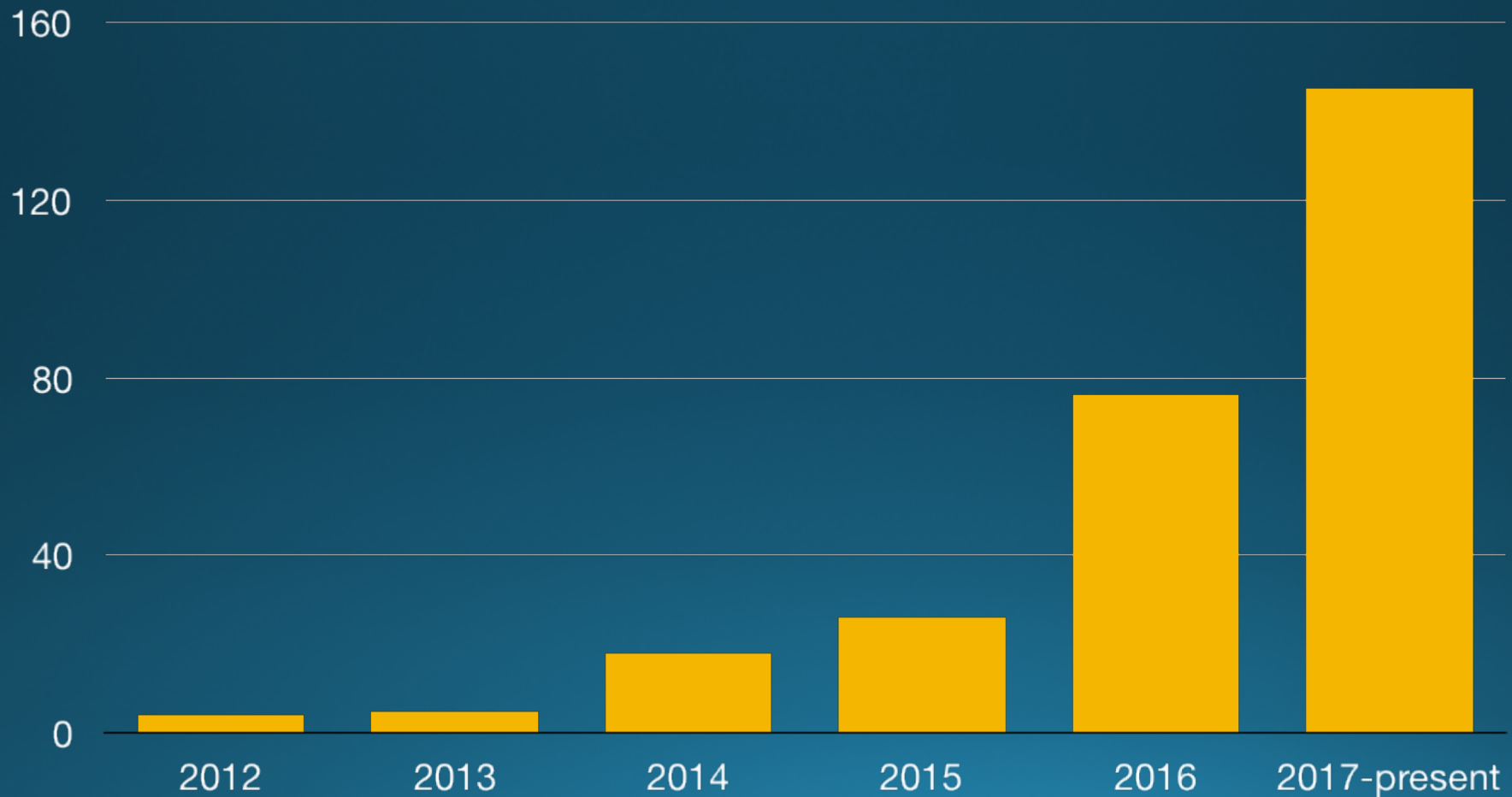Tseng Jing-Ren, MD

Nuclear Medicine and Molecular Imaging Center

CGMH, Linkou

Ga68-PSMA PET scan:
Is the role too important to ignore?

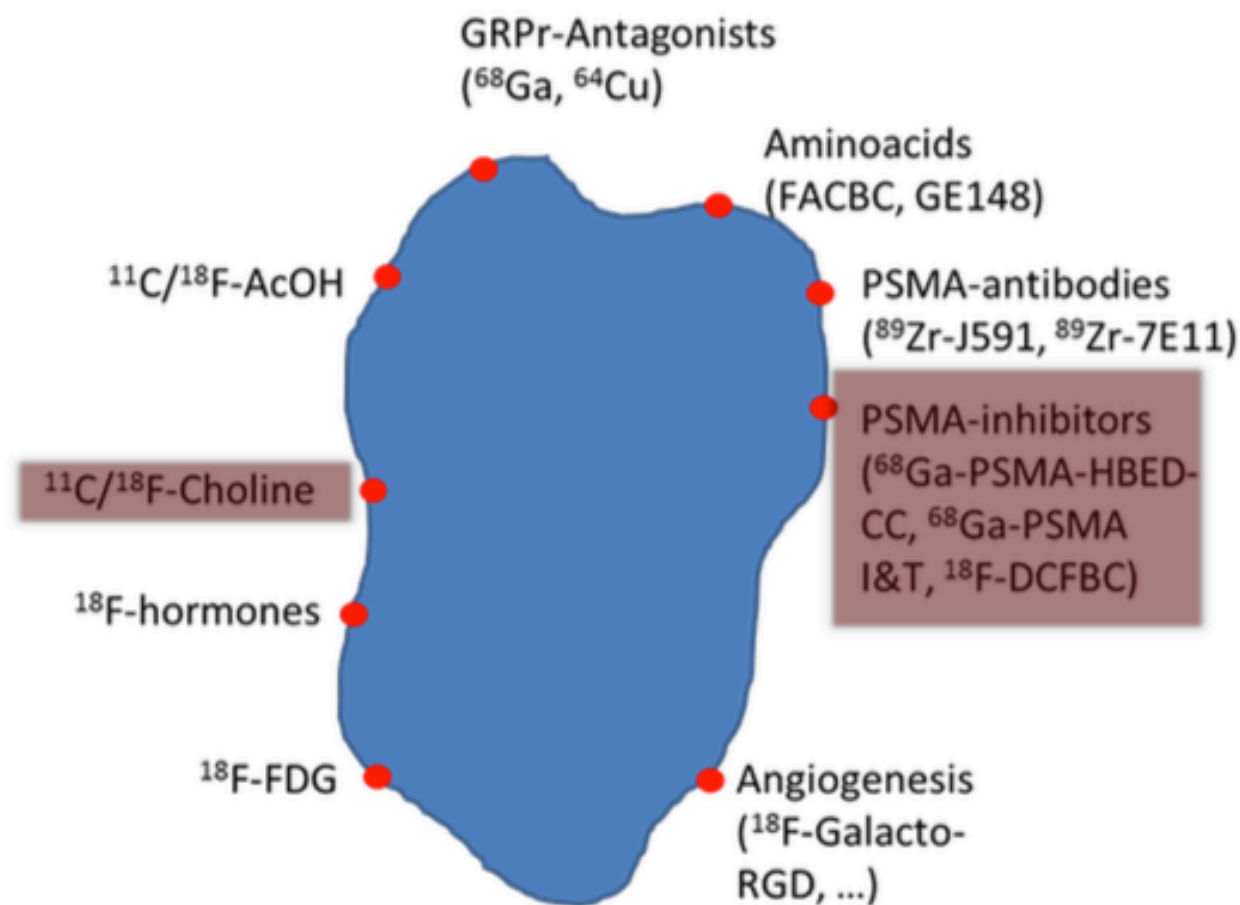Exponential Growth of Publications Using "PSMA PET"

Updated 2017 EAU guidelines

6.9.4.6.   Guidelines for imaging in patients with biochemical recurrence
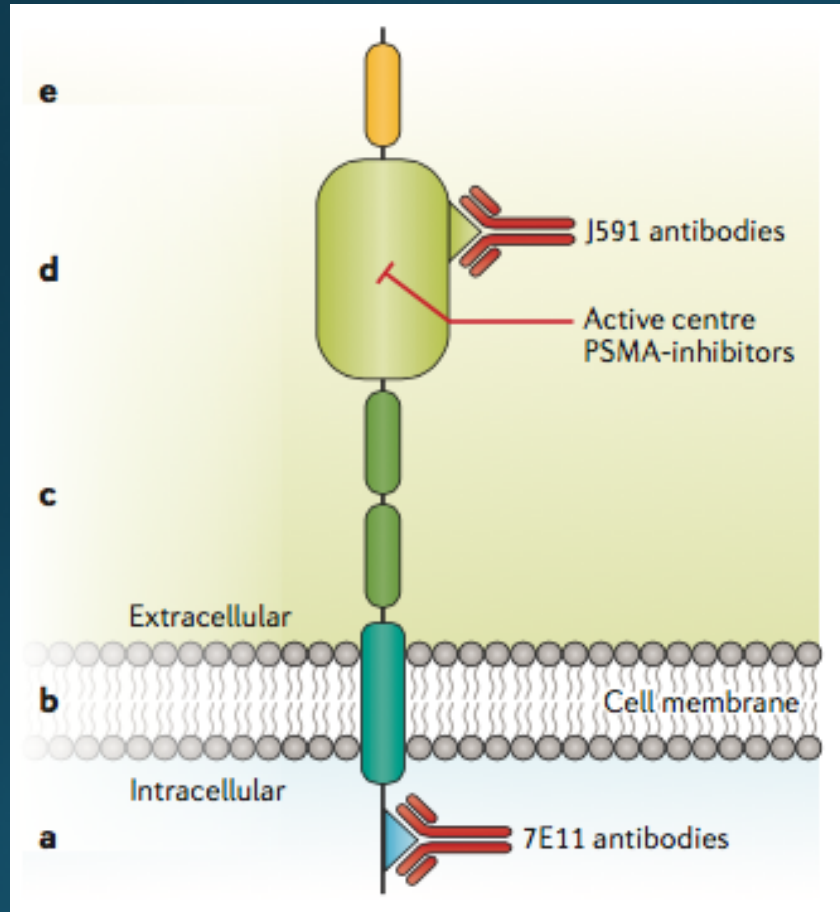
Prostate-specific antigen (PSA) recurrence after radical prostatectomy	LE	GR
PSA < 1 ng/mL: no imaging is recommended.	3	A
PSA ≥ 1 ng/mL: positon emission tomography (PET)/computed tomography (CT) imaging is recommended using choline or prostate-specific membrane antigen (PMSA).	2b	A
Perform bone scan and/or abdominopelvic CT only in patients with PSA > 10 ng/mL, or with adverse PSA kinetics (PSA-doubling time (DT) < 6 months, PSA velocity > 0.5 ng/mL/month).	3	A
PSA recurrence after radiotherapy		
Perform prostate multiparametric magnetic resonance imaging (mpMRI) only in patients who are considered candidates for local salvage therapy, use mpMRI to localise abnormal areas and guide biopsies.	3	B
Choline PET/CT imaging is recommended to rule out lymph nodes or distant metastases in patients fit enough for curative salvage treatment.	2b	B
Perform bone scan and/or abdominopelvic CT only in patients with PSA > 10 ng/mL, or with adverse PSA kinetics (PSA-DT < 6 months, PSA velocity > 0.5 ng/mL/month).	3	A

"Molecular targets" for hybrid PET-imaging in PCa

GRPr-Antagonists (^{68}Ga, ^{64}Cu)

Aminoacids (FACBC, GE148)

^{11}C/^{18}F-AcOH

PSMA-antibodies (^{89}Zr-J591, ^{89}Zr-7E11)

PSMA-inhibitors (^{68}Ga-PSMA-HBED-CC, ^{68}Ga-PSMA I&T, ^{18}F-DCFBC)

^{11}C/^{18}F-Choline

^{18}F-hormones

^{18}F-FDG

Angiogenesis (^{18}F-Galacto-RGD, ...)

# Prostate-specific membrane antigen (PSMA)

- 100-fold to 1,000 fold over-expression on the cell membrane of prostatic cancer cells
- Increased expression in advanced-stage and castration-resistant prostate cancers

^{68}Ga-PSMA HBED-CC

- **"Heidelberg Compound"**

- Glu-NH-CO-NH-Lys-(Ahx)-[^{68}Ga(HBED-CC)] *

- preliminary studies: high detection rate[1] and high lesion-to-background ratio [2]
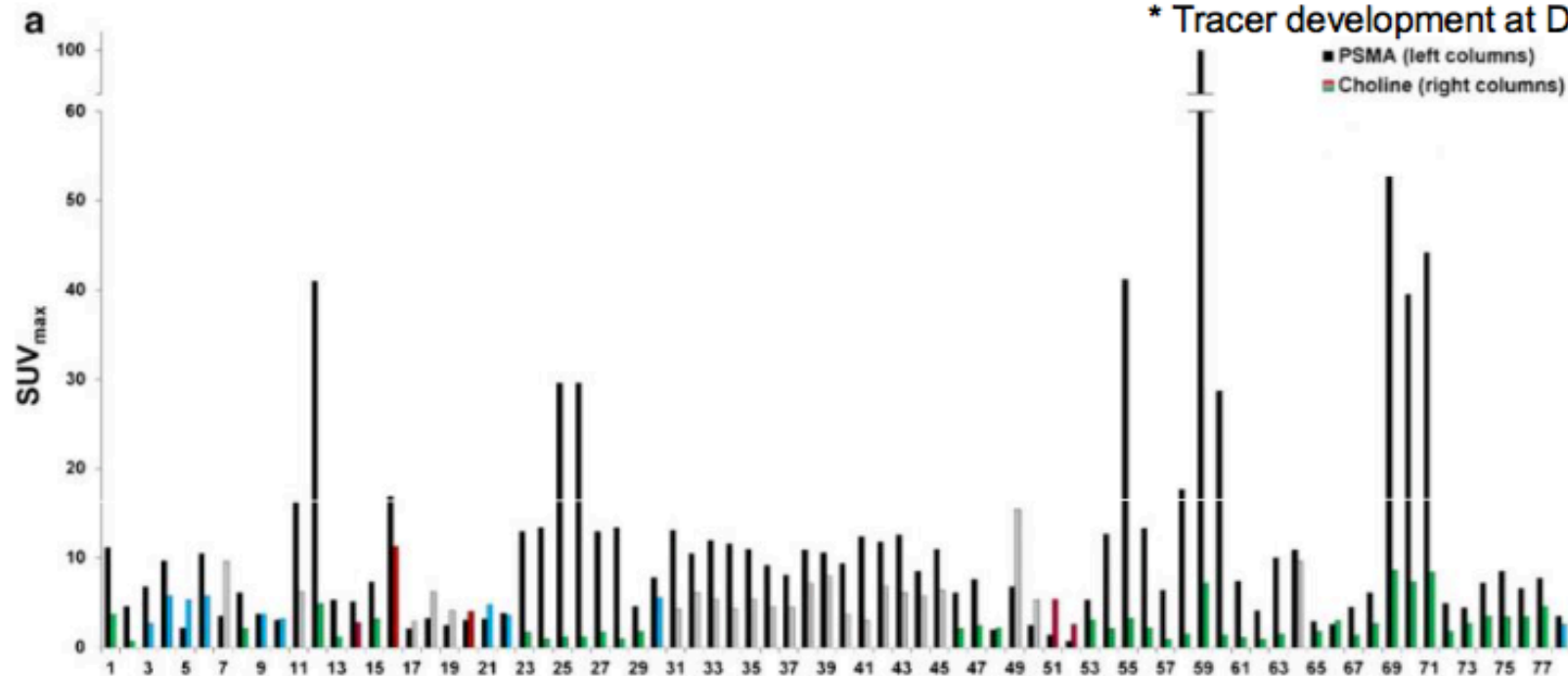
  [1] Afshar-Oromieh A et al. EJNMMI 2013
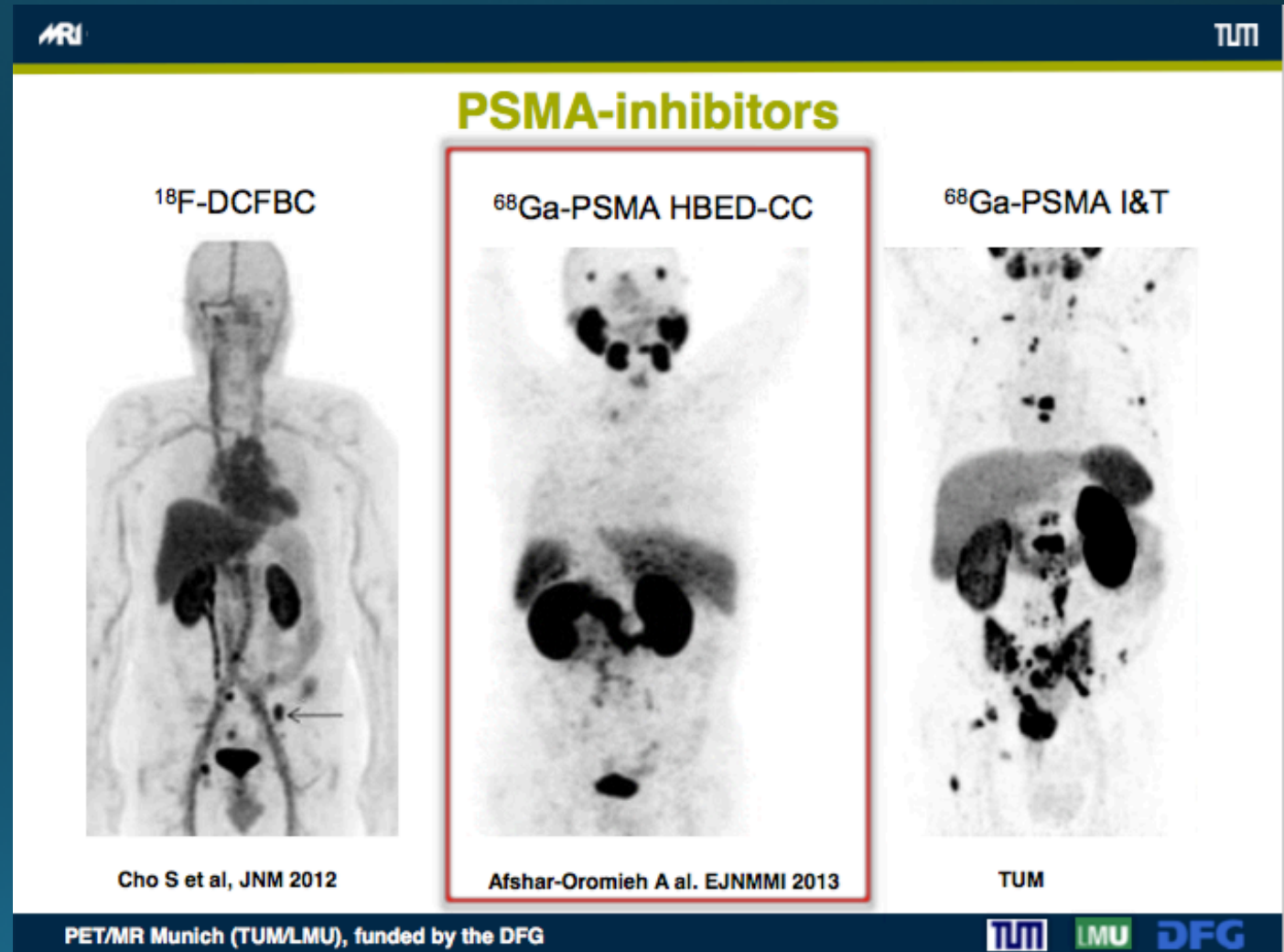 [2] Afshar-Oromieh A et al. EJNMMI 2014
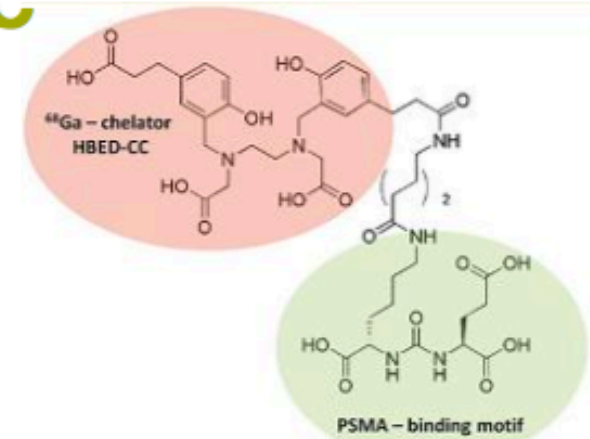
Eder M et al. Bioconjugate Chem 2012
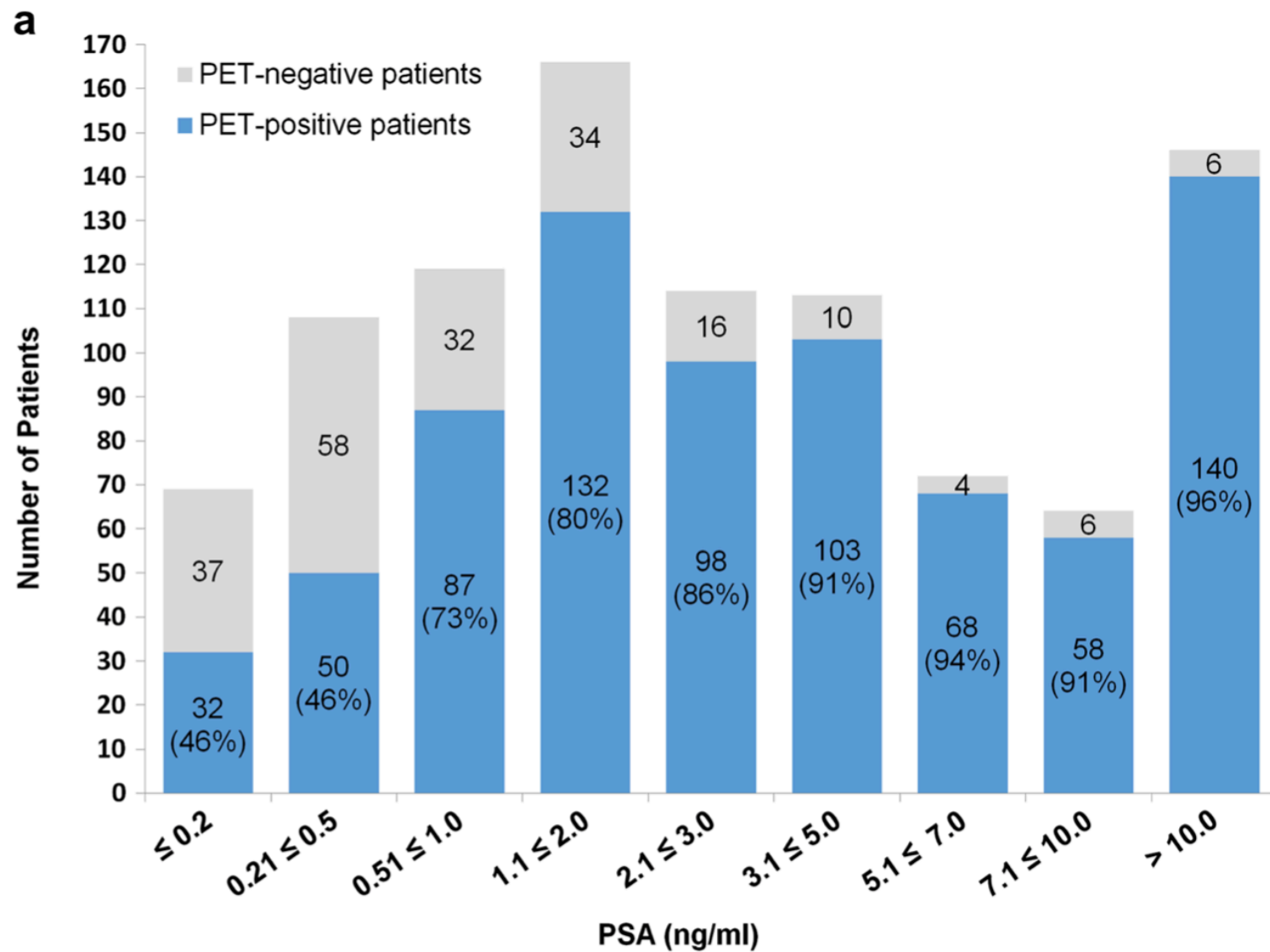
* Tracer development at DKFZ Eisenhu[...]

■ PSMA (left columns)
■ Choline (right columns)

Outline

1. **PSMA PET and biochemical recurrence**

2. PSMA PET and primary staging

3. PSMA Theranostics

4. The role of PSMA PET in CRPC cases?

PSMA-inhibitors

^{18}F-DCFBC

^{68}Ga-PSMA HBED-CC

^{68}Ga-PSMA I&T

Cho S et al, JNM 2012

Afshar-Oromieh A al. EJNMMI 2013

TUM

PET/MR Munich (TUM/LMU), funded by the DFG

Fig. 1 Probabilities of a pathological ^{68}Ga-PSMA-11 PET/CT scan (*a*) and plot of the rates of pathological PET/CT scans with confidence intervals (*b*) in relation to PSA levels in 971 patients. *Blue columns* Numbers of patients with a pathological PET/CT scan together with the rates which also represent the patient-based sensitivities of ^{68}Ga-PSMA-11 PET/CT in detecting recurrent PCa in relation to PSA level. Amongst all patients with a PSA level less than 0.2 ng/ml, 15 had values less than 0.1 ng/ml

It's still "Lumpology"

- CT and bone scan underperform when characterizing lymph nodes, local recurrence, and bone lesions

- MRI offers excellent resolution to image the pelvis

  – See tiny "lumps"

  – DWI of some value but still not good enough to characterize tiny nodes

- PET imaging can help

Outline

1. PSMA PET and biochemical recurrence

2. PSMA PET and primary staging

3. PSMA Theranostics

4. The role of PSMA PET in CRPC cases?
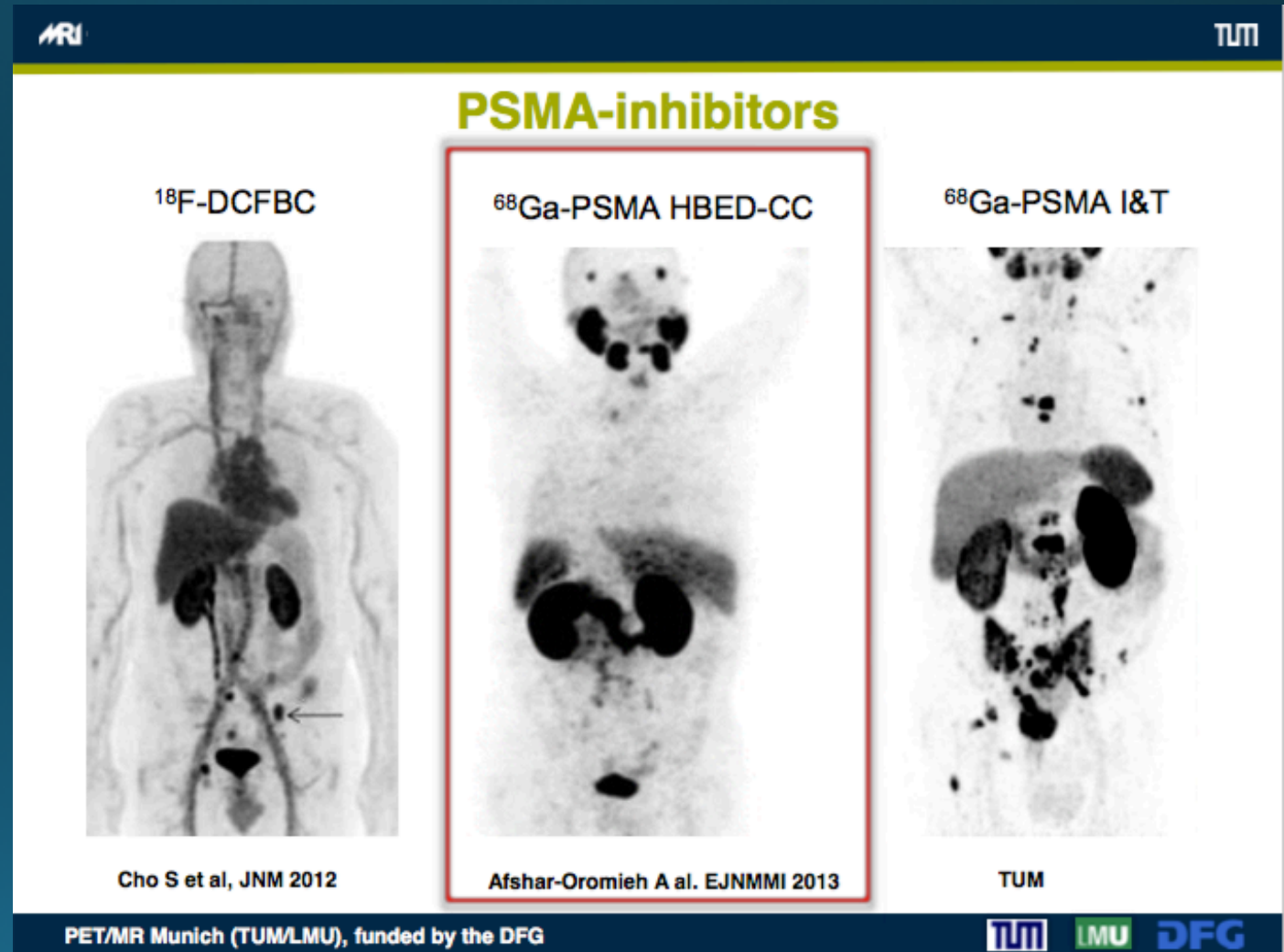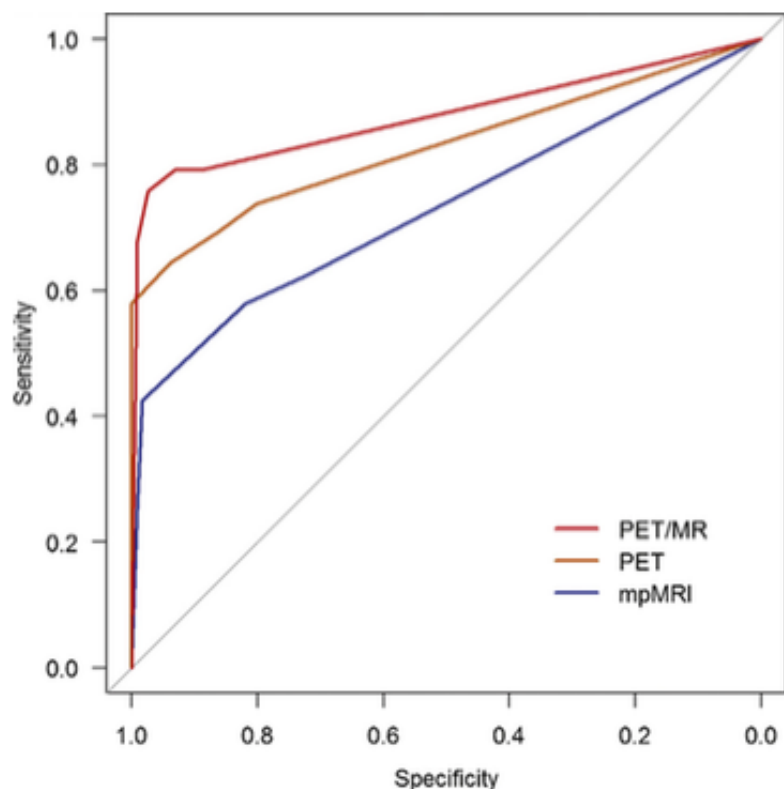
Fig. 3 – Receiver operating characteristic curves for multiparametric magnetic resonance imaging (mpMRI), positron emission tomography (PET), and gallium 68 (^{68}Ga)-prostate-specific membrane antigen (PSMA) HBED-CC PET/MRI on a sextant-based analysis.

	AUC (95% CI)	Youden-selected threshold	Sensitivity, %, at threshold (95% CI)	Specificity, %, at threshold (95% CI)
mpMRI	0.73[*,†] (0.66–0.80)	4[§]	43 (33–53)	98 (94–100)
		3	58 (49–66)	82 (69–90)
PET	0.83[*,#] (0.78–0.87)	4	64 (56–72)	94 (86–98)
PET/MRI	0.88[#,†] (0.84–0.92)	4	76 (68–82)	97 (90–99)

AUC = area under the curve; CI, confidence interval; mpMRI = multiparametric magnetic resonance imaging; MRI = magnetic resonance imaging; PET = positron emission tomography.
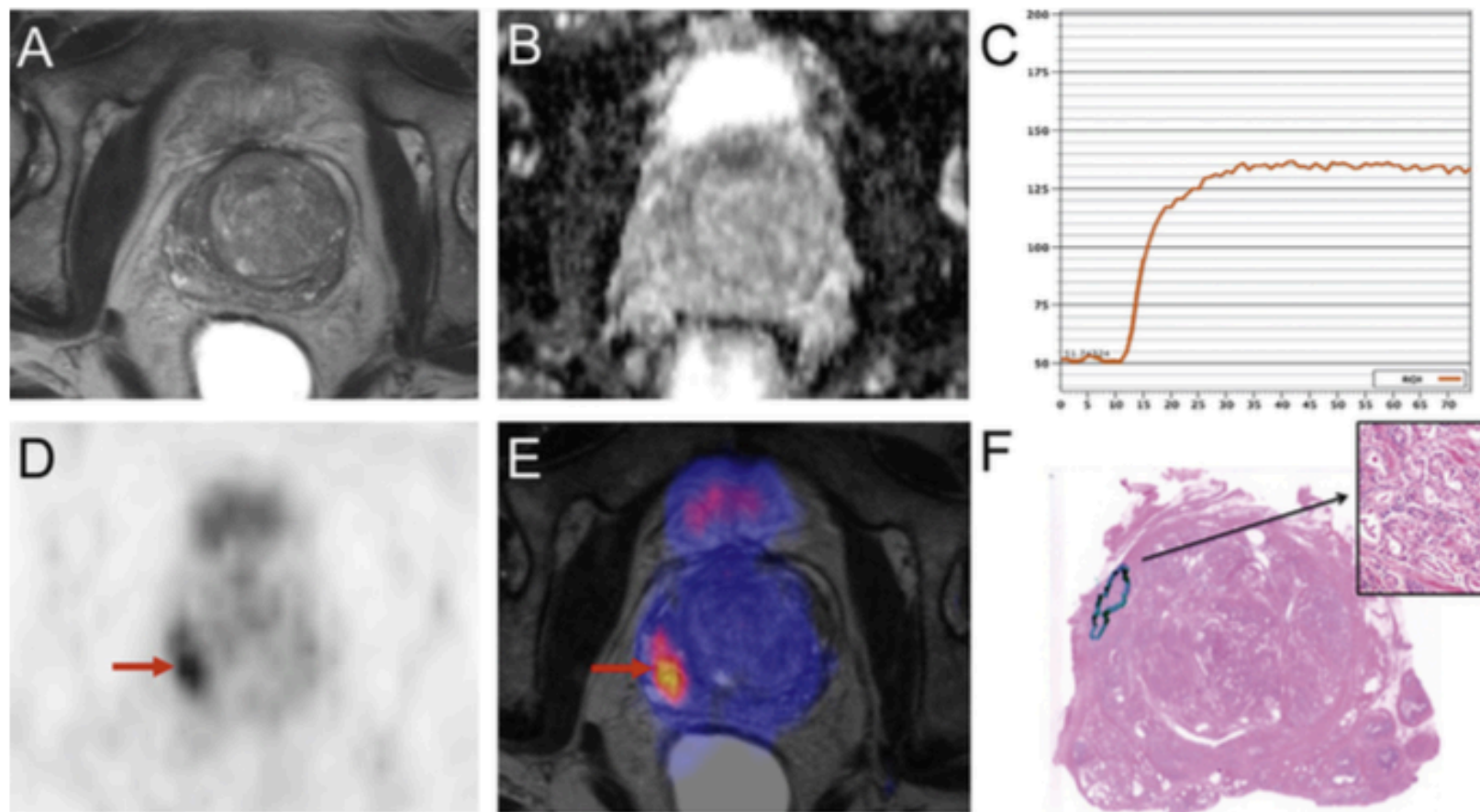
[*] mpMRI versus PET, $p = 0.003$.

[†] mpMRI versus PET/MRI, $p < 0.001$.

[§] The threshold of 4 for mpMRI is presented to show data with the same threshold for all imaging methods; the threshold of 3 is the calculated optimal cut-off as described in the Material and methods section.
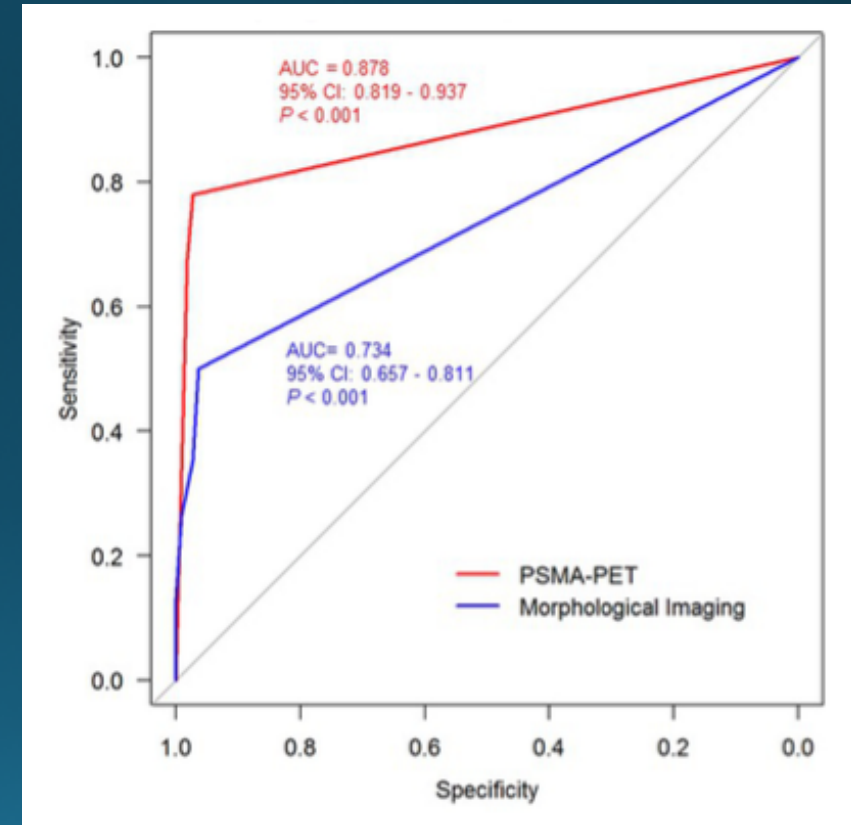
[#] PET versus PET/MRI, $p = 0.002$.

Fig. 1 – A 65-year-old patient with a biopsy-proven prostate cancer Gleason score of 6 and a prostate-specific antigen of 24.5 ng/ml. (A) Transverse T2-weighted images show considerable benign prostatic hyperplasia in the central zone presenting with one large and multiple surrounding small nodules. Prostate Imaging Reporting and Data System (PI-RADS) scoring using information from diffusion-weighted imaging (apparent diffusion coefficient map shown in B) and dynamic contrast-enhanced (enhancement curve in C) resulted in a PI-RADS scores of 2 for the right and left midgland sextants. Positron emission tomography (PET) and fused T2-weighted/PET images show intense focal uptake projecting on the right peripheral zone. Note that only slight diffuse uptake is present in the central gland. (D) In PET a score of 5 was given. (E) In the combined PET/ magnetic resonance imaging (MRI), due to missing clearly suspicious findings on MRI, a score of 4 was given for the right midgland sextant. (F) Hematoxylin and eosin gross section histopathology shows an oval Gleason score 6 tumor focus in the right peripheral zone. Note that the different anteroposterior positive focus of the tumor nodus in imaging and histopathology is related to slightly different planes.

^{68}Ga-PSMA HBED-CC PET for lymph node metastasis

^{68}Ga-PSMA HBED-CC PET Rating	Histology: LN metastasis		
	Positive	Negative	
Positive	53	3	PPV: 94.6%
Negative	15	108	NPV: 87.8%
Total	68	111	179
	Sensitivity: 77.9%	Specificity: 97.3%	Accuracy: 89.9%

Morphological Rating (CT/MR)	Histology: LN metastasis		
	Positive	Negative	
Positive	18	1	PPV: 94.7%
Negative	49	110	NPV: 69.2%
Total	67	111	178
	Sensitivity: 26.9%	Specificity: 99.1%	Accuracy: 71.9%

AUC = 0.878
95% CI: 0.819 - 0.937
$P < 0.001$

AUC = 0.734
95% CI: 0.657 - 0.811
$P < 0.001$

— PSMA-PET
— Morphological Imaging

CT/MR: Mean size 13.0 ± 4.9 mm (range 4-25 mm)

Table 2 Value of PSMA PET/CT in predicting the occurrence of LN metastases in the whole patient group and in those with ≥15 lymph nodes removed

	All patients ($n = 51$)	Patients with ≥15 lymph nodes removed ($n = 37$)
Sensitivity	53.3%	66.6%
Specificity	85.7%	88%
Accuracy	76%	81%
Positive predictive value	61.5%	72.7%
Negative predictive value	81%	84.6%

Reference	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
[6]	33	100	100	69
[8]	66	99	96	86
[7]	84	84	82	84
[9]	64	95	88	82
Present study				
Entire cohort	53.3	85.7	61.5	81
Patients with ≥15 LNs removed	66.6	88	72.7	84.6