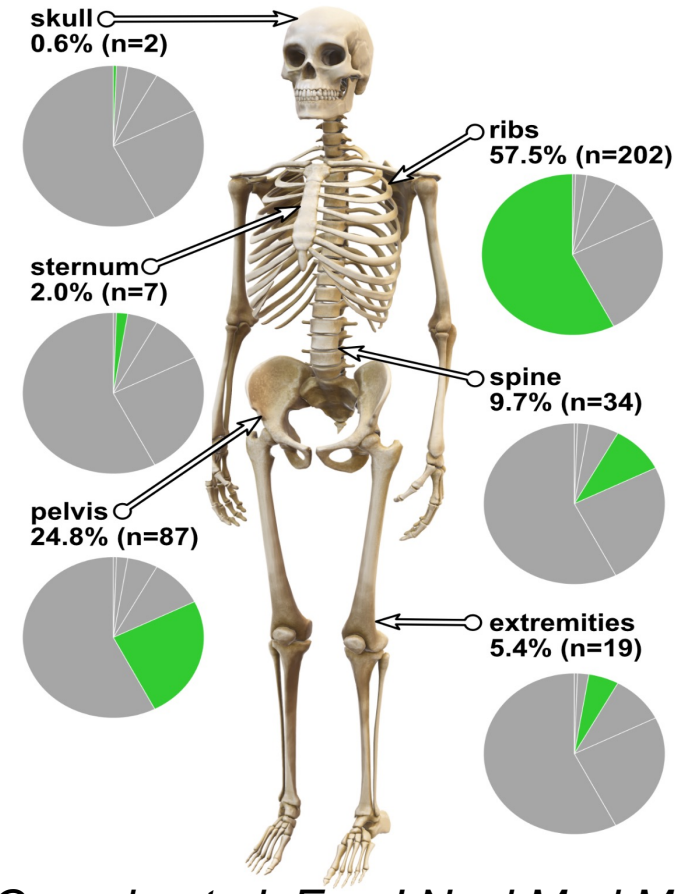
2) PSMA PET tracer heterogeneity: bone

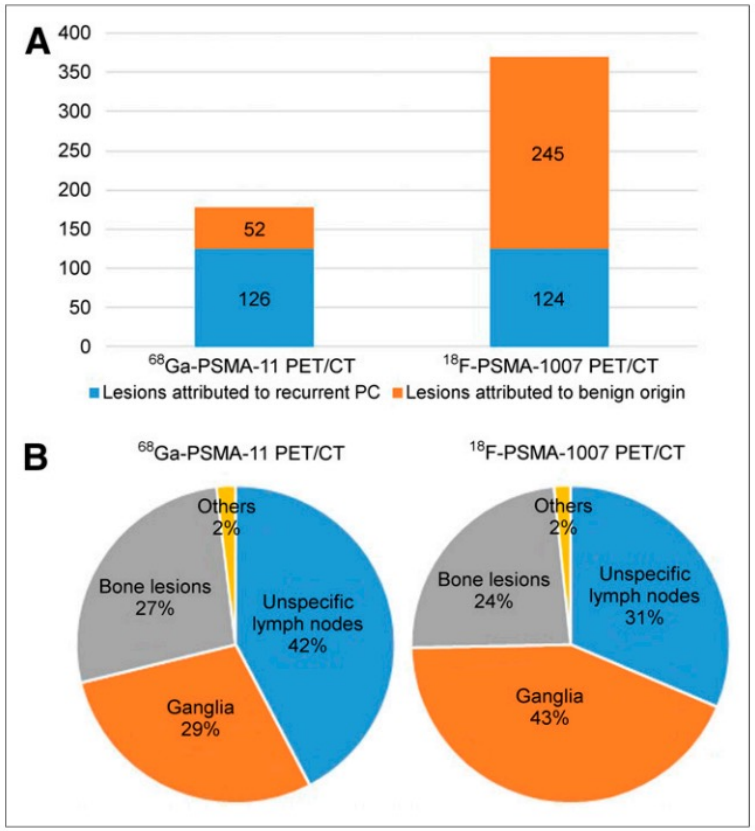
UBUs (unclear uptake with an SUV_{max}<10)
179 out of 348 patients (51.4%), and in 44.7% considered clinically relevant.



Gruenig et al. Eur J Nucl Med Mol Imaging. 2021 Dec;48(13):4483-4494.

Matched pair analysis (18F- vs. 68Ga)

- each 102 patients
- **245 vs. 52 unspecific lesions**



Rauscher I, et al, JNM 2020

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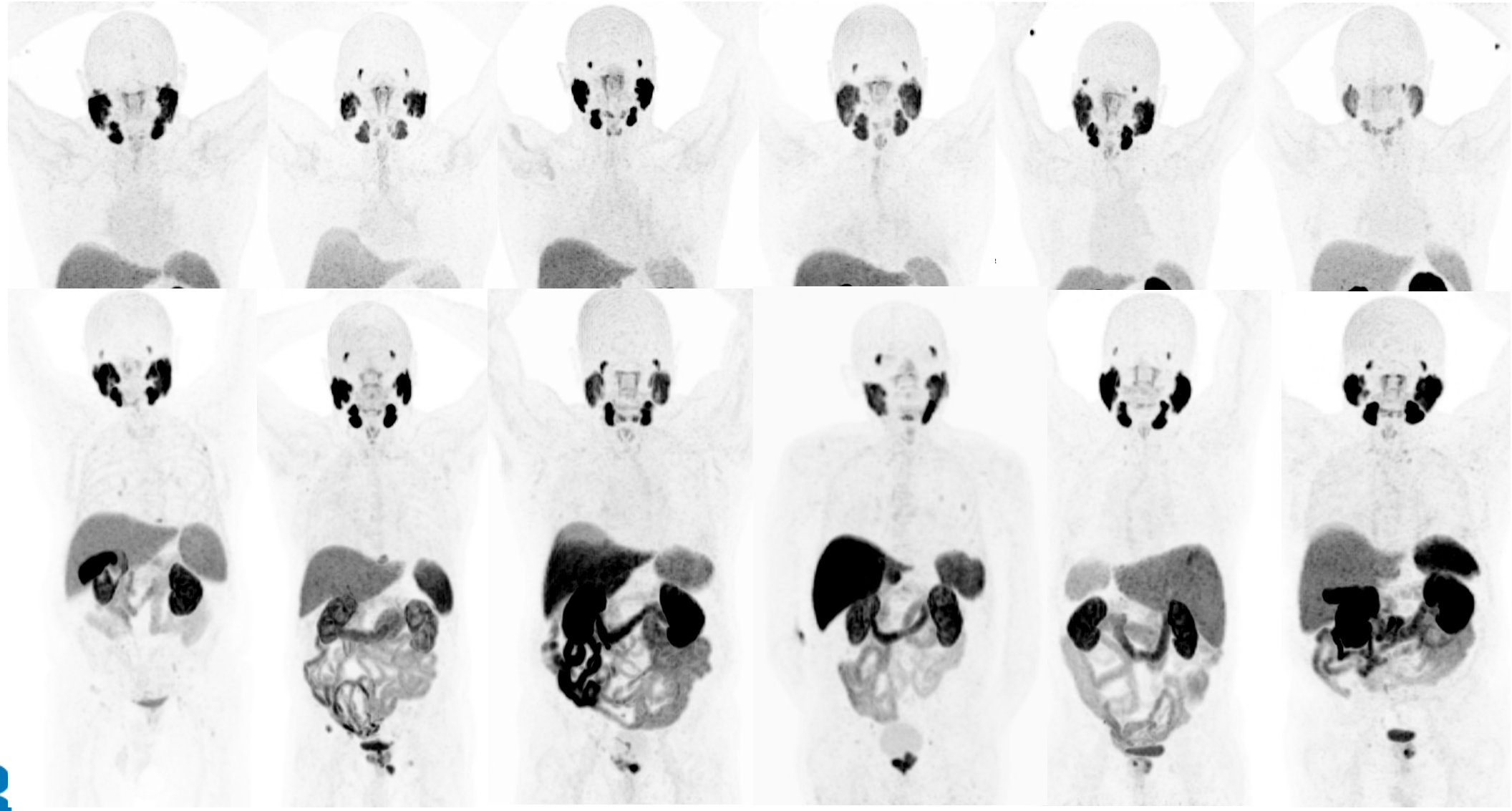
2) PSMA PET tracer heterogeneity: ^{18}F-DCFPyl (Pylclari)



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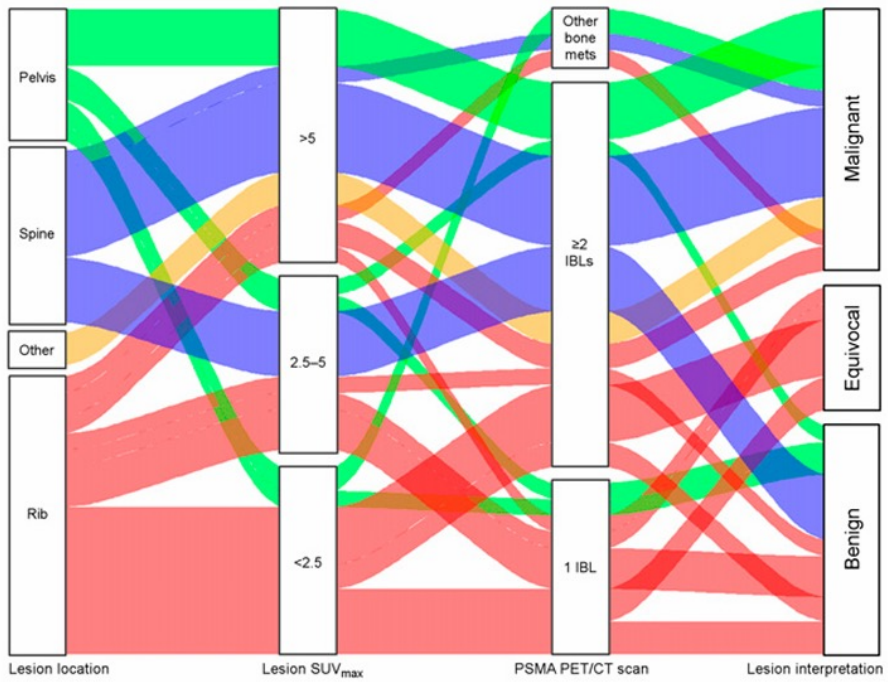
2) PSMA PET tracer heterogeneity: ^{18}F-DCFPyl (Pylclari)

It is less lipophilic compared to ^{18}F-PSMA-1007

- UBU in **19.8%** of patients (compared to **51.4% for ^{18}F-PSMA-1007**)
- 37 of 98 were determined as benign (37%), 42 malignant

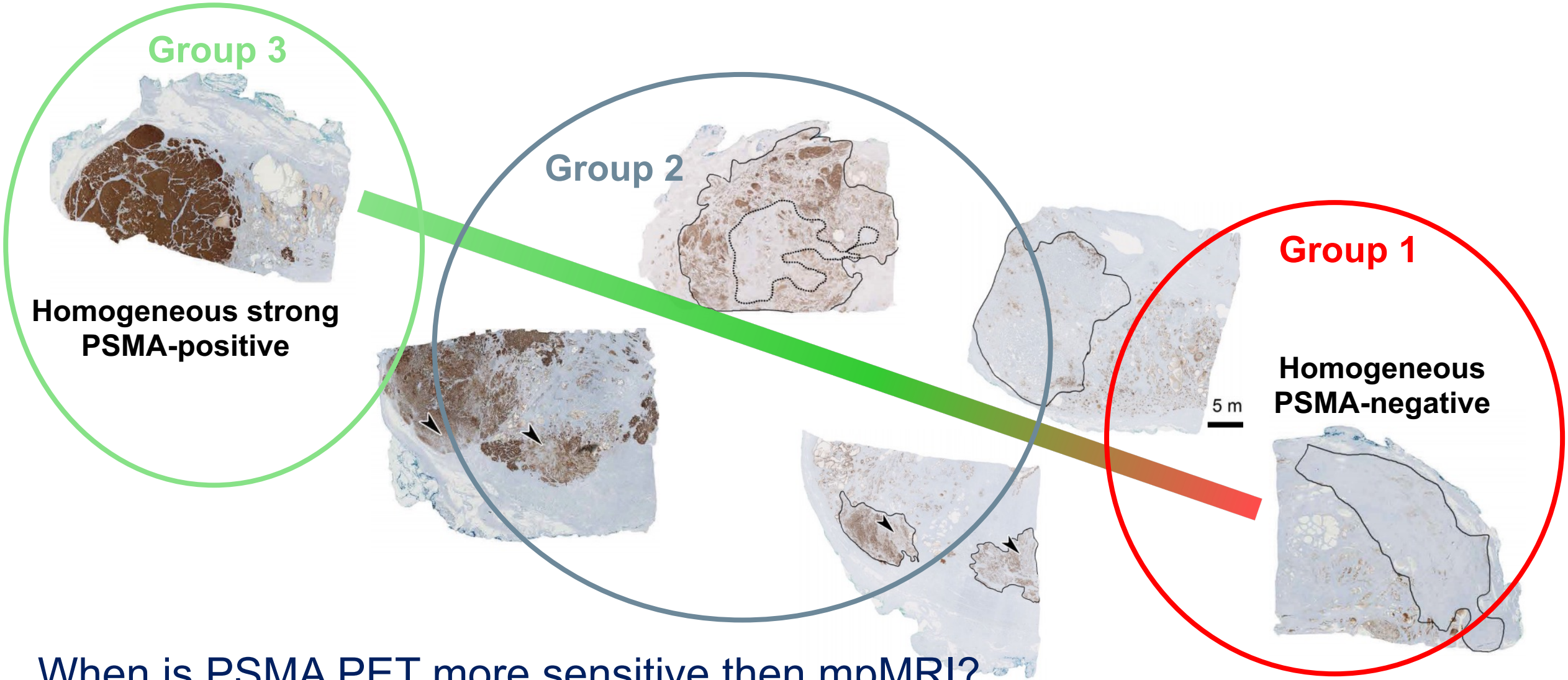


SUVmax > 5 or coexisting bone metastases rise the risk for malignancy.

SUVmax < 5 in atypical locations (ribs) without other bone metastases are likely benign.

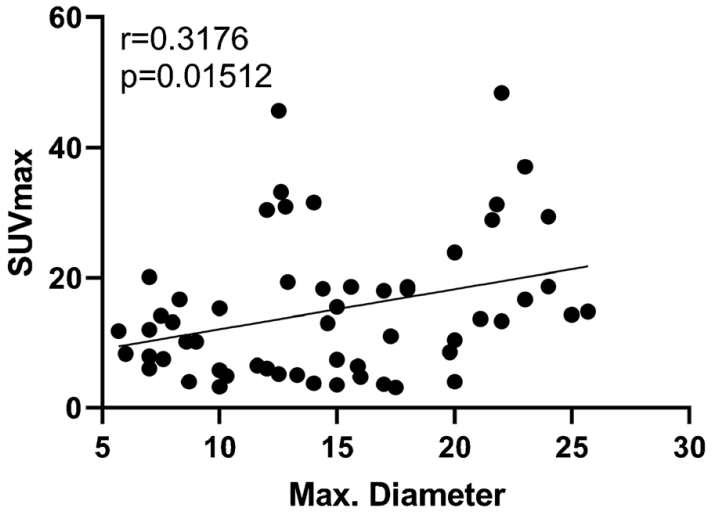
Phelps TE. et al. J Nucl Med 2023; 64:395–401

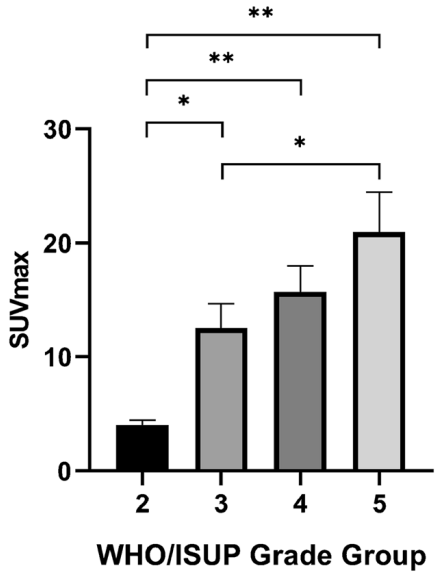
3) PSMA and prostate cancer heterogeneity:

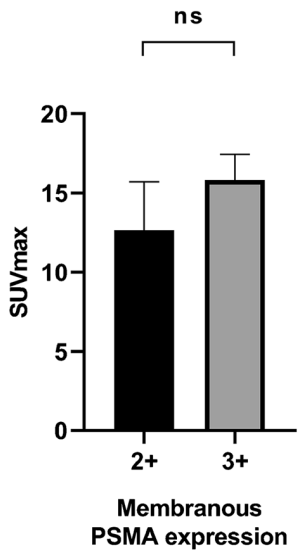


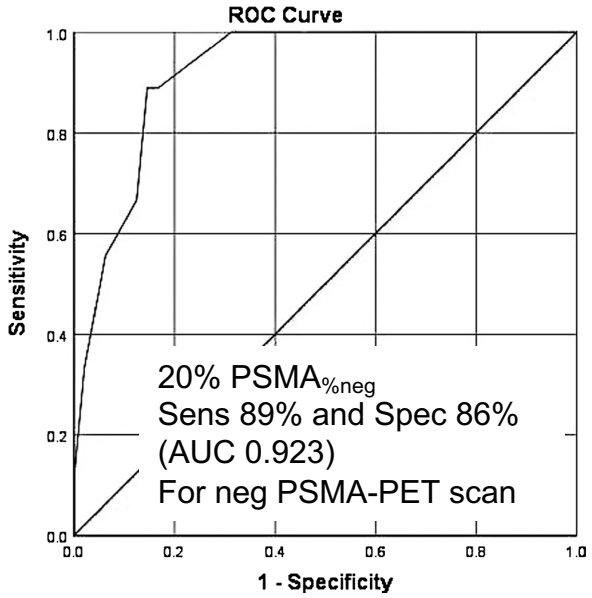
When is PSMA PET more sensitive then mpMRI?

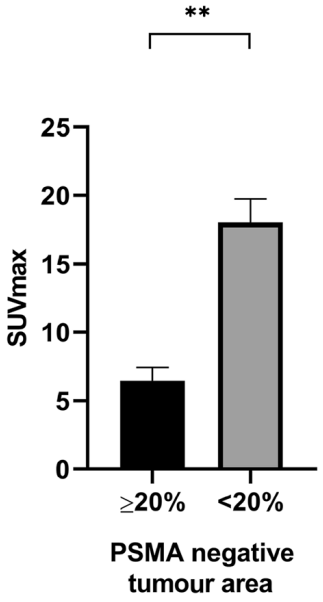
3) PSMA and prostate cancer heterogeneity:

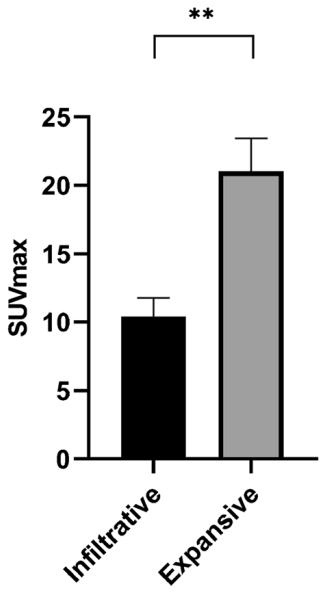












Rüschoff et al. Eur J Nucl Med Mol Imaging. 2022; 48:4042-4053

3) PSMA and prostate cancer heterogeneity:

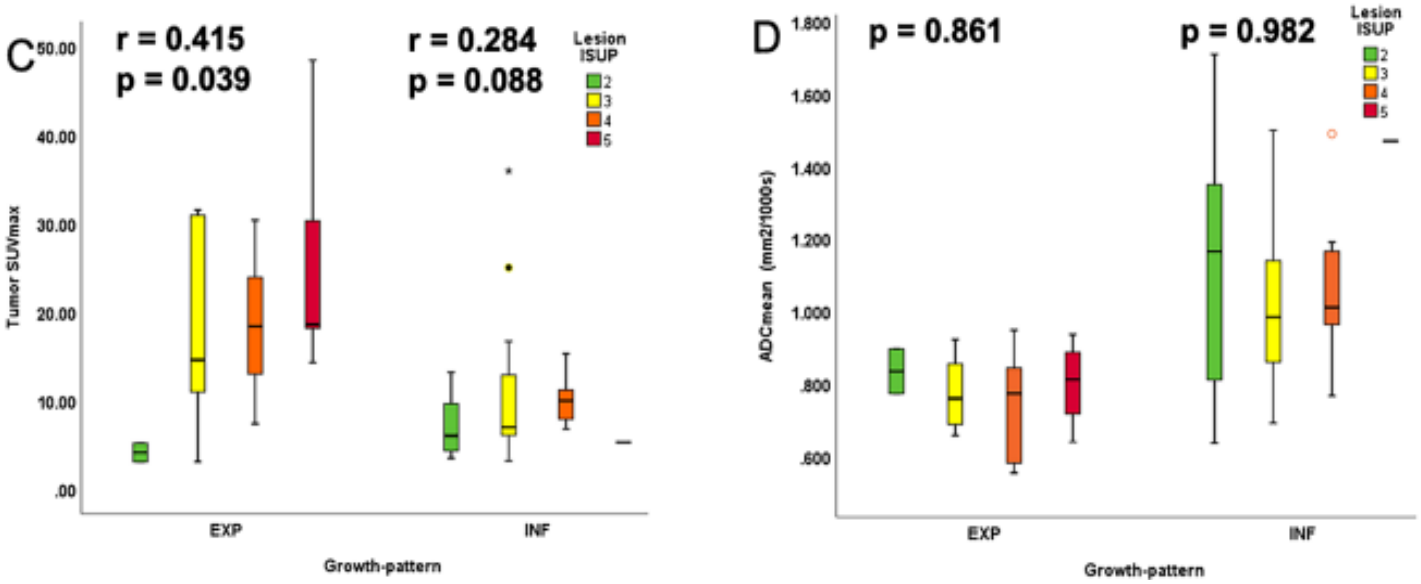
European Journal of Nuclear Medicine and Molecular Imaging (2022) 49:3917–3928
https://doi.org/10.1007/s00259-022-05787-9

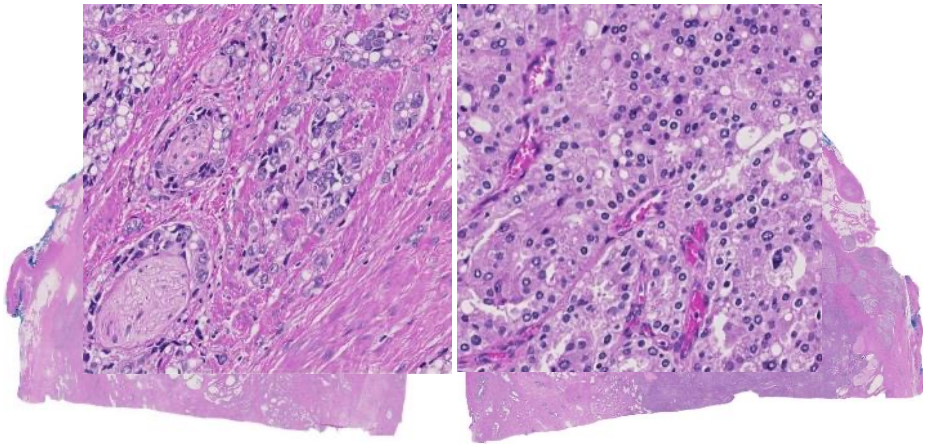
ORIGINAL ARTICLE

Check for updates

Infiltrative growth pattern of prostate cancer is associated with lower uptake on PSMA PET and reduced diffusion restriction on mpMRI

Riccardo Laudicella[1,2] · Jan H. Rüschoff[3] · Daniela A. Ferraro[1,4] · Muriel D. Brada[3] · Daniel Hausmann[5,6] · Iliana Mebert[1,7] · Alexander Maurer[1] · Thomas Hermanns[7] · Daniel Eberli[7] · Niels J. Rupp[3] · Irene A. Burger[1,8]





GS 4+5

MD/PhD

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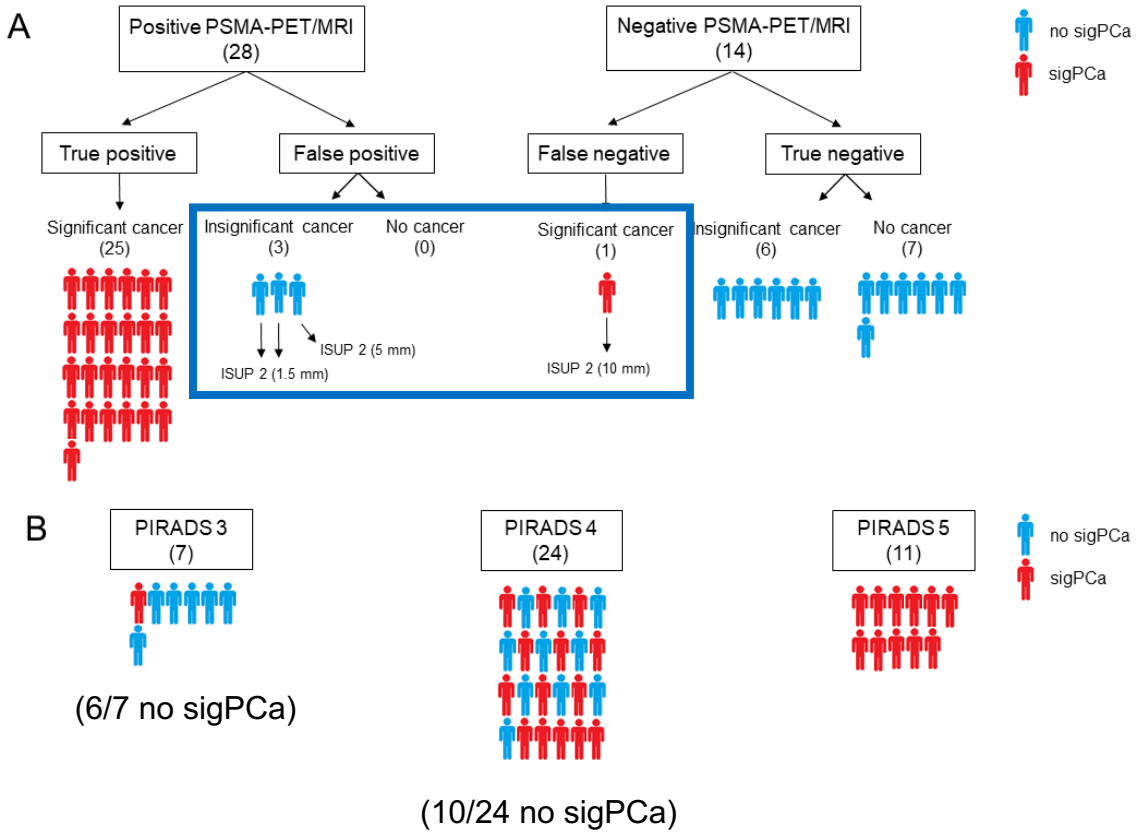
USZ

Laudicella et al. Eur J Nucl Med Mol Imaging. 2022; 49:3917-3928

3) PSMA and prostate cancer heterogeneity: do we catch all?

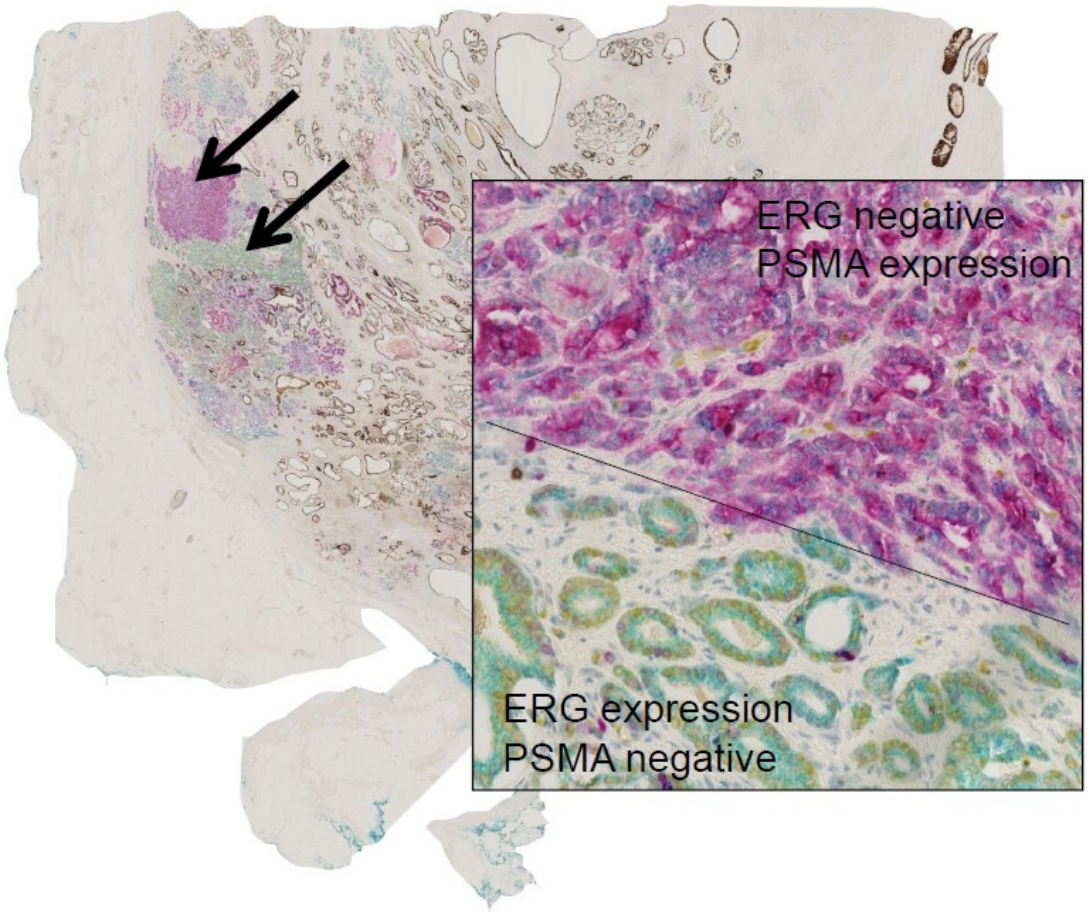
PSMA PET/MR für Biopsie Targets: 42 Patienten mit steigendem PSA und einer mpMRI PIRADS 3-5 Läsion:

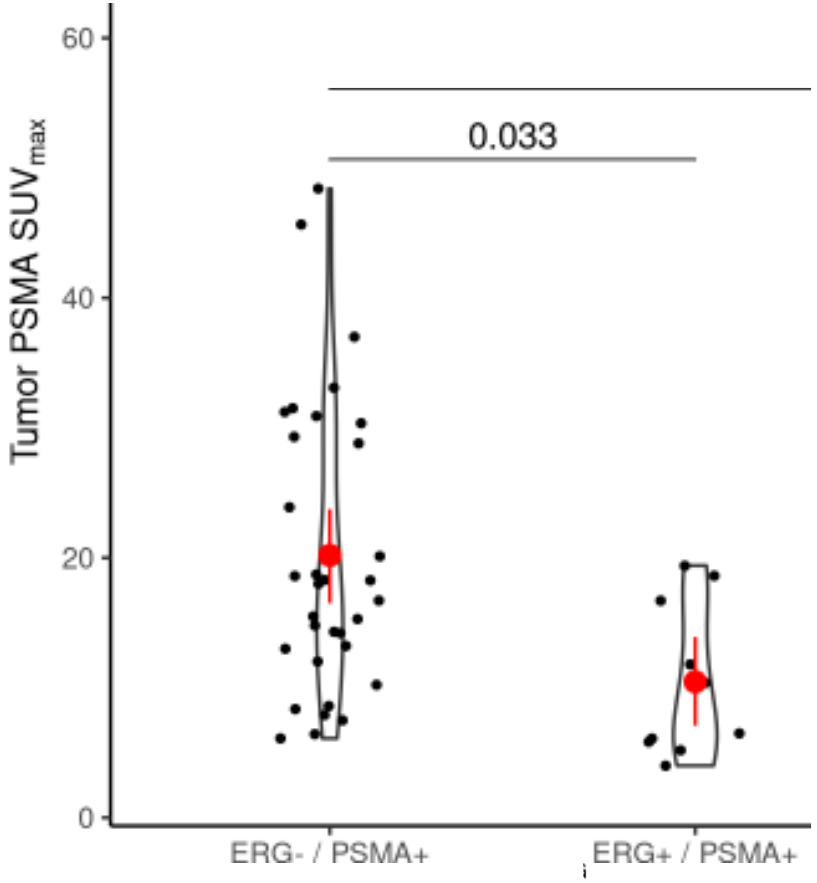


Ferraro et al. Eur J Nucl Med Mol Imaging. 2021; 48(10):3315-3324.

3) PSMA and prostate cancer heterogeneity:

TMPRSS2-ERG gen fusion, homogeneous and robust on IHC + negative correlation to PSMA:





Rupp et al. under submission.

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Thank you for your attention!