Not all that shines is positive

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Nuclear Medicine & Molecular Imaging

UZ Leuven – KU Leuven

Session ‘Follow-up after radical therapy’

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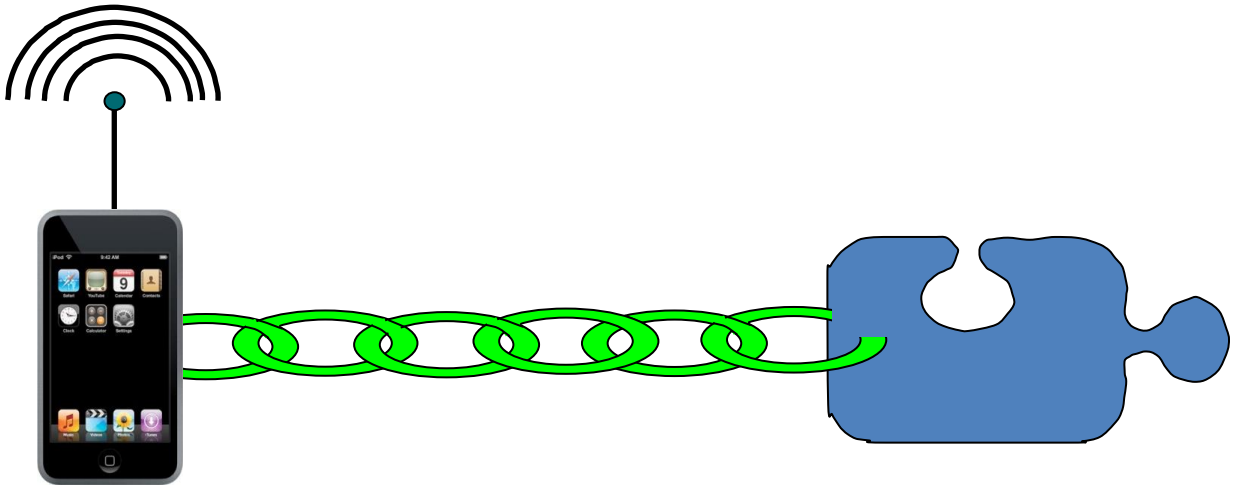
Conflicts of interest

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports	
Receipt of honoraria or consultation fees	Bayer, Telix, Lightpoint, GE Healthcare
Stock shareholder	
Other support (please specify):	

How? Tracers for molecular diagnostic imaging

^{68}Ga



PSMA-11

Radionuclide

Emits radiation upon decay.
This radiation can be detected by nuclear medicine camera.

Vectormolecule

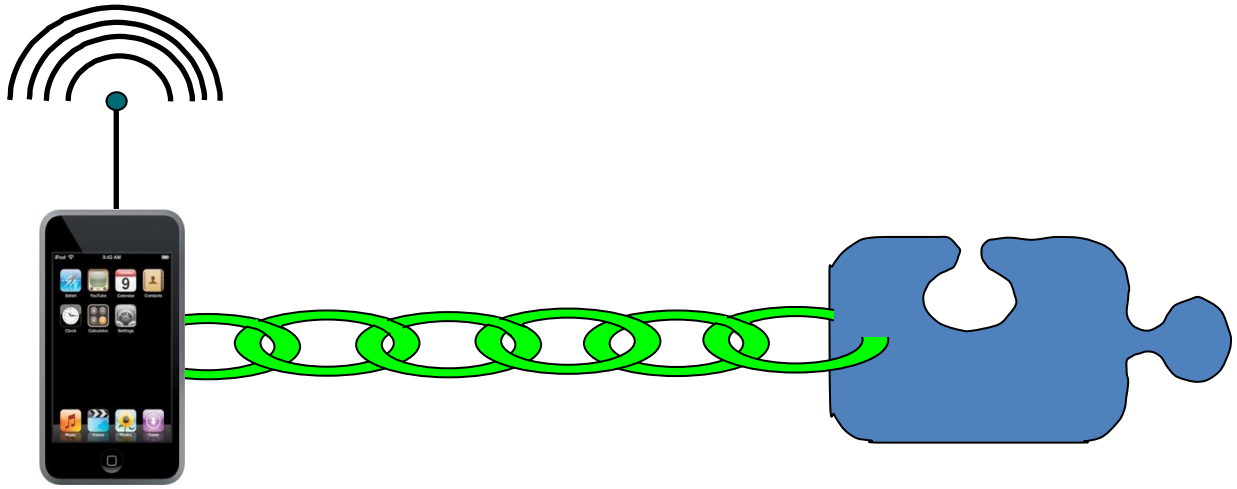
Is responsible for a specific interaction with the target

Disadvantages gallium-68

- Gallium-68
  - Generator product (^{68}Ge/^{68}Ga-generator)
    - Very expensive
    - Only limited amount of tracer produced per batch
  - Physical characteristics
    - High positron energy => lower spatial resolution
    - Half life of 68 min => no transport to other sites possible
  - ^{68}Ga-PSMA-11: excretion through kidneys -> bladder
- Fluor-18
  - Cyclotron product
    - Can be producted in large batch
  - Physical characteristics
    - Lower positron energy => better spatial resolution
    - Half life ~ 2h => central production with distribution to other sites possible
  - Some ^{18}F-PSMA compounds (f.e. ^{18}F-PSMA-1007): limited bladder activity (hepatobiliary excretion)

Tracers for molecular diagnostic imaging

- ^{68}Ga
- ^{18}F
- …



Radionuclide

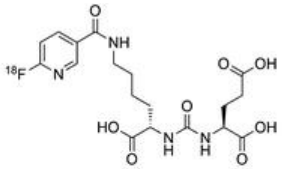
Emits radiation upon decay.
This radiation can be detected by nuclear medicine camera.

Vectormolecule

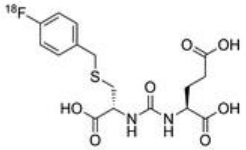
Is responsible for a specific interaction with the target

- PSMA-11
- PSMA-1007
- DCFPyL
- rhPSMA-7.3
- rhPSMA-7
- FACBC
- …

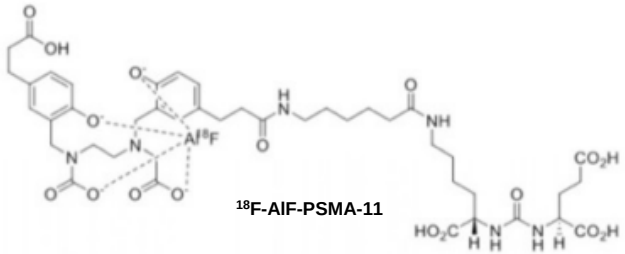
PSMA ligands



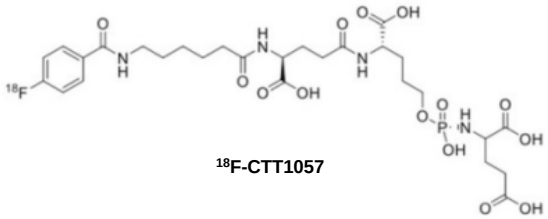
^{18}F-DCFPyL



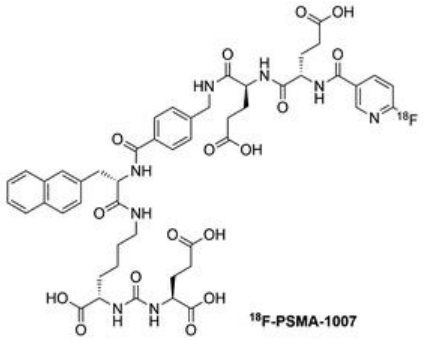
^{18}F-DCFBC



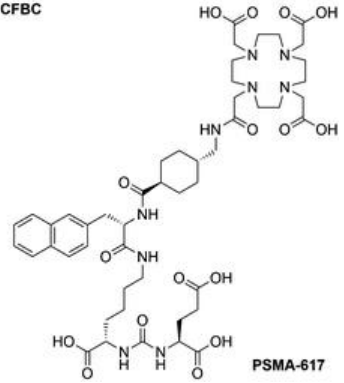
^{18}F-AlF-PSMA-11



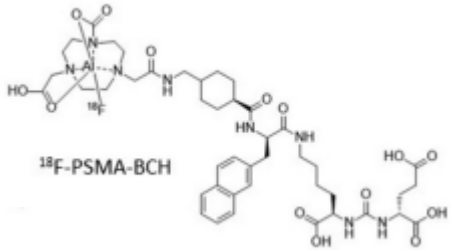
^{18}F-CTT1057



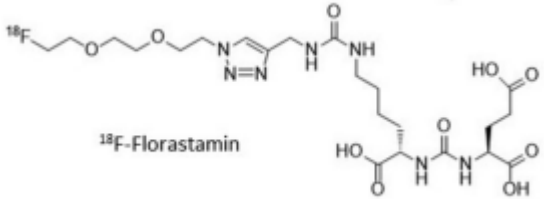
^{18}F-PSMA-1007



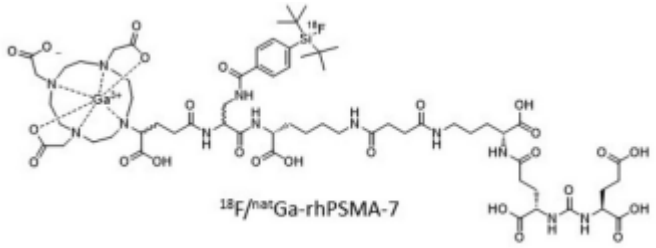
PSMA-617



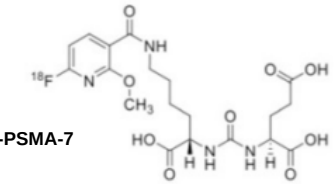
^{18}F-PSMA-BCH



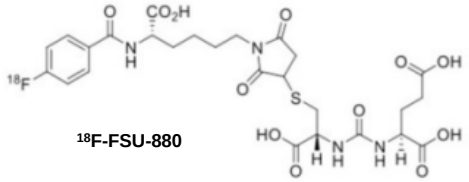
^{18}F-Florastamin



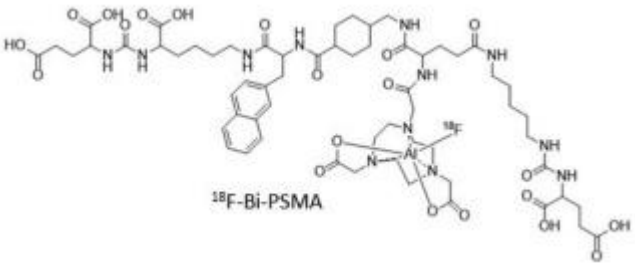
^{18}F/^{nat}Ga-rhPSMA-7



^{18}F-JK-PSMA-7

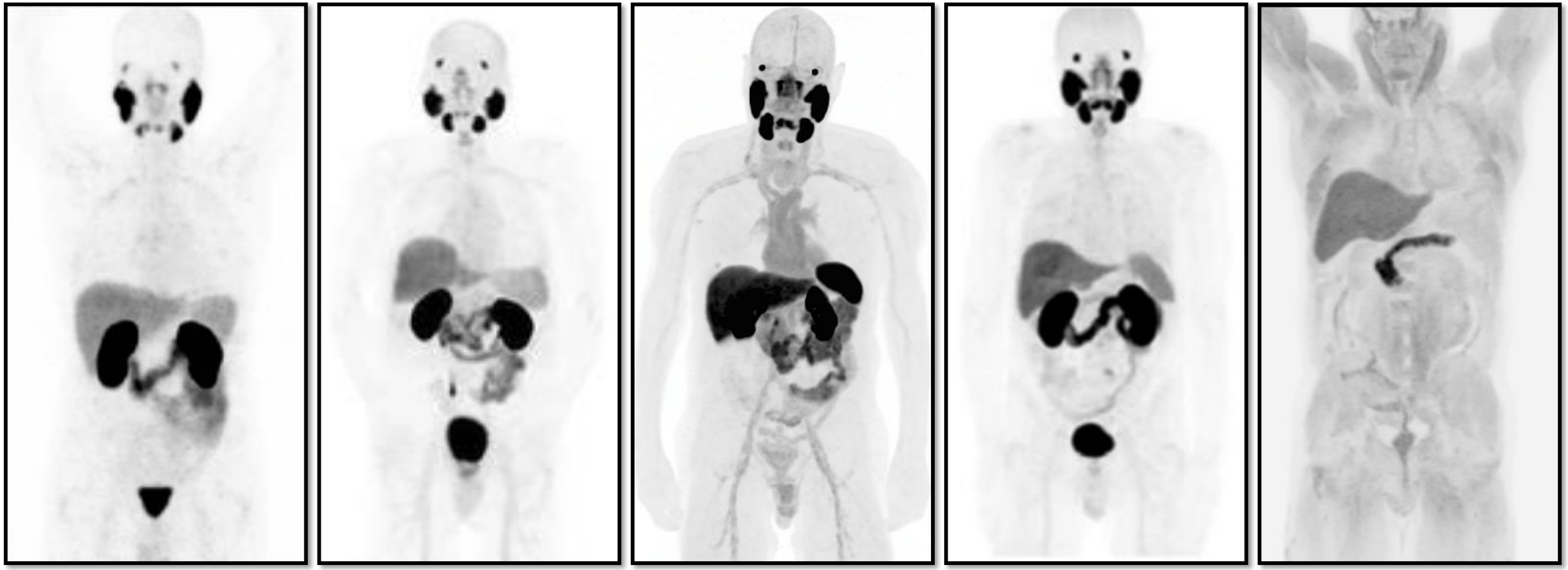


^{18}F-FSU-880



^{18}F-Bi-PSMA

Biodistribution



^{68}Ga-PSMA-11 | ^{18}F-DCFPyL | ^{18}F-PSMA-1007 | ^{18}F-rhPSMA-7.3 | ^{18}F-FACBC (Axumin)

Afshar-Oromieh et al., EJNMMI 2013 - Szabo et al., Molecular Imaging Biol 2015 – Tolvanen et al., JNM 2020

Biodistribution

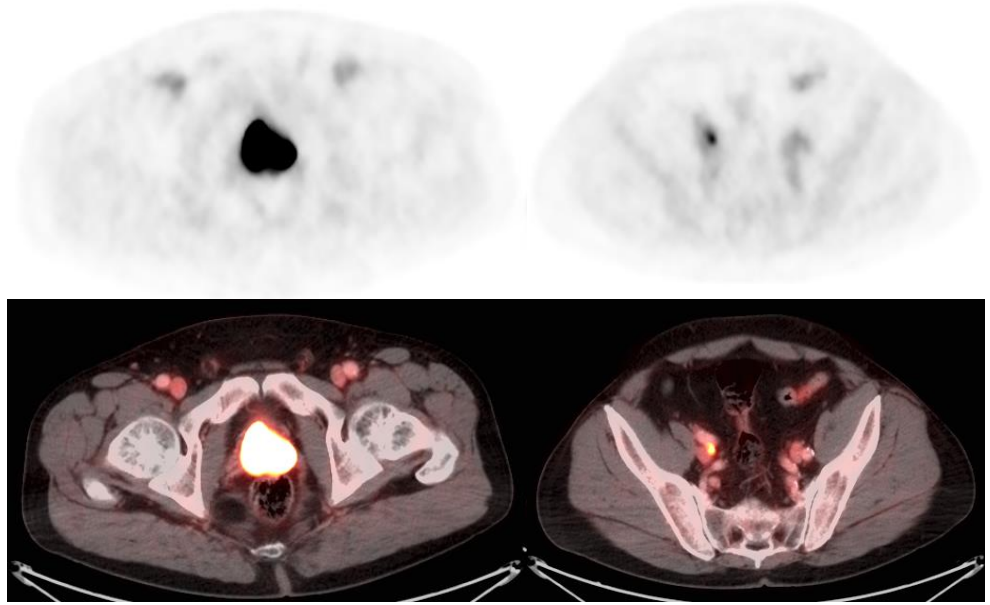
^{68}Ga-PSMA-11

- Salivary and lacrimal glands
  - Salivary excretion -> mild uptake in oropharynx, larynx, esophagus
- Liver, spleen
- Small bowel
- Kidneys, bladder

^{18}F-PSMA-1007

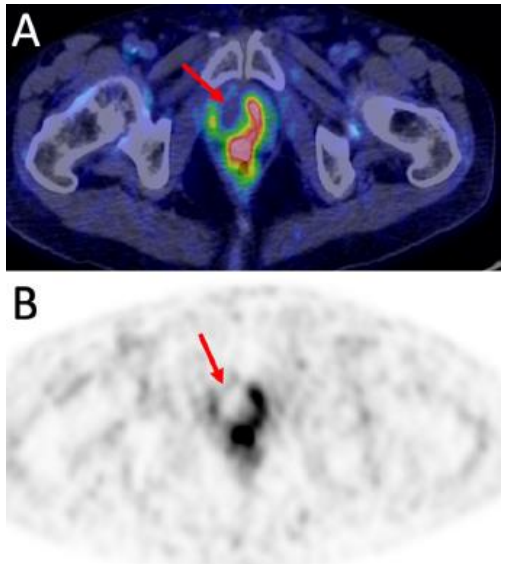
What is positive?

- High specificity
- Moderate sensitivity (in primary LN staging compared to histology)

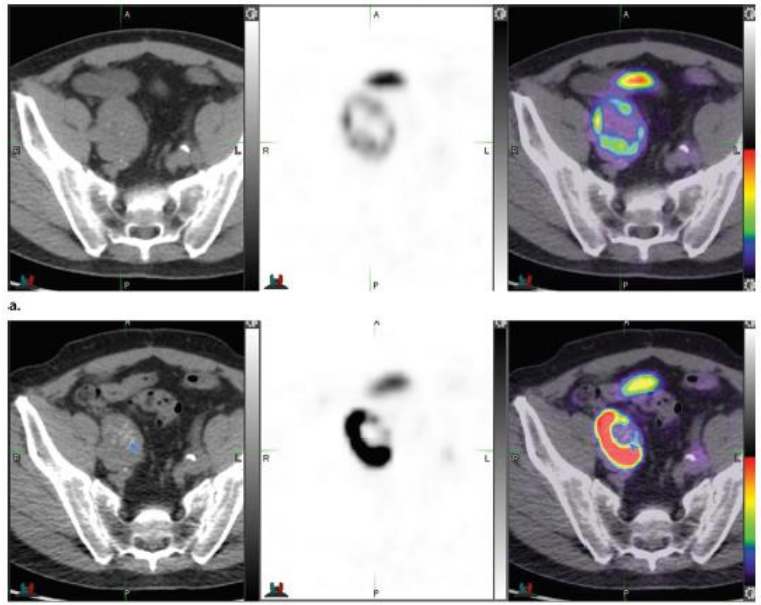


False negative

- Prostate cancer is PMSA negative
  - ± 10% of primary PCa
  - Neuro-endocrine differentiation
  - Advanced mCRPC

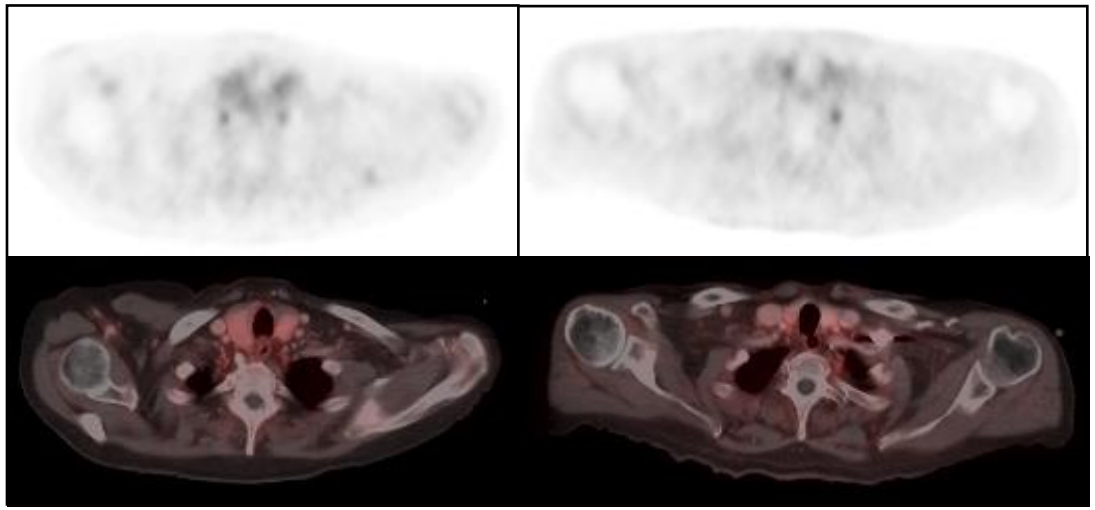


- Effect of ADT
  - Short-term ADT may increase PSMA expression
  - Long-term ADT may decrease PSMA expression

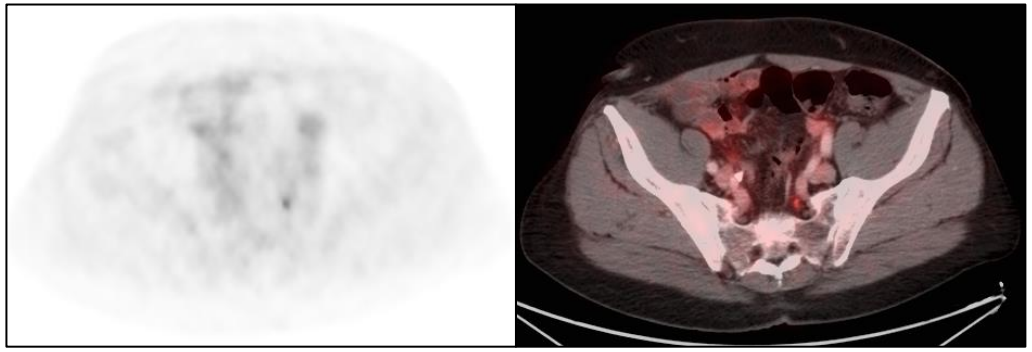


- ! LiverM+ when using ^{18}F-PSMA-1007

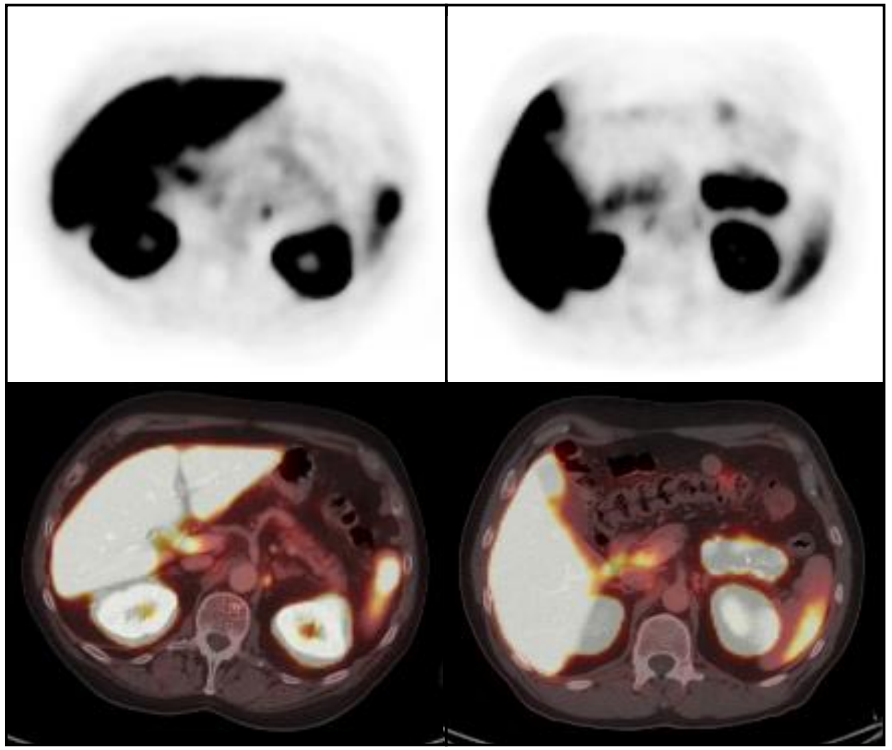
Pitfalls - ganglia



Cervical



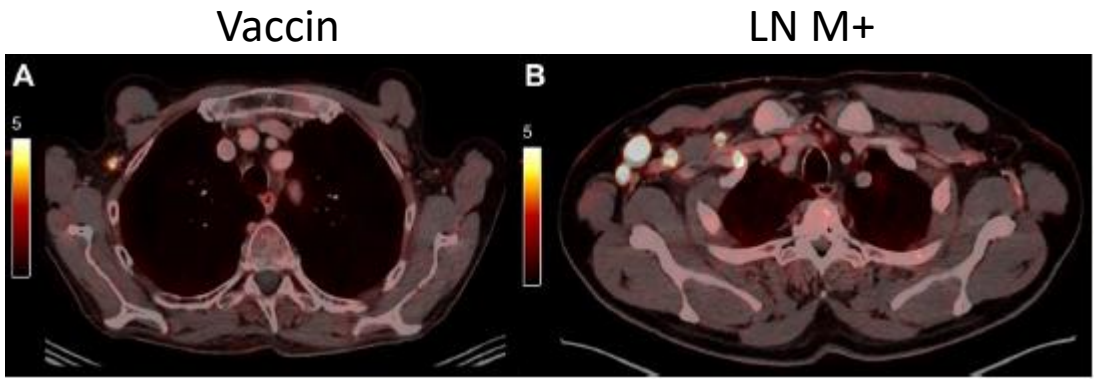
Pre-sacral

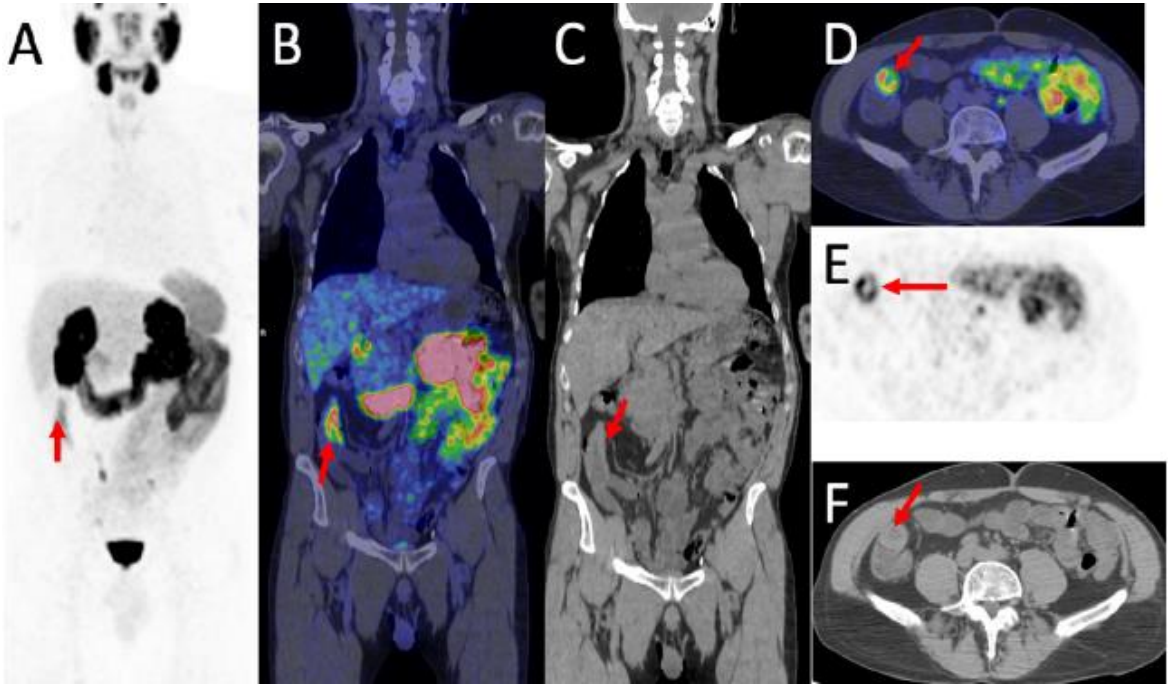


Coeliac

Pitfalls - benign lesions

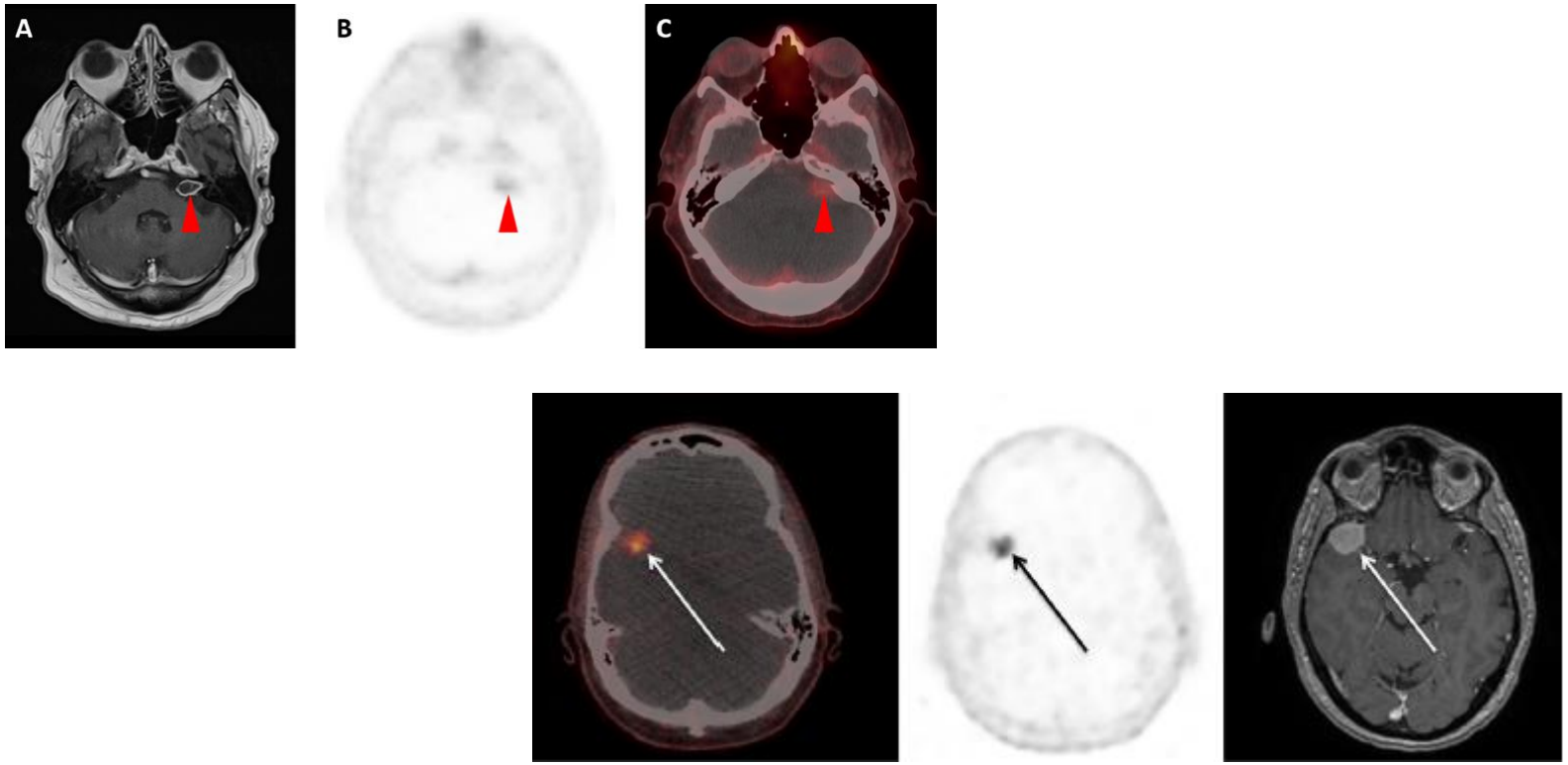
- Acute and chronic inflammatory processes
  - Inflammatory LNs (after COVID-vaccination)
  - Granulomatous disease and sarcoidosis
  - Bowel disease (Crohn,…)

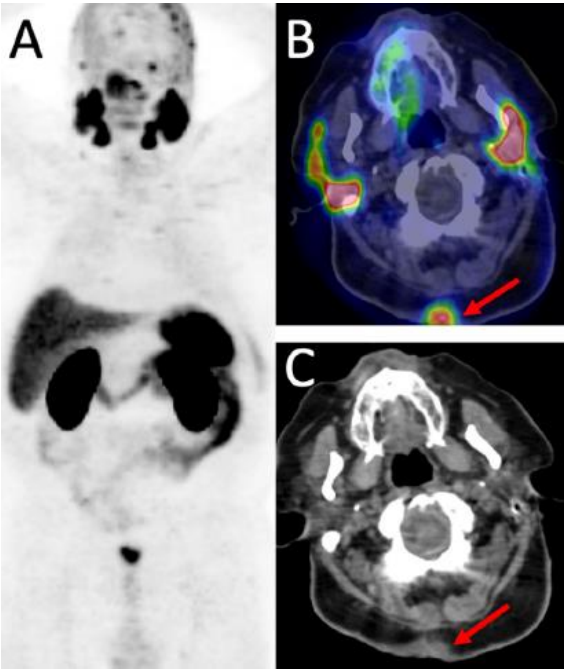




Pitfalls - benign lesions

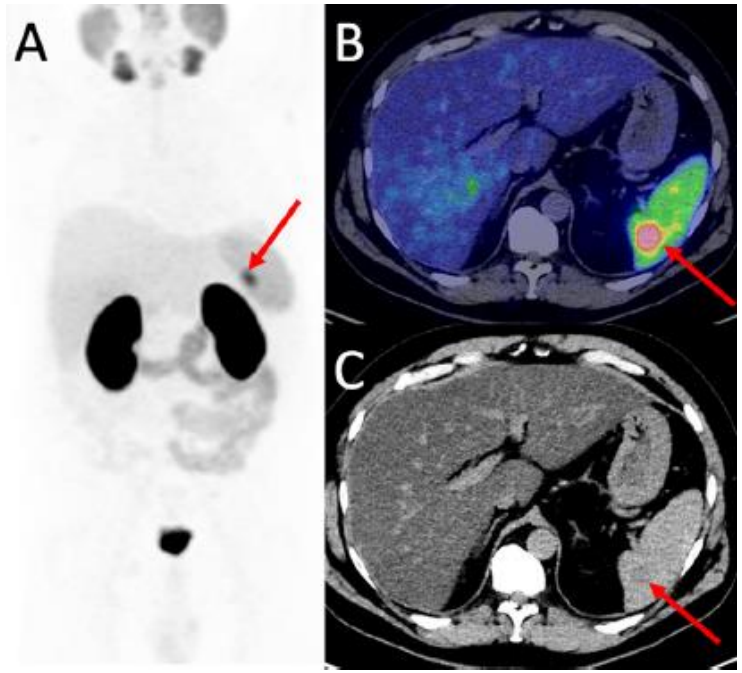
- Benign tumors of neurogenic origin
  - Meningioma, schwannoma, peripheral nerve sheath tumor





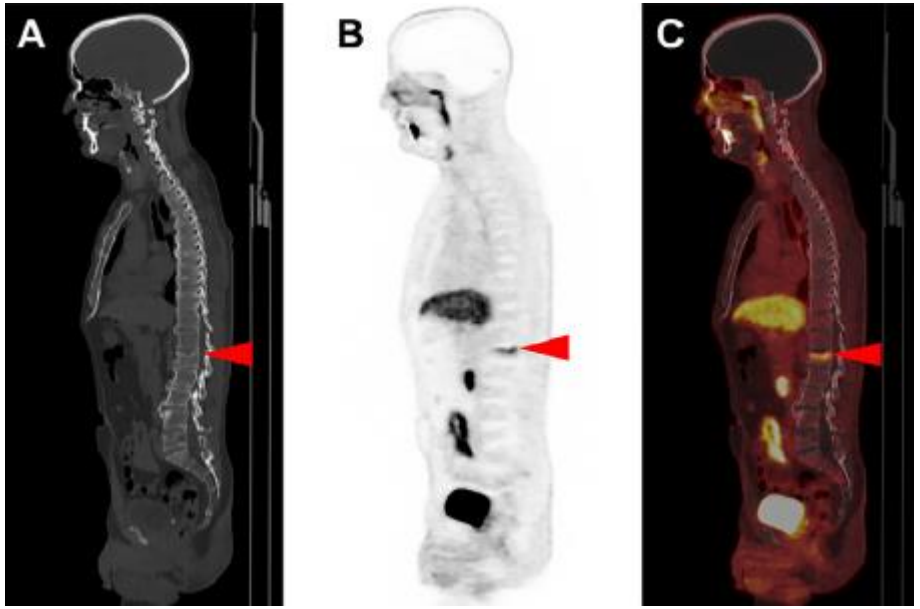
Pitfalls - benign lesions

- Hemangiomas
  - Due to high number of endothelial cells and vascular density
- Ischemic stroke, radionecrosis



Pitfalls - benign lesions

- Osteoblastic activity
  - Osteoarthritis, fractures, fibrous dysplasia, degenerative changes
  - Paget's disease may also resemble bone metastases
  - In case of uncertainty, conventional imaging techniques (bone scintigraphy, CT, MRI) can help to discriminate benign bone lesions from PCa metastases



Disadvantages of ^{18}F-PSMA-tracers

- Unspecific lesions

	^{18}F-PSMA-1007	^{68}Ga-PSMA-11
Positive lesions	369	178
Suspicious lesions	124 (34%)	126 (71%)
Benign lesions	245 (66%)	52 (29%)

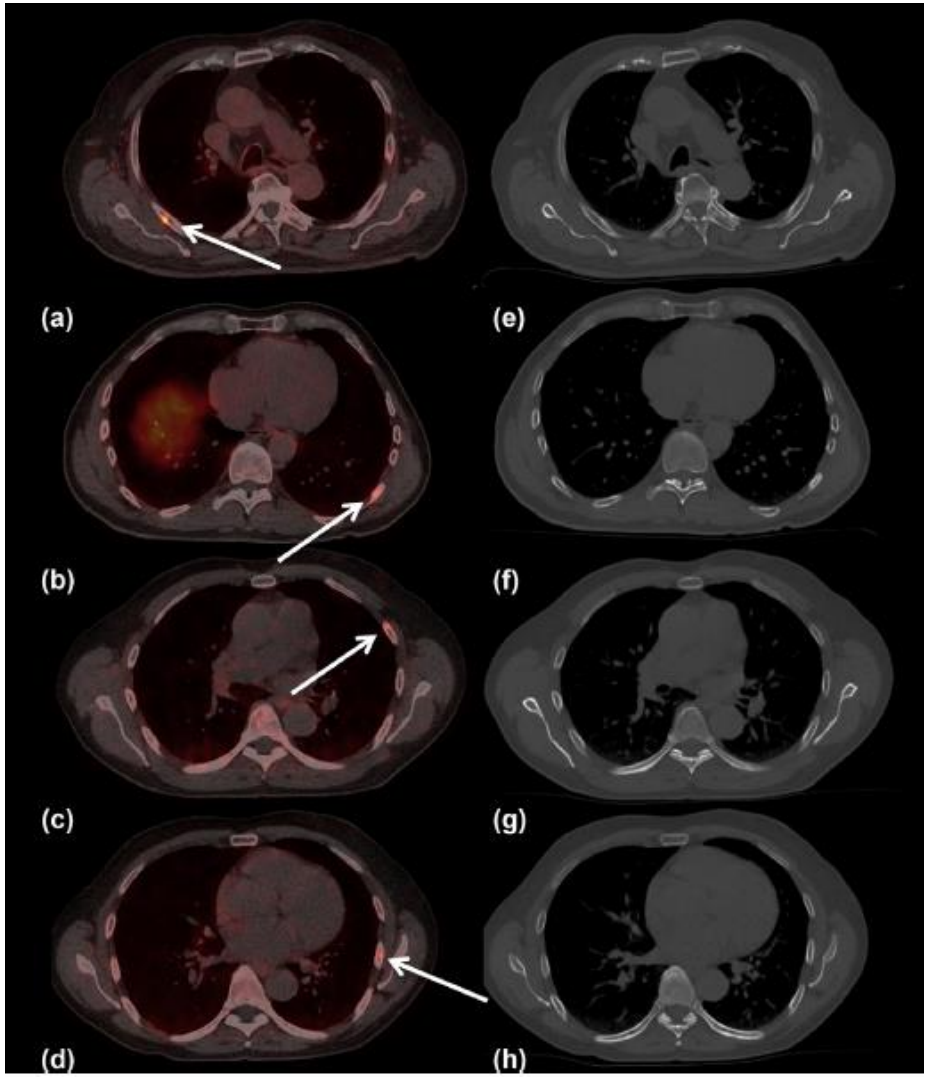
Benign lesions	**^{18}F-PSMA-1007 (n=245)**	**^{68}Ga-PSMA-11 (n=52)**
Ganglia	106 (43%)	15 (29%)
Unspecific LNs	77 (31%)	22 (42%)
Bone lesions	58 (24%)	14 (27%)

Bone lesions	**^{18}F-PSMA-1007**	**^{68}Ga-PSMA-11**
Fracture	3 (5%)	2 (14%)
Degeneration	13 (22%)	3 (21%)
Unclear	6 (10%)	3 (21%)
Unspecific uptake	36 (62%)	6 (43%)

- Different biodistribution (liver)
  - Use for patient selection RLT

Rauscher et al., JNM 2020

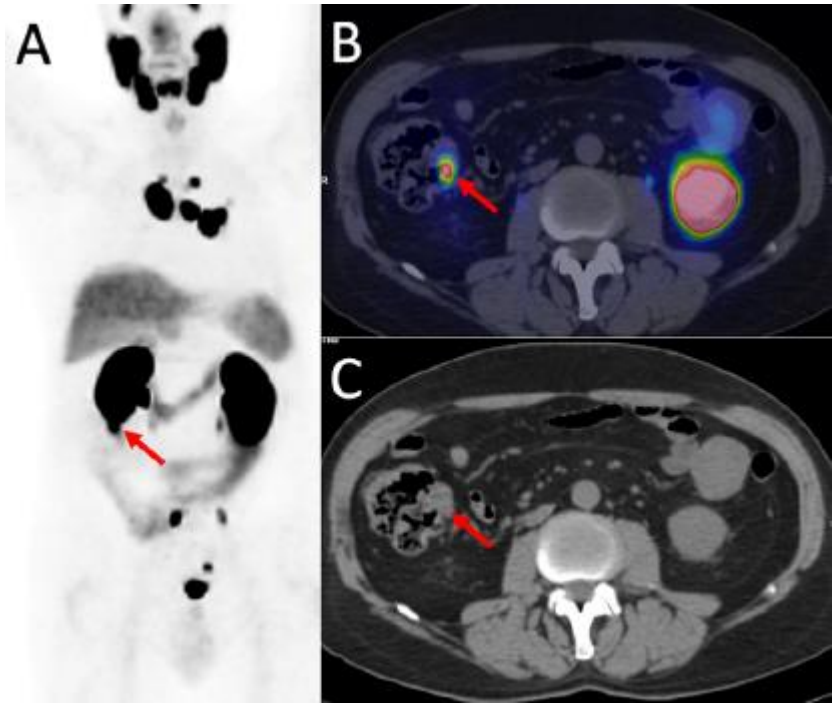
Unspecific bone lesions



Foley et al., Clin Radiol 2020

Other malignant disease

- Many other malignant tumors exhibit increased PSMA uptake
  - Related to tumor neo-angiogenesis
- Examples
  - RCC
  - HCC
  - Benign and malignant pancreatic lesions
  - Bladder adenocarcinoma
  - Glioblastoma
  - Breast carcinoma
  - Gastric and colorectal cancer
  - Adenoid cystic carcinoma of the salivary gland
  - Thymic carcinoma
  - Multiple myeloma, lymphoma
  - Papillary thyroid carcinomas



Colon adenocarcinoma

Standardized reporting: E-PSMA

1. Qualitative (PSMA expression V) and quantitative (PSMA expression Q = SUV_{max}) evaluation of lesions

PSMA expression V (visual score)	Grade of PSMA expression
Score=0	Below blood pool
Score=1	Equal to or above blood pool and lower than liver
Score=2	Equal to or above liver and lower than parotid gland
Score=3	Equal to or above parotid gland

2. Interpretation of PSMA-PET findings based on PSMA expression scores

Score	Definition
1	Benign lesion without abnormal PSMA uptake
2	Probably benign lesion: faint PSMA uptake (equal or lower than background) in a site atypical for prostate cancer
3	Equivocal finding: faint uptake in a site typical for prostate cancer or intense uptake in a site atypical for prostate cancer
4	Probably prostate cancer: intense uptake in typical site of prostate cancer, but without definitive findings on CT*
5	Definitive evidence of prostate cancer: intense uptake in typical site of prostate cancer, with definitive findings on CT

*A definitive finding on CT means the presence of a real anatomical substrate on the CT

3. Regional classification of PSMA-PET findings

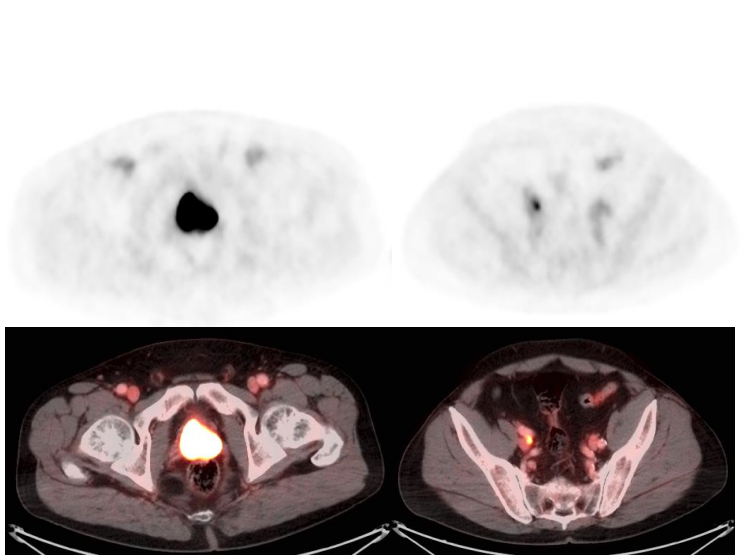
Class	Description
Local tumor (T)	
miT0	No local tumor
miT2	Organ-confined tumor
miT3a	Non-organ-confined tumor (extracapsular extension)
miT3b	Non-organ-confined tumor (seminal vesicles invasion)
miT4	Tumor invading adjacent structures (other than seminal vesicles)
miTr	Presence of local recurrence after radical prostatectomy
Regional nodes (N)	
miN0	No positive regional lymph nodes
miN1	Positive regional lymph nodes
Distant metastases (M)	
miM0	No distant metastases
miM1a	Extra-pelvic lymph nodes
miM1b	Bone metastasis
miM1c	Non-nodal visceral metastasis: report involved organ(s)

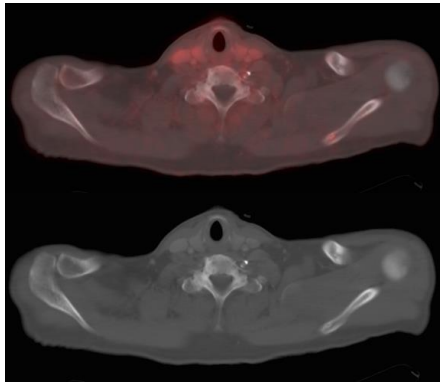
Standardized reporting: E-PSMA

	Prostate	LN iliaca externa R	Scapula L
PSMA expression V	Score 3	Score 2	Score 1
PSMA expression Q	SUV_{max} 33,5	SUV_{max} 6,8	SUV_{max} 1,8
Interpretation	Score 5	Score 5	Score 2

=> Regional classification: miT3bN1M0

Physiologic uptake (SUV_{mean})	
Liver	7,7
Spleen	7,6
Parotid	12,6





Take home messages

- When reading PSMA PET images
  - Indication
  - Tracer
  - Pitfalls
    - FN
    - FP (general – tracer specific)
  - Standardized reporting E-PSMA

- NucMed presence at MDC

- When in doubt, contact NucMed physician!

10th edition
GLOBAL CONGRESS ON PROSTATE CANCER
JUBILEE EDITION