Integrating MRI and PSMA PET Imaging in Prostate Cancer

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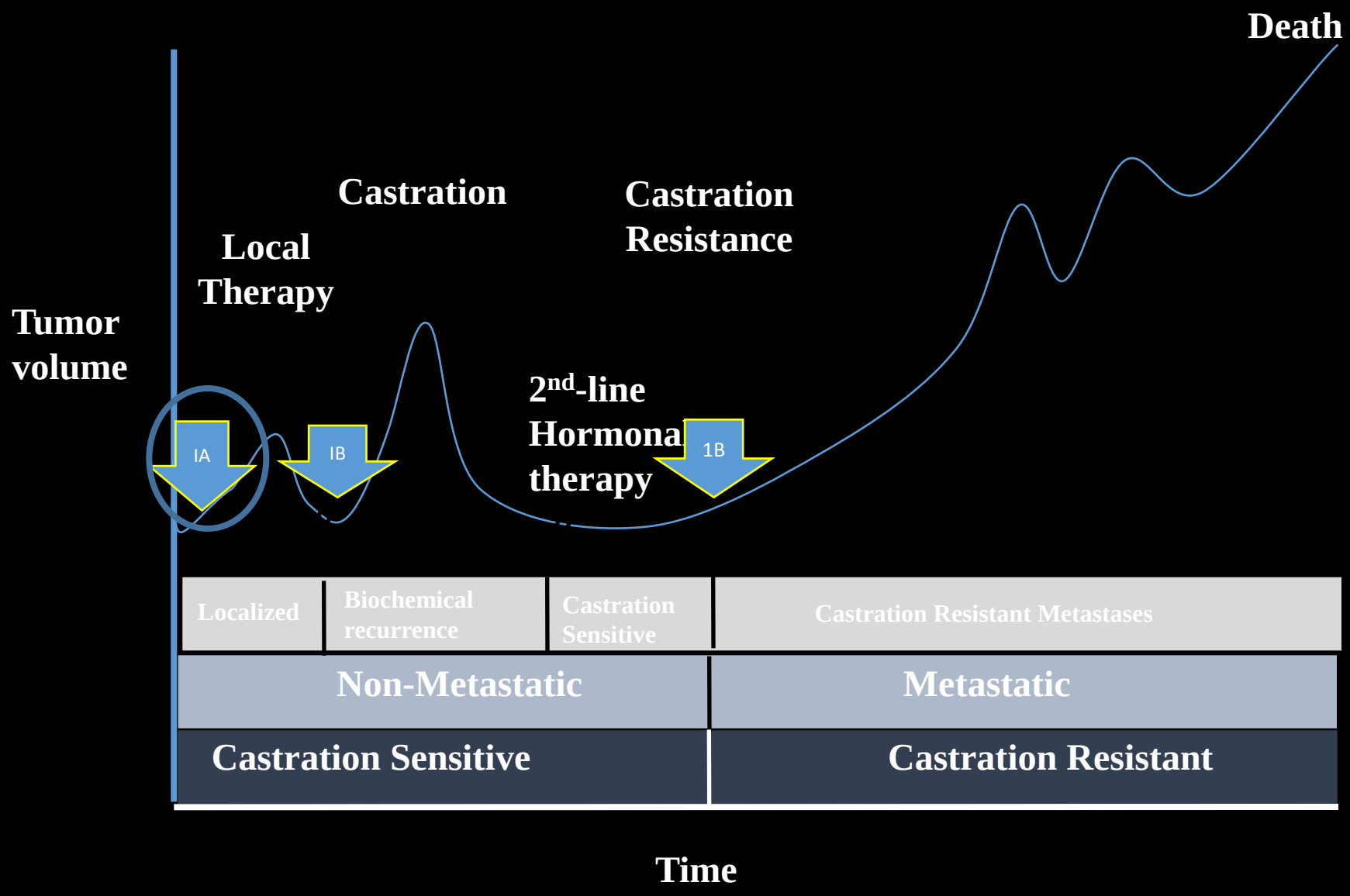
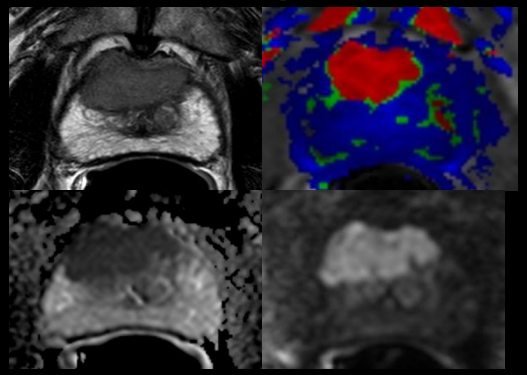
Natural History of Prostate Cancer



How can PET imaging help?

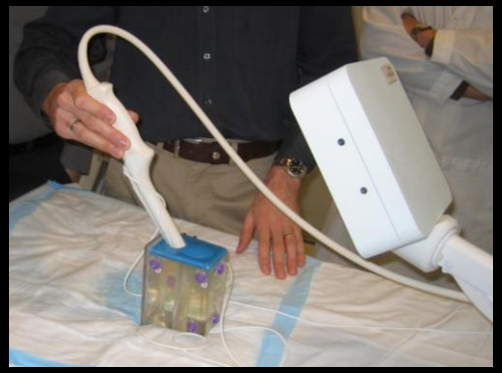
- For localized disease: Staging
  - Is there disease in nodes or bones?
  - Is there disease in seminal vesicles?
- For Recurrent disease: Restaging
  - Is there residual tumor in prostate bed?
  - Is there nodal or bony disease?
- For Metastatic disease:
  - What is extent of disease?
  - Is it progressing or responding to therapy?

The Development of Prostate Imaging and Image Guided Biopsy 2000-2016



Multiparametric MRI 2000's

In gantry biopsy 2003-6



MRI-TRUS-GPS-2006

Clinic MR-TRUS Fusion 2008

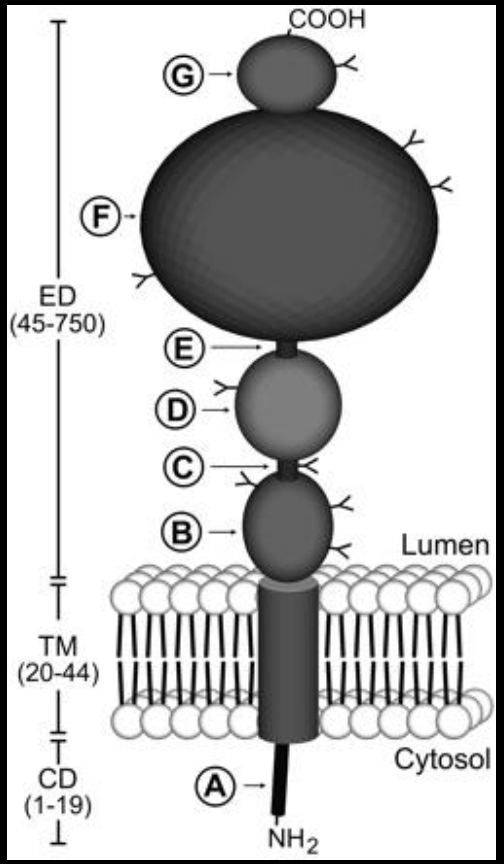
Commercial MR-TRUS fusion Devices 2013

World wide- Image Guided Bx (IGB) 2016

Prostate Specific Membrane Antigen (PSMA)

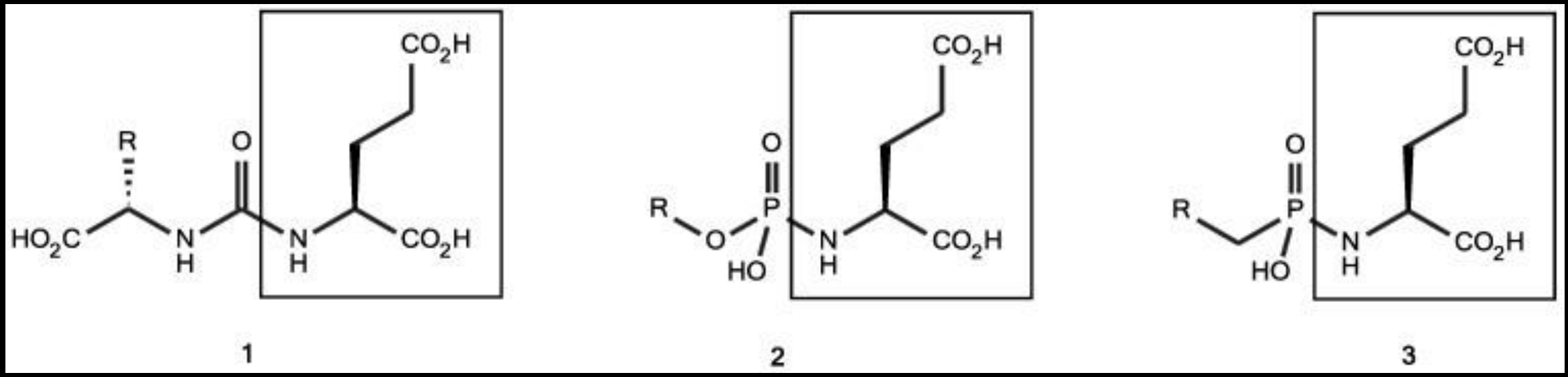
- PSMA (prostate specific membrane antigen) is a transmembrane protein, which is highly expressed in many prostate cancers, particularly high grade cancers.

- Urea-based compounds have high affinity for the enzymatic domain of PSMA and are used for PET imaging

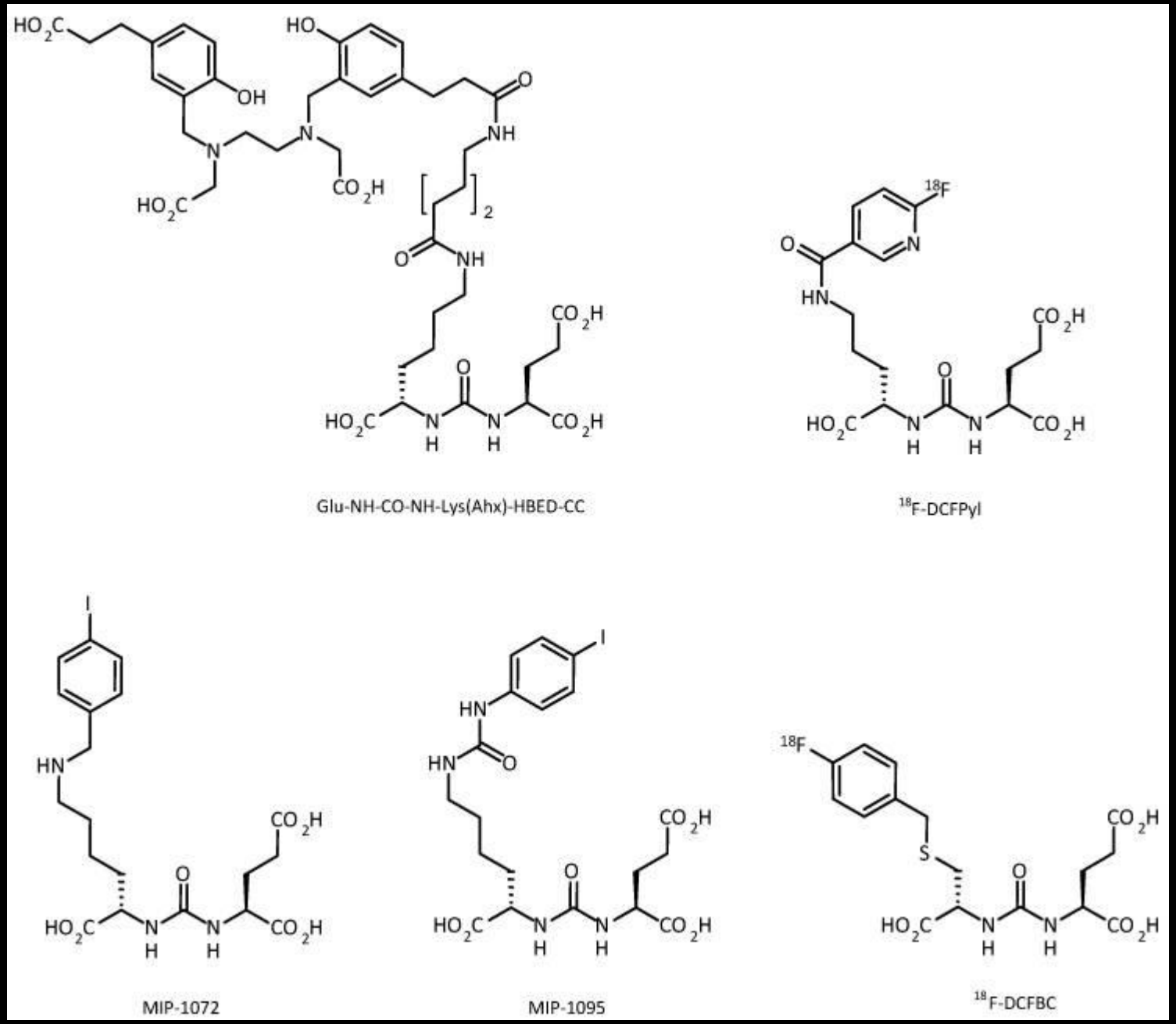


PSMA receptor

http://ajpcell.physiology.org/content/288/5/C975



Lutje et al Theranostics 2016



Lutje et al Theranostics 2016

PSMA PET Imaging

- Available PSMA targeting PET tracers:
  - ^{68}Ga Labelled:
    - ^{68}Ga-PSMA-11 (^{68}Ga-PSMA-HBED-CC)
  - ^{18}F Labelled:
    - 18F-DCFBC
    - 18F-DCFPyL

Comparison of ^{68}Ga and ^{18}F

^{68}Ga		^{18}F
68	half life (min)	110
generator	production	cyclotron
1899	Positron energy (keV)	633
89%	Positron yield	96%

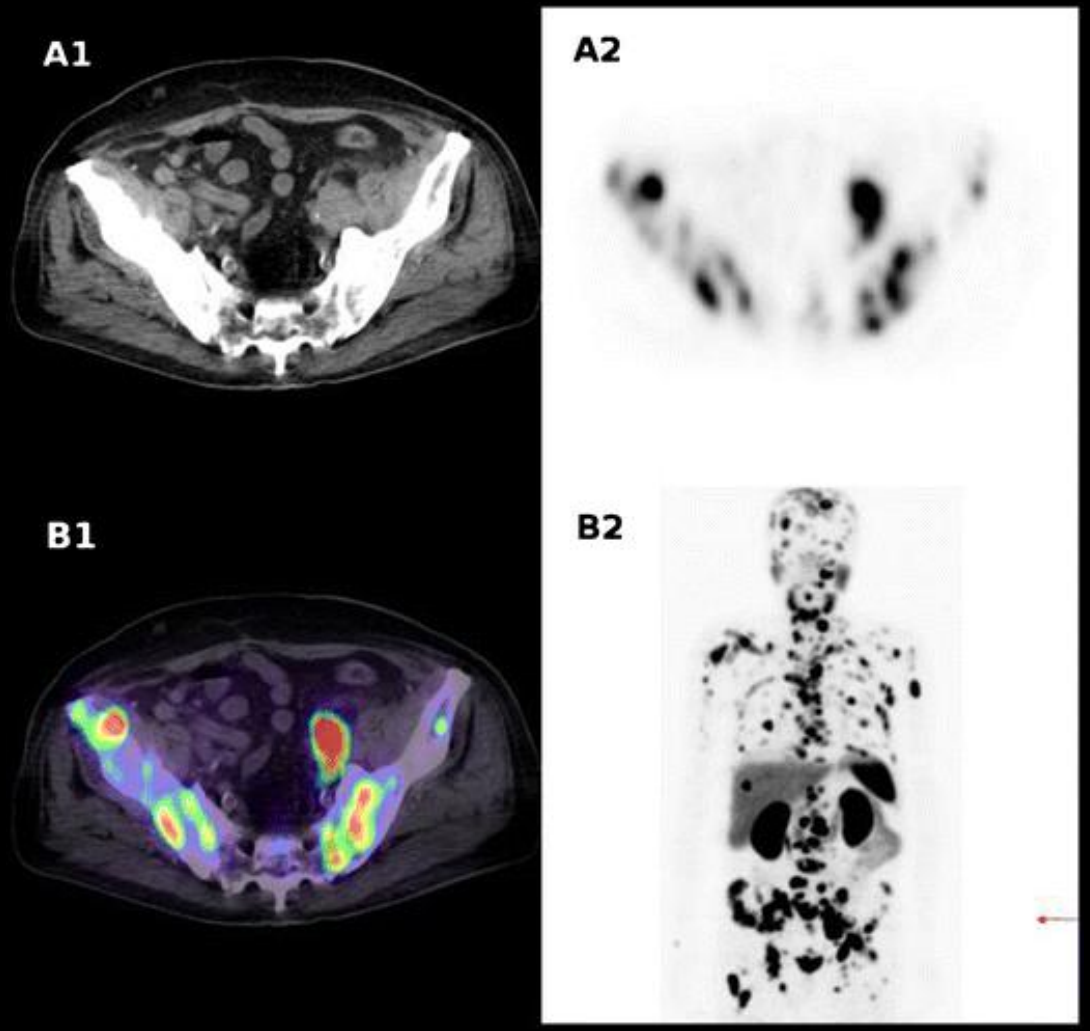
^{68}Ga PSMA-11 PET

- Small ligand, imaged 60 minutes after injection
- 319 PC pts Afshar-Oromieh et al 2015
  - Lesion-based analysis: Sens, Spec, NPV, PPV: 76.6%, 100%, 91.4% and 100%
  - Patient-based analysis : sensitivity 88.1%
  - 416 histological lesions: 30 false negative on ^{68}Ga
- BCR in 248 pts after RP Eiber et al 2015
- PET/MR more accurate than PET/CT Afshar-Oromieh et al 2014

Tumor detection rate (%)	PSA (ng/ml)
58	0.2-0.5
73	0.5-1
93	1-2
97	≥2

^{68}Ga PSMA

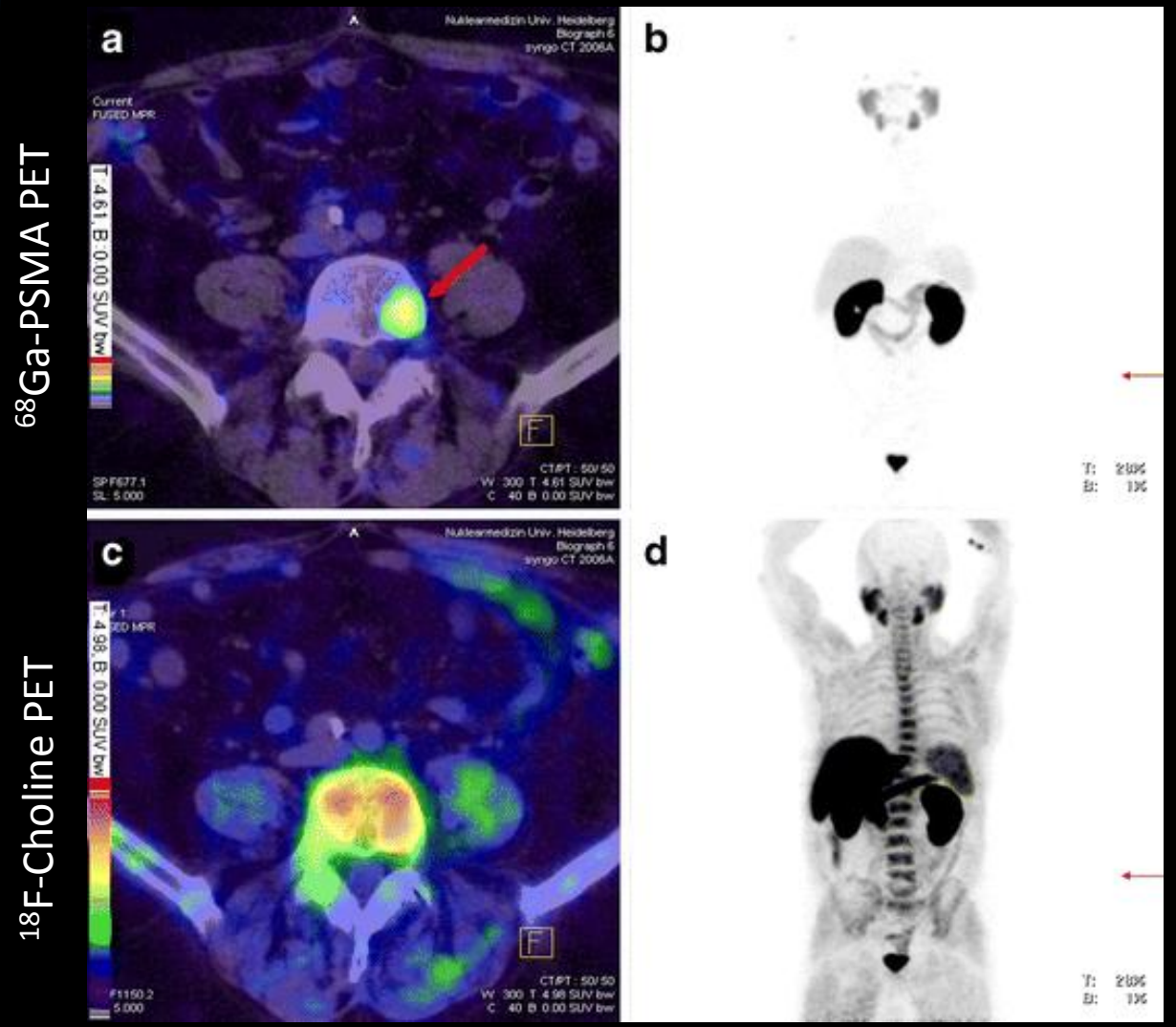
Afshar-Oromeih et al, EJNMMI 2013



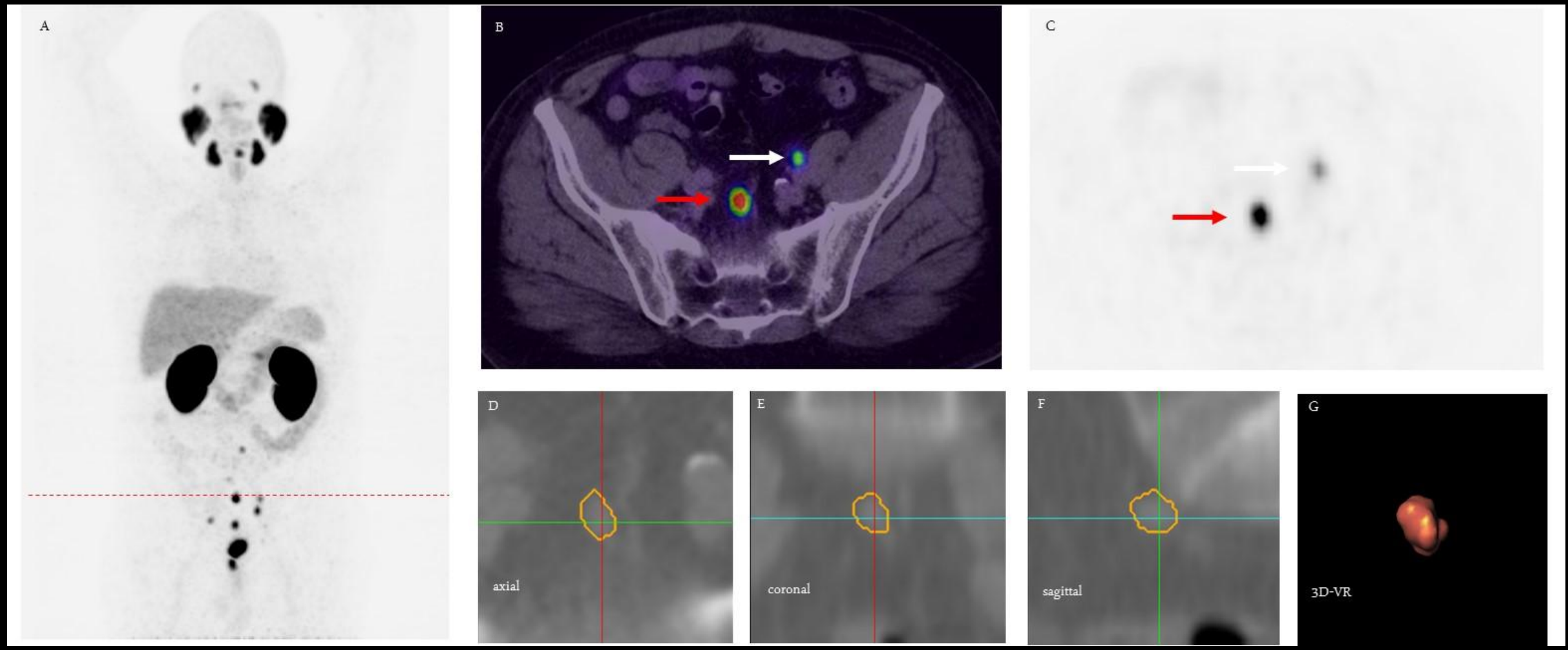
^{68}Ga-PSMA PET/CT demonstrating a patient representative for disseminated lymph node and bone metastases of prostate cancer.

^{68}Ga PSMA vs ^{18}F-Choline

Afshar-Oromieh et al, EJNMMI 2014



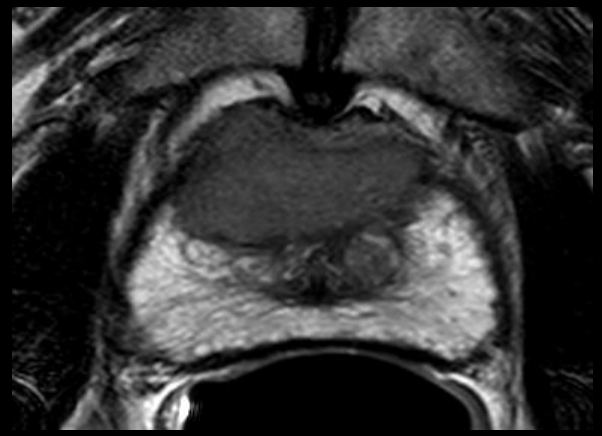
71-year old man with PSA=4ng/ml after radical prostatectomy.



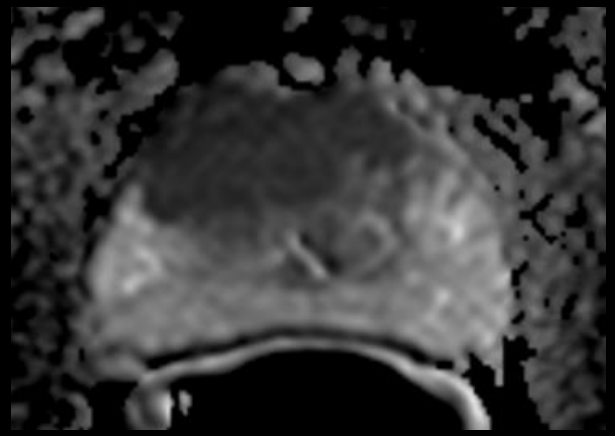
Courtesy of Dr. Frederik Giesel from University of Heidelberg, Germany

^{18}F-DCFBC PET

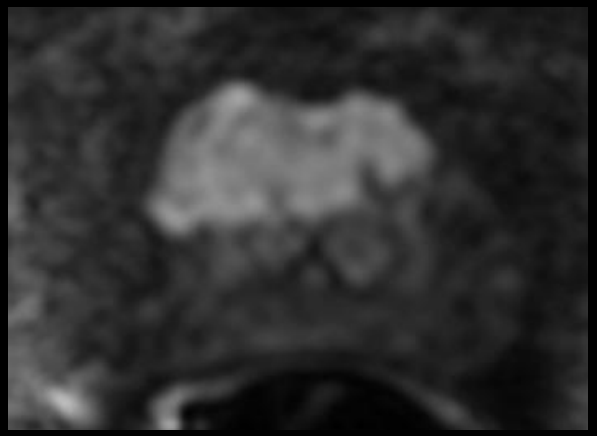
- ^{18}F- *N*-[*N*-[(*S*)-1,3-dicarboxypropyl] carbamoyl]-4-[^{18}F]fluorobenzyl-l-cysteine
- Low molecular weight PSMA inhibitor
- 5 pts with PCa metastases Cho et al 2012
  - Biodistribution, dosimetry
  - 32 PET positive lesions
    - 21 concordant with conventional imaging
    - 11 only with DCFBC, most in bone



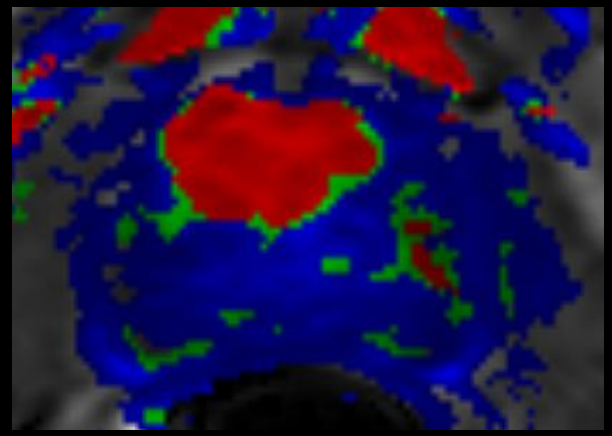
T2W MRI



ADC map

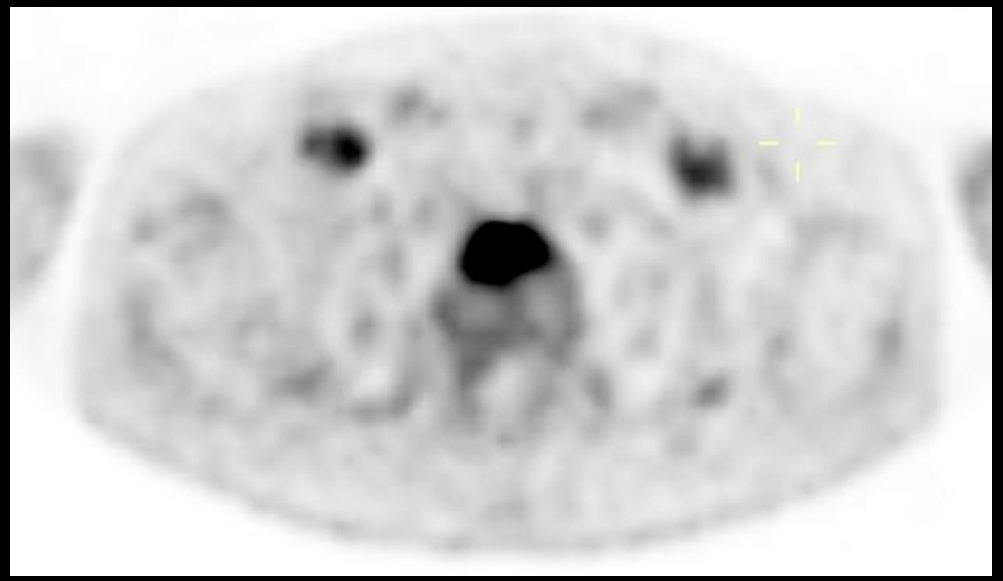


B=2000 DWI



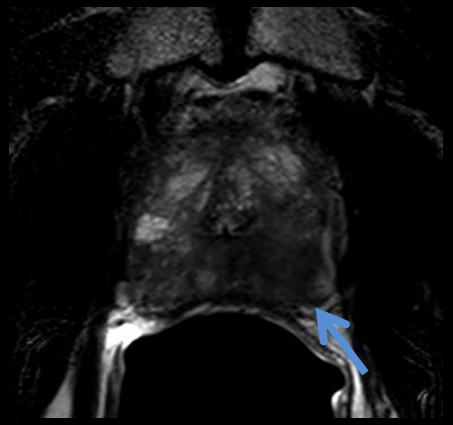
DCE MRI permeability map

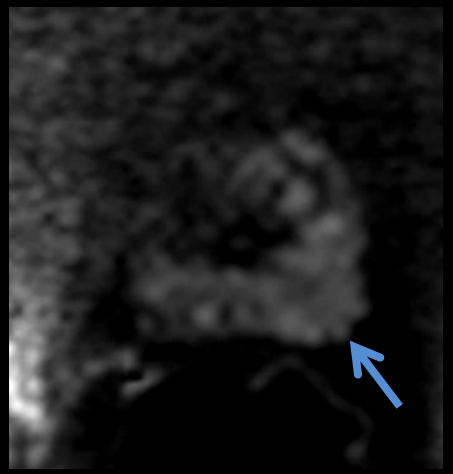
TRUS/MRI fusion guided biopsy Gleason 4+5 prostate cancer

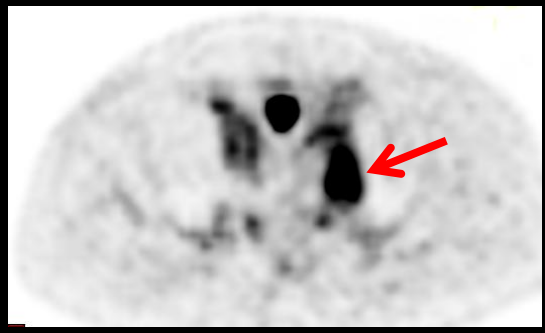


18F-DCFBC PET study localizes the anterior TZ lesion

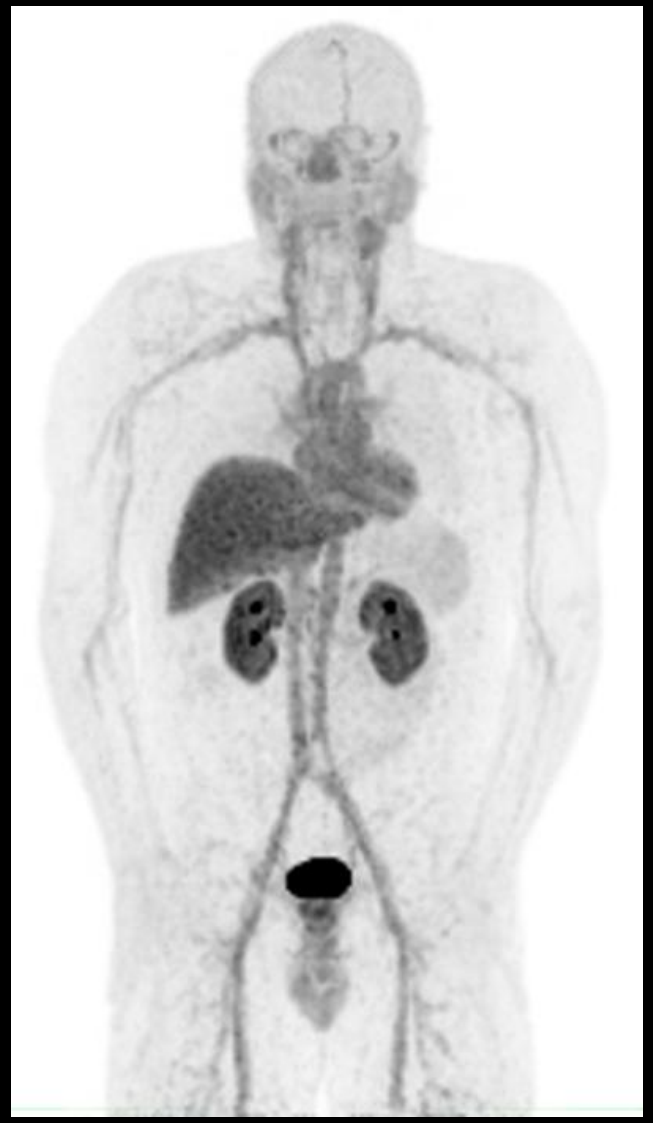
66-year old man, Gleason 4+5 PSA=216ng/ml

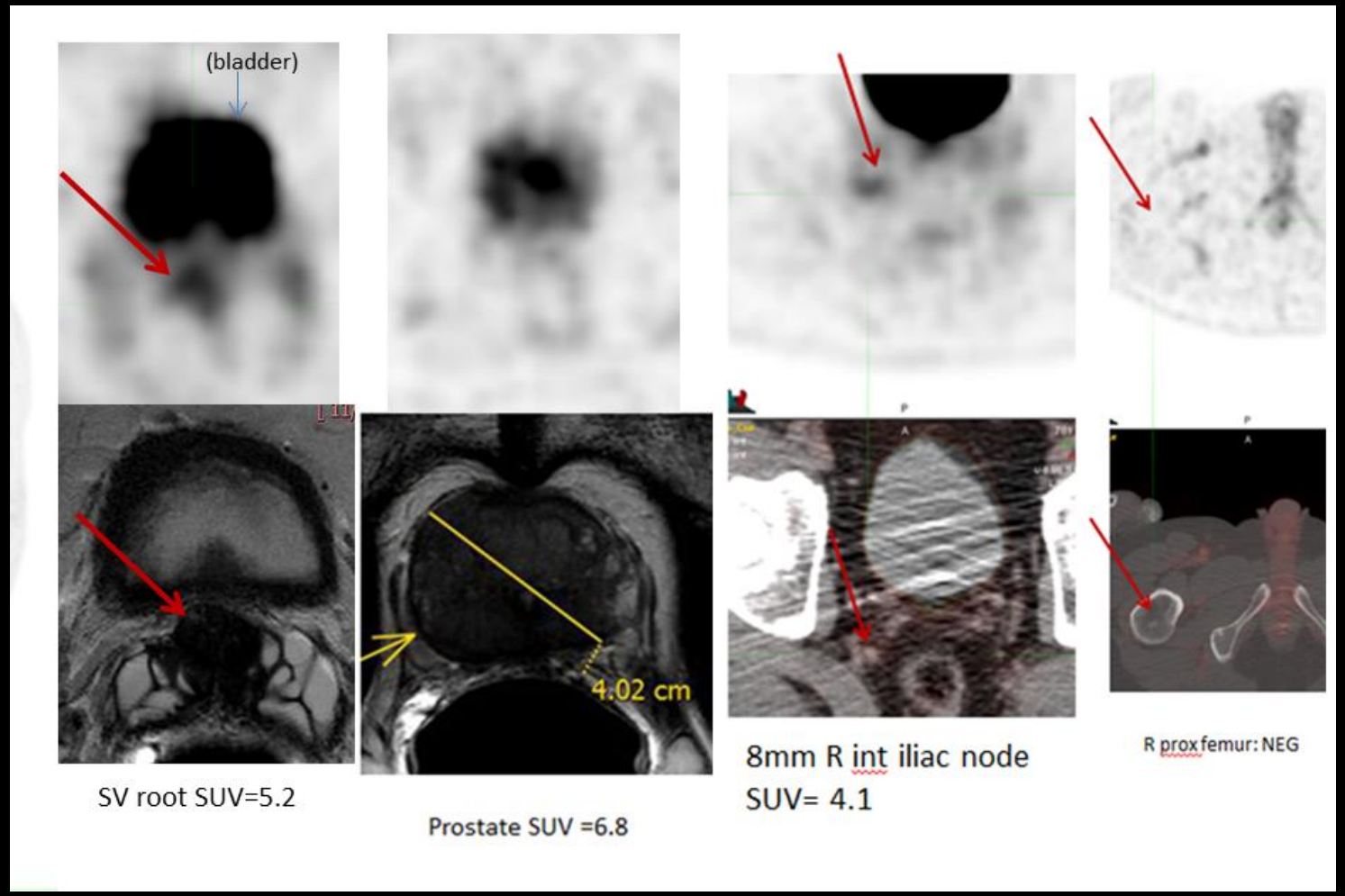




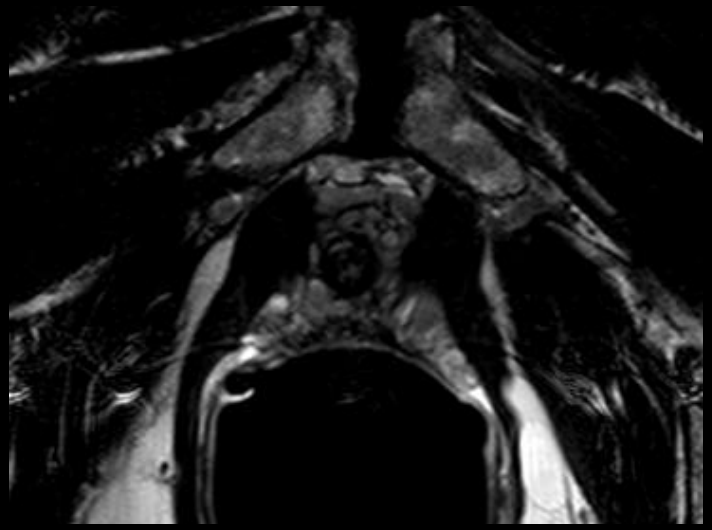


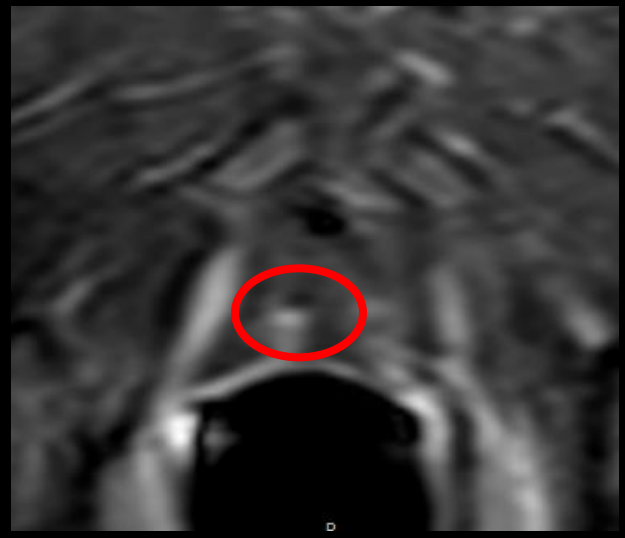
64-year old man, Gleason 5+4 PSA=39ng/ml with seminal vesicle and nodal metastases

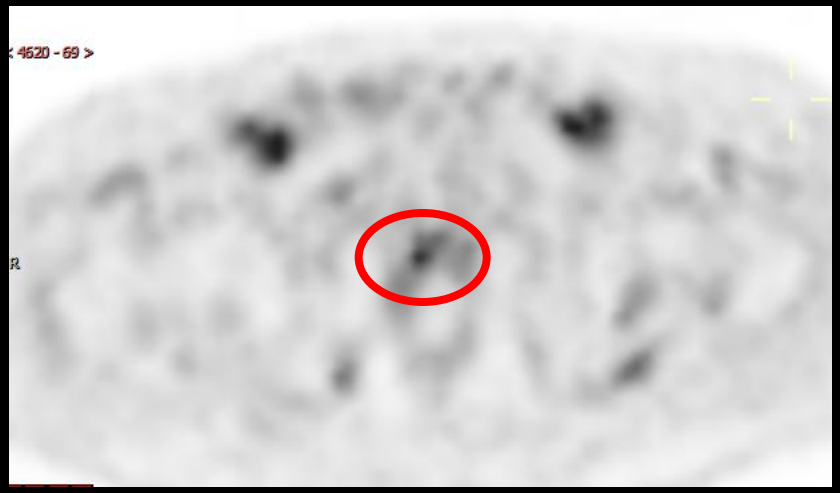


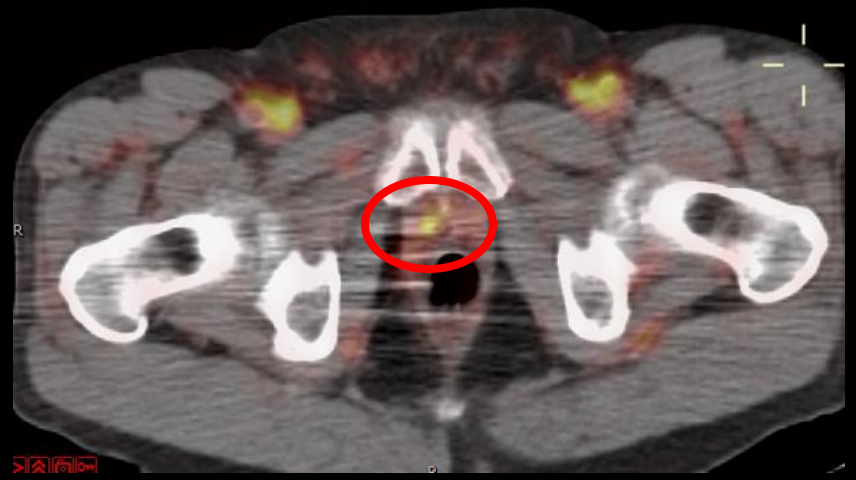


69-year old man, S/P RP 6 years ago, PSA=0.25ng/ml



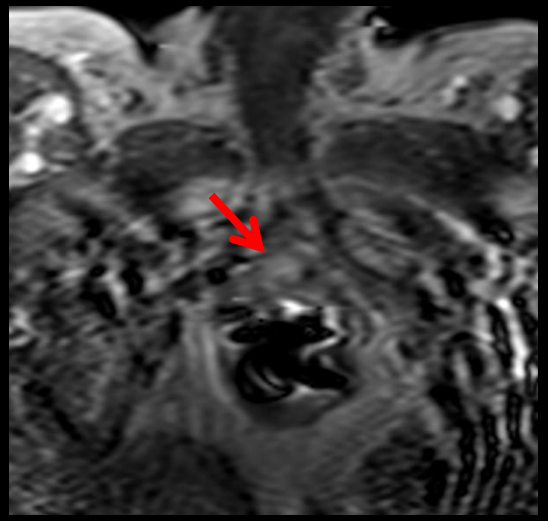




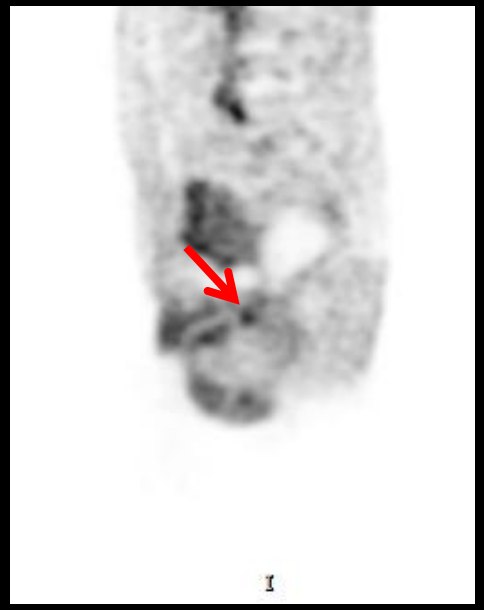


58-year old man, S/P radical prostatectomy, PSA=1.4ng/ml with recurrence at anastomosis

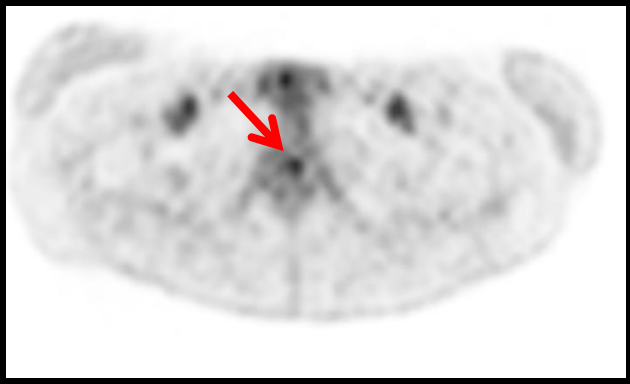
Axial T2W MRI



DCE MRI

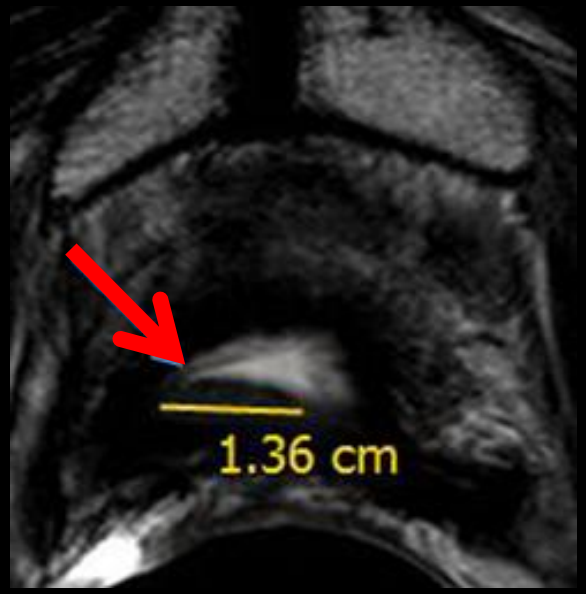


Sagittal ^{18}F-DCFBC PET

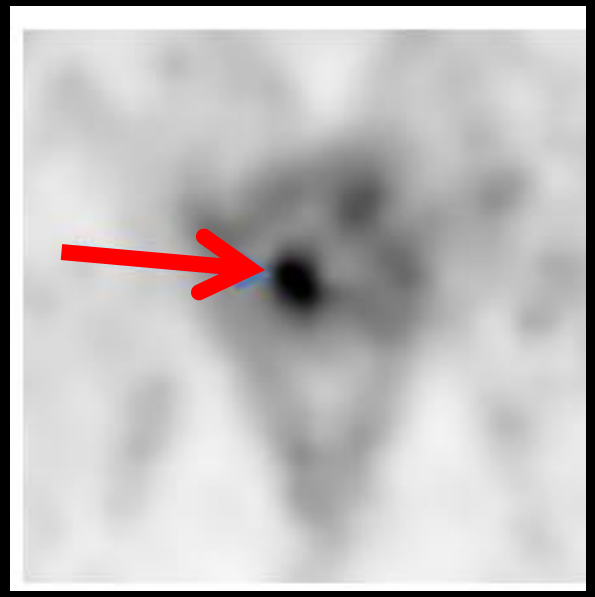


Axial ^{18}F-DCFBC PET

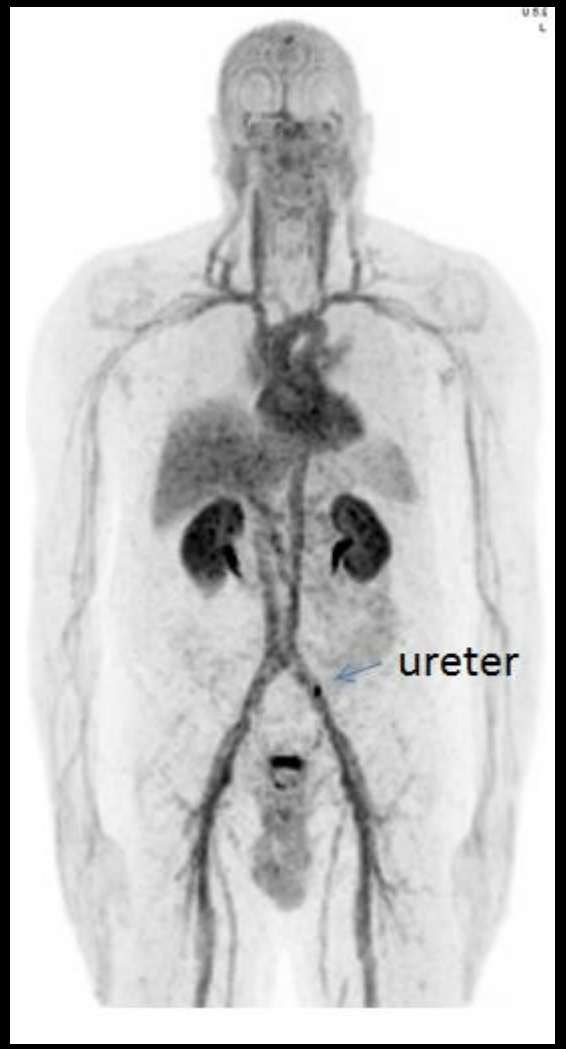
54-year old man, S/P radical prostatectomy, PSA=0.6ng/ml



Axial T2W MRI

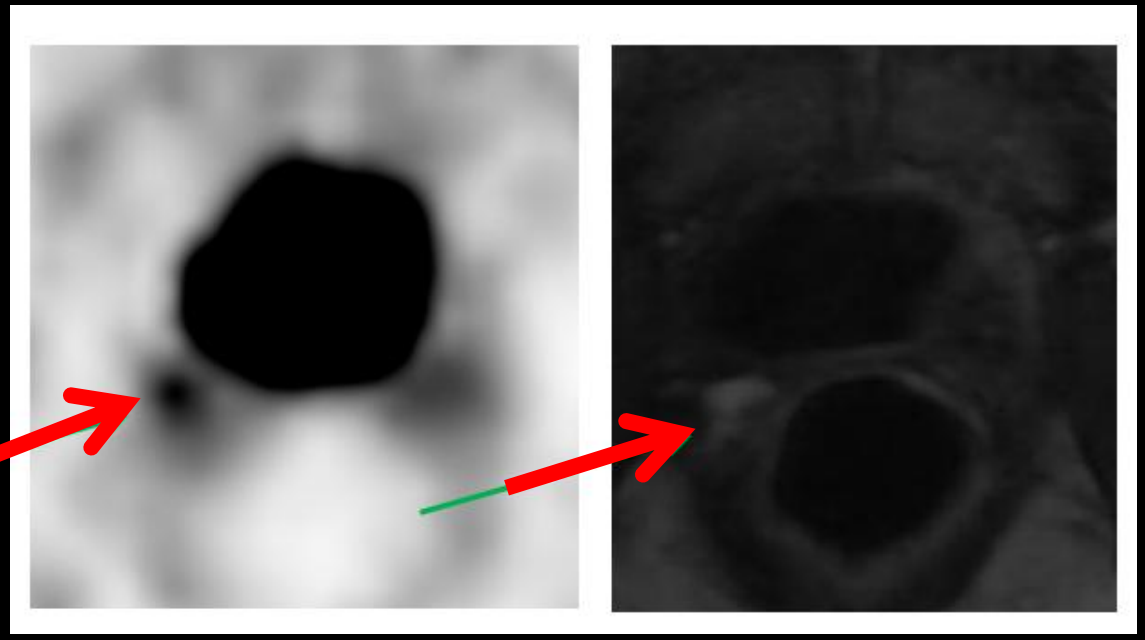


Axial ^{18}F-DCFBC PET



Coronal
^{18}F-DCFBC PET

54-year old man, S/P radical prostatectomy, PSA=0.9ng/ml with recurrence at right seminal vesicles

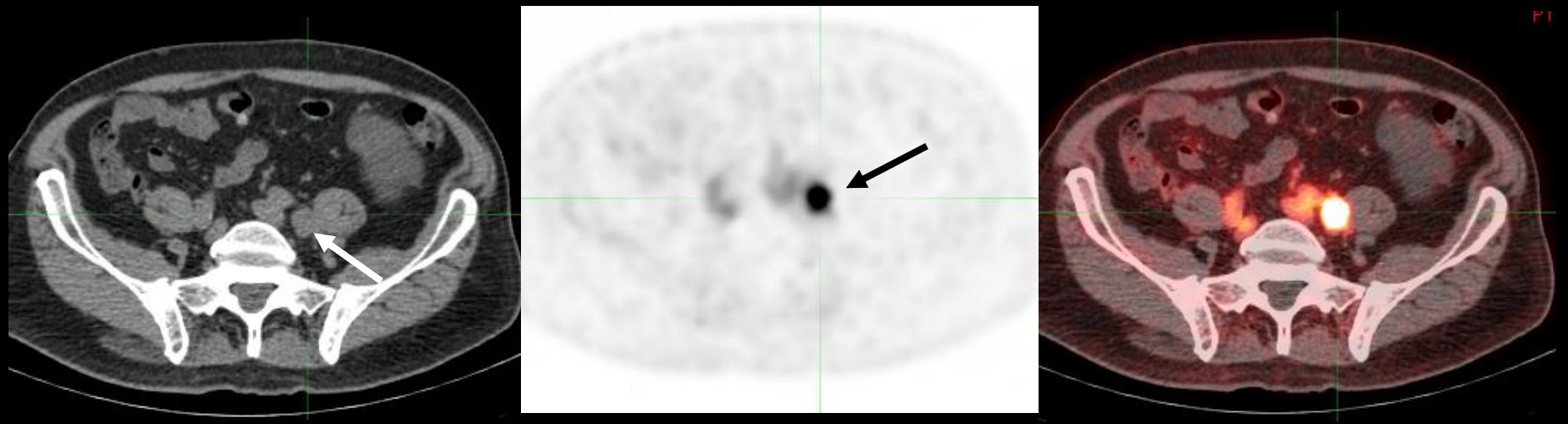


Axial ^{18}F-DCFBC PET

DCE MRI

Sagittal
^{18}F-DCFBC PET

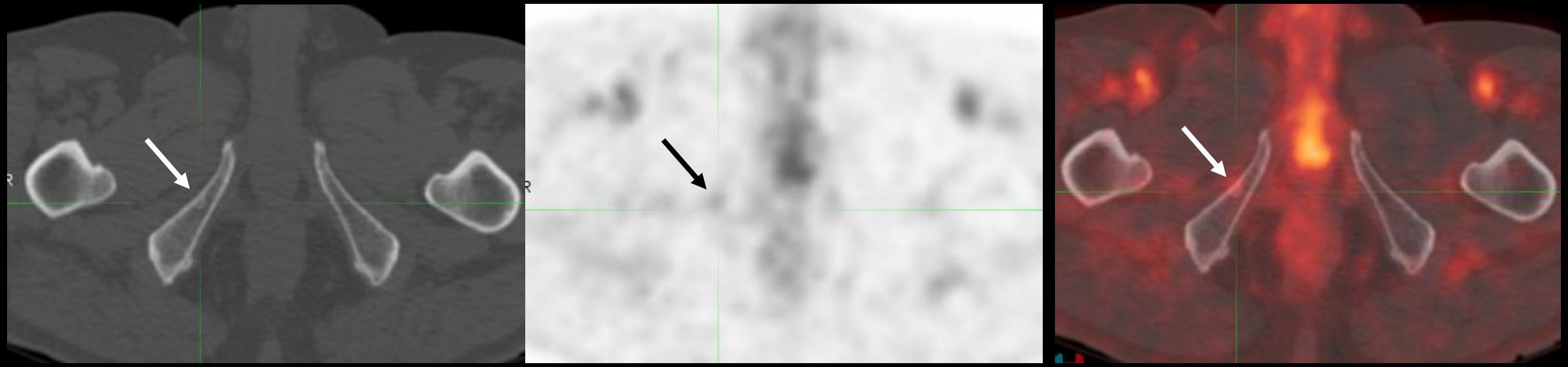
DCFBC 107 (JM) -
Arm 2: s/p RP + RT. , PSA = 1.97 ng/ml (09/12/2016)



Focal abnormal DCFBC uptake fusing to a 1.6x1.9 cm

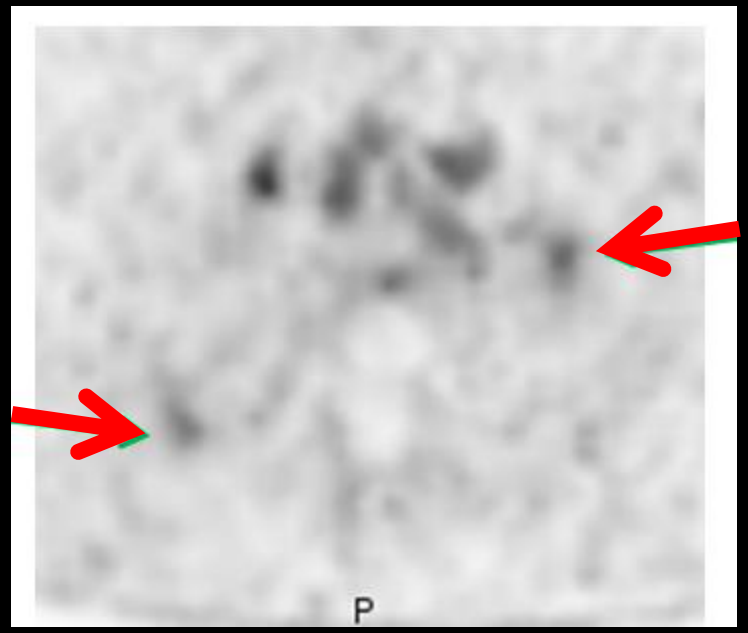
left common iliac lymph node [SUV_{max} 12.3]

DCFBC 107 (JM) -
Arm 2: s/p RP + RT. , PSA = 1.97 ng/ml (09/12/2016)



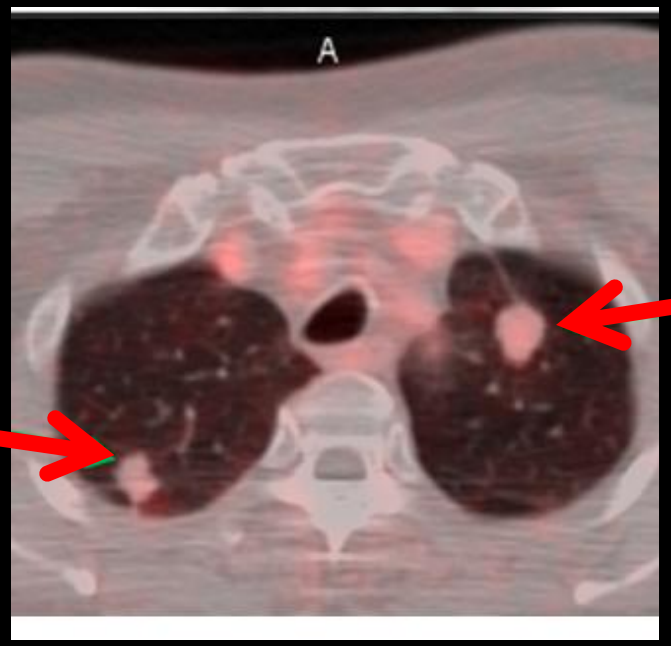
Very subtle DCFBC uptake fusing to a small sclerotic bony lesion in the right ischium.

68-year old man, S/P radical prostatectomy, PSA=9ng/ml



Axial ^{18}F-DCFBC PET

2hr SUV= 2.7



2hr SUV= 3.0

Axial ^{18}F-DCFBC PET/CT

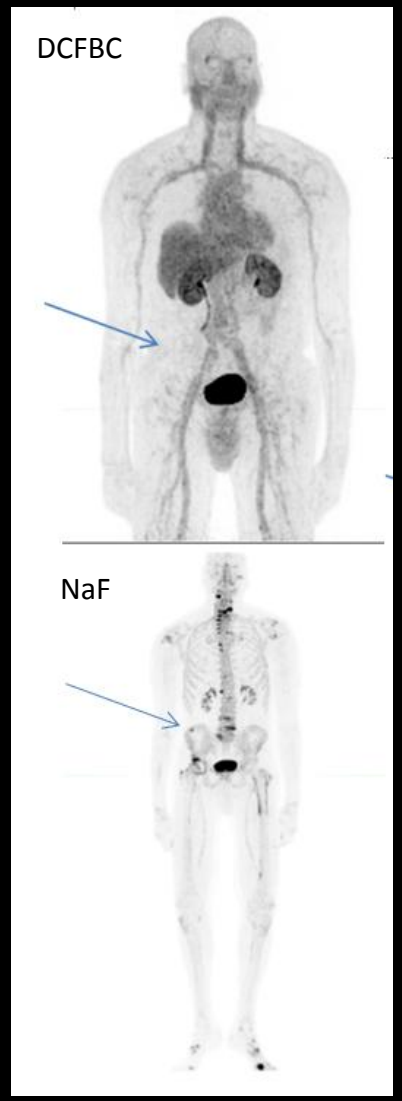
Coronal ^{18}F-DCFBC PET

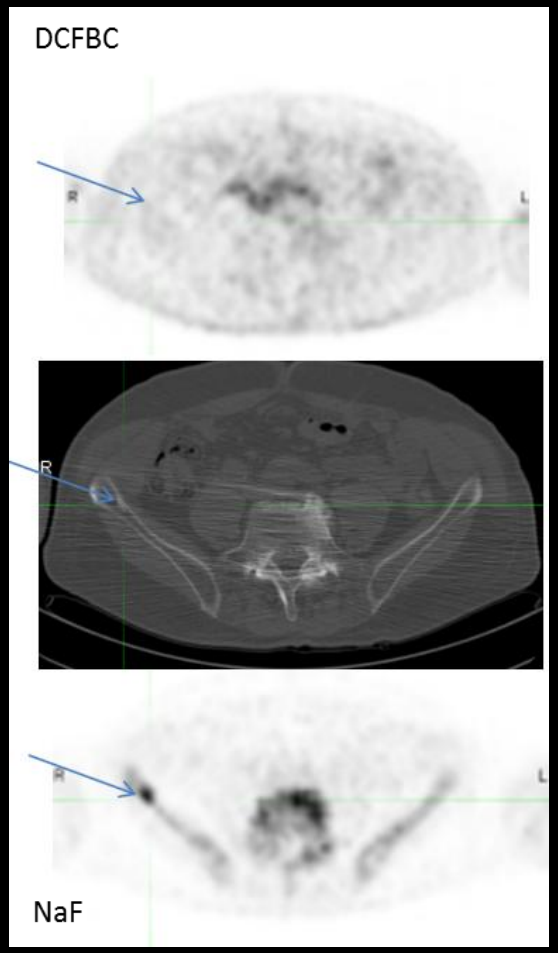
65-year old man on ADT, PSA=7.1ng/ml

18F-DCFBC PET
Paraaortic and
iliac nodes

18F- NaF PET:
negative for
metastases

73-year old man on ADT, PSA<0.01ng/ml





R Ilium bone lesion: Positive on NaF, negative on DCFBC PET

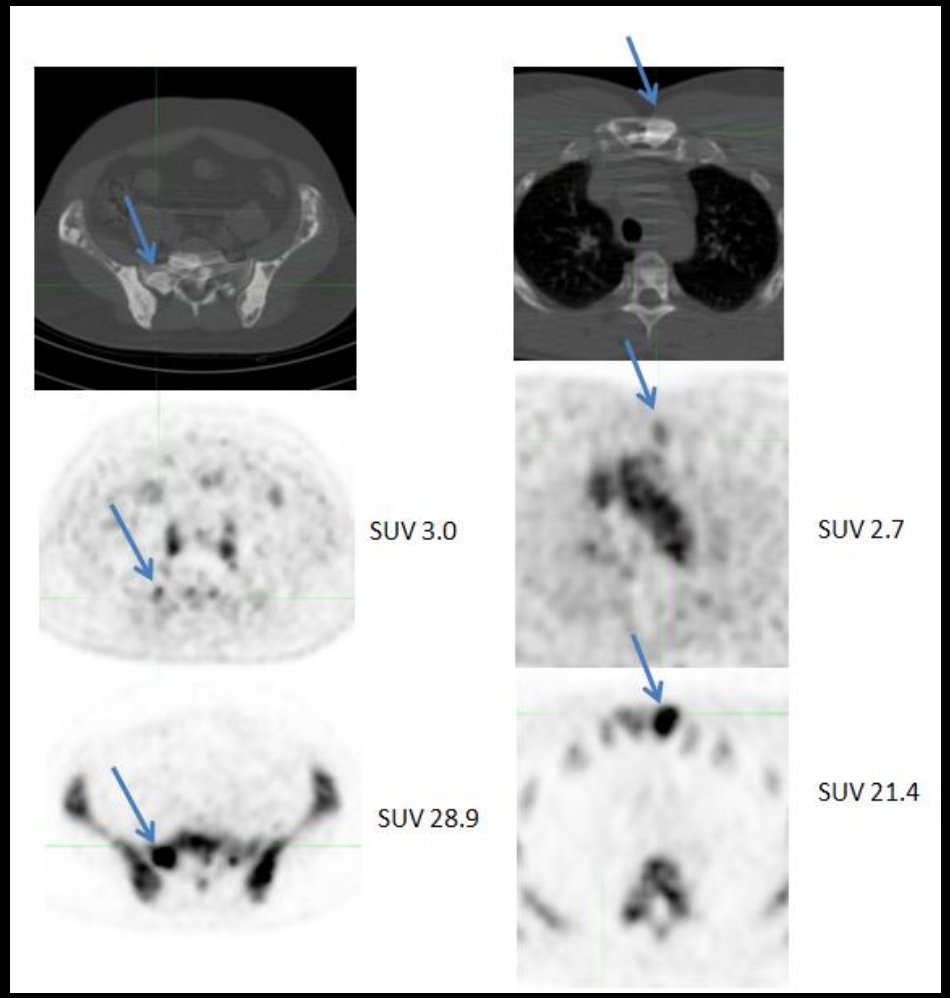
72 year old man on ADT: PSA 1.2ng/ml NaF(+) DCFBC (±). Is this patient in transition to AR status?

18F-NaF

18F-DCFBC

18F-DCFBC

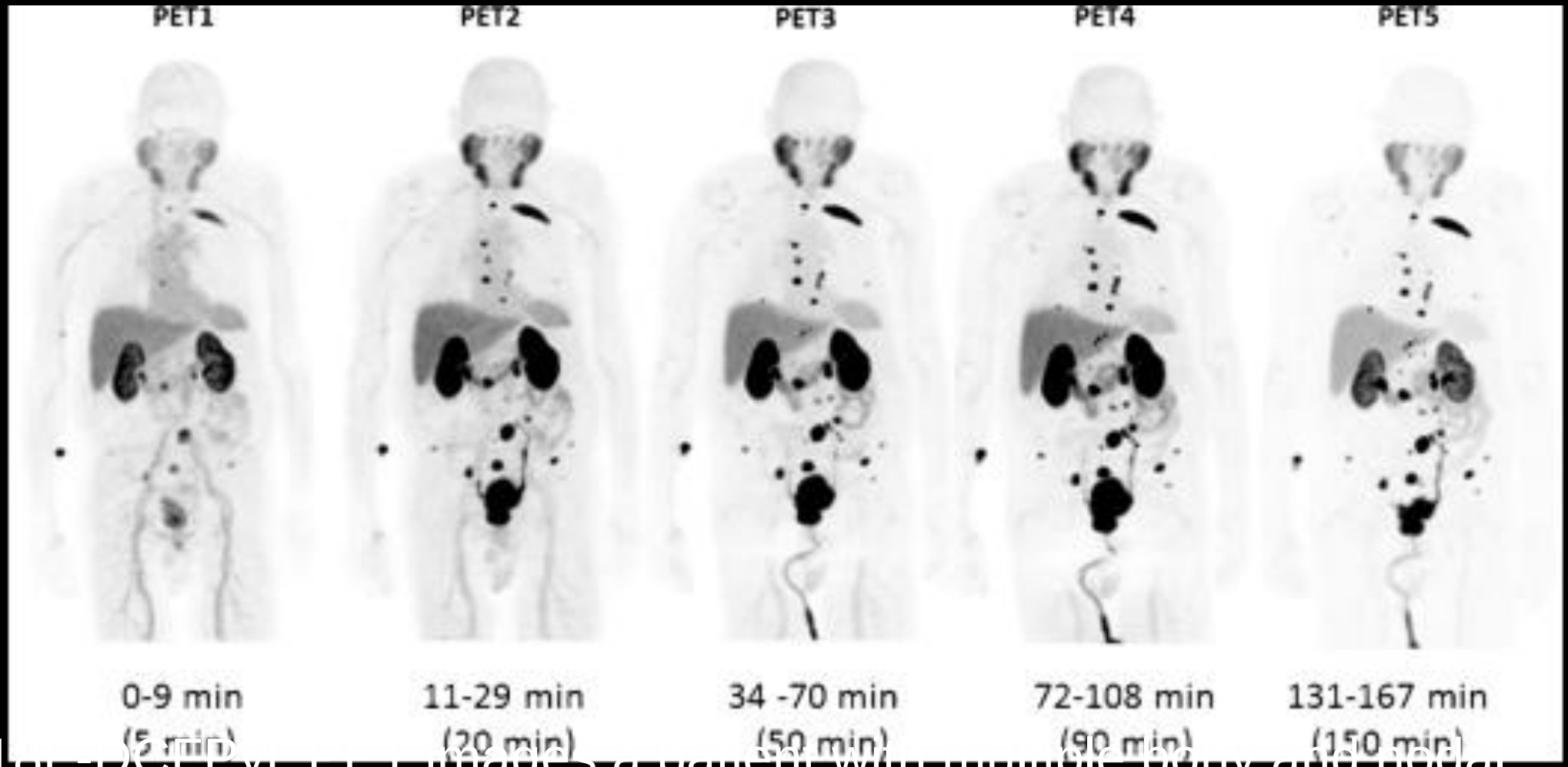
18F-NaF



^{18}F-DCFPyL PET

- 2-(3-{1-carboxy-5-[(6-[^{18}F]fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid.
- Markedly reduced blood pool activity with corresponding overall higher uptake in prostate cancer
- Superior to conventional imaging (8 patient pilot study by Rowe et al 2016).
- Commercial sponsor (now in phase 3 study).

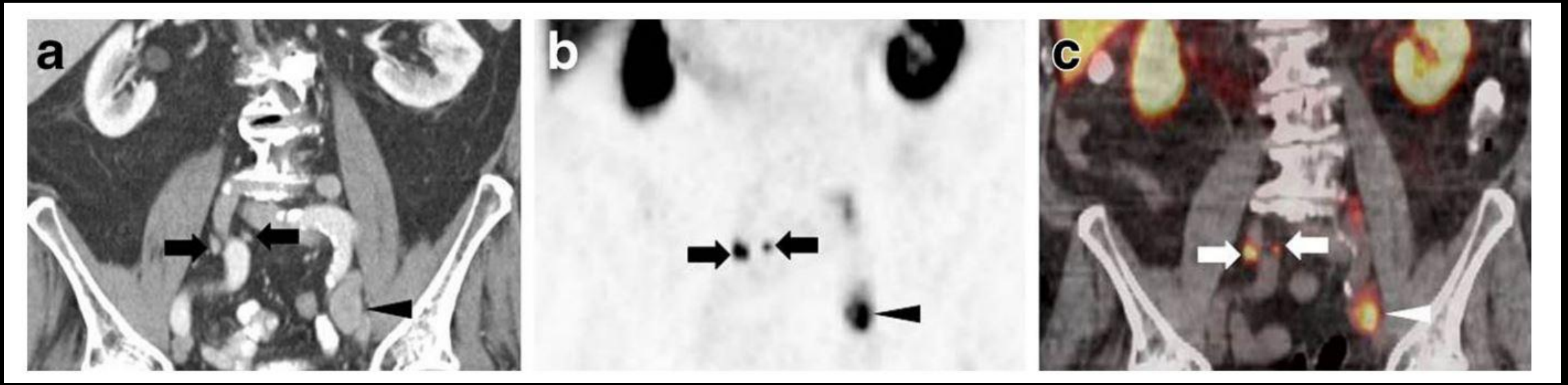
^{18}F-DCFPyL PET



18F-DCFPyL PET images a patient with multiple bony and nodal metastases.

Image courtesy of Dr. Martin Pomper, JHU

^{18}F-DCFPyL PET



Metastatic lymph nodes with variable sizes (4-6mm [arrows] and 20mm[arrowhead]) with selective uptake of 18F-DCFPyL in a prostate cancer patient.

Fig. 4.

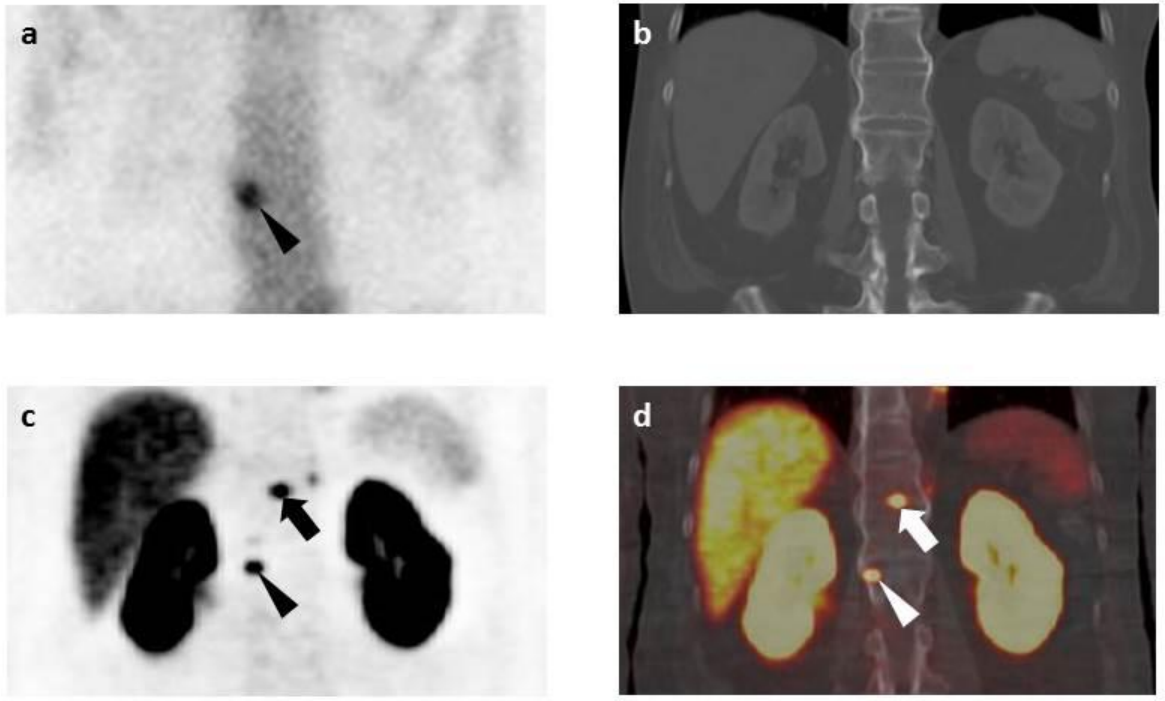
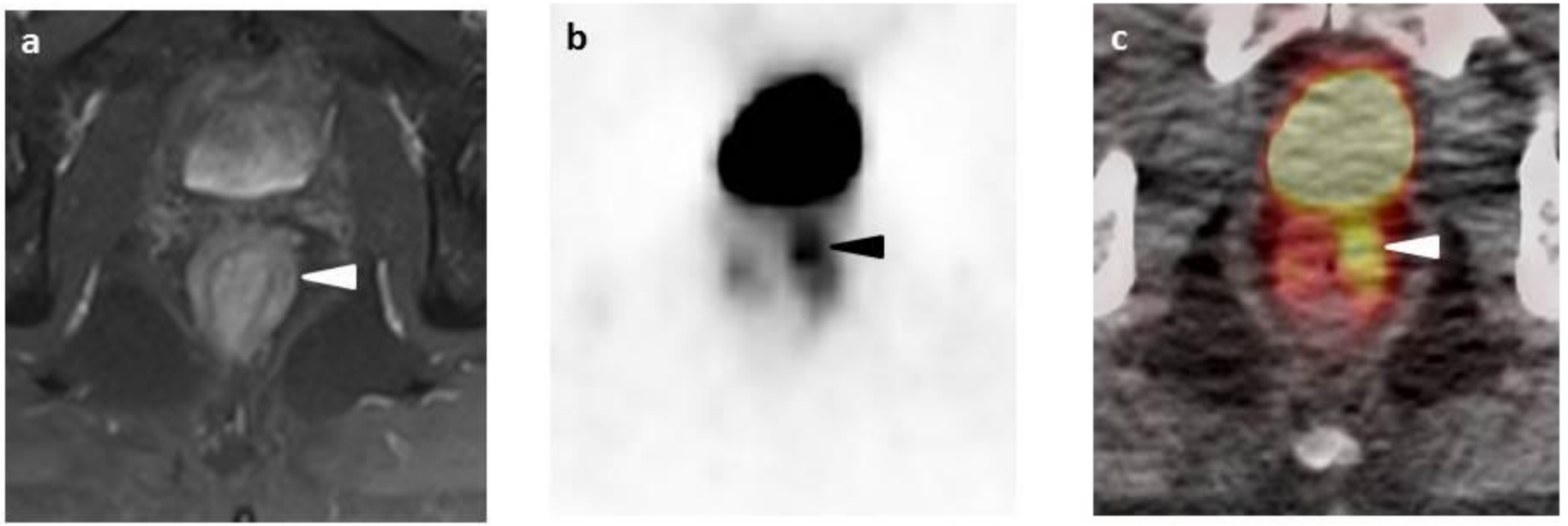
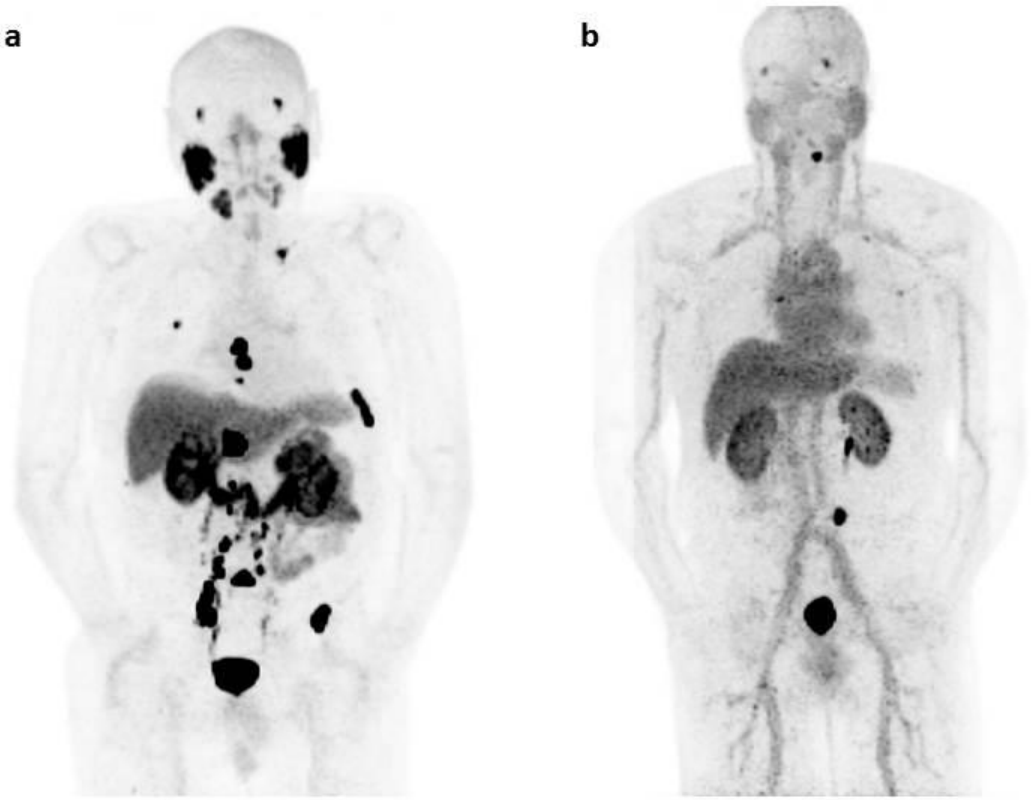


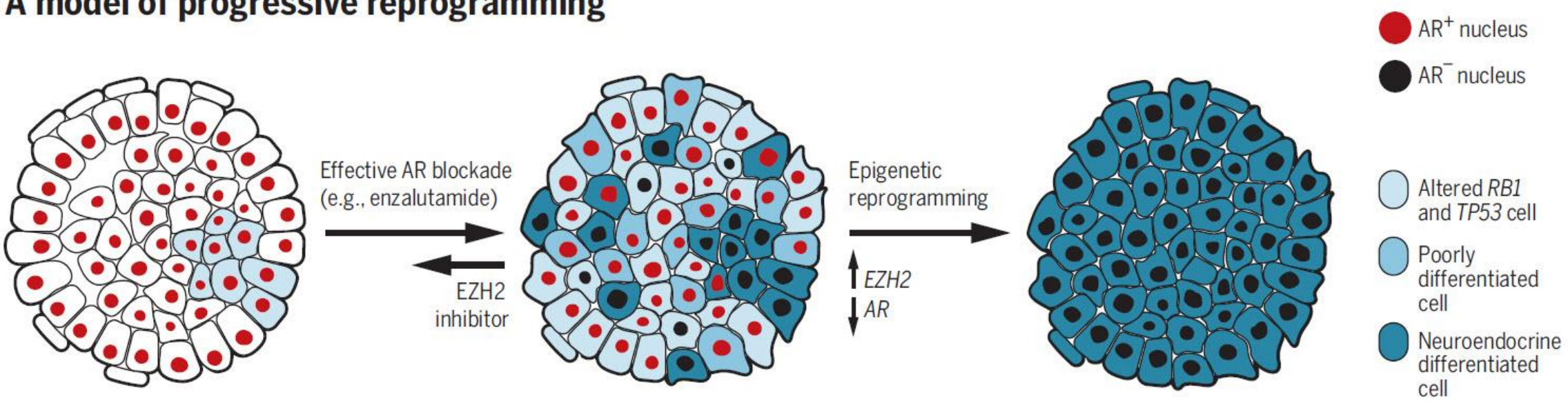
Fig. 6.



Supplementary Fig. 3.



A model of progressive reprogramming

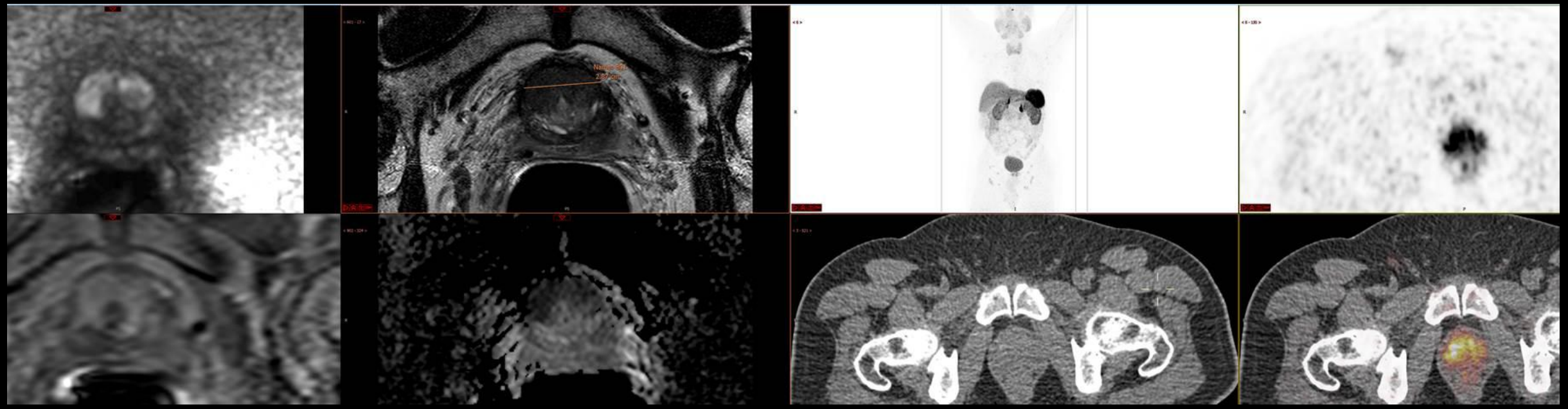


Androgen-dependent, AR^{+}
In castrate-resistant prostate cancer (luminal epithelial adenocarcinoma), cells express and depend upon androgen receptor (AR^{+}) for growth.

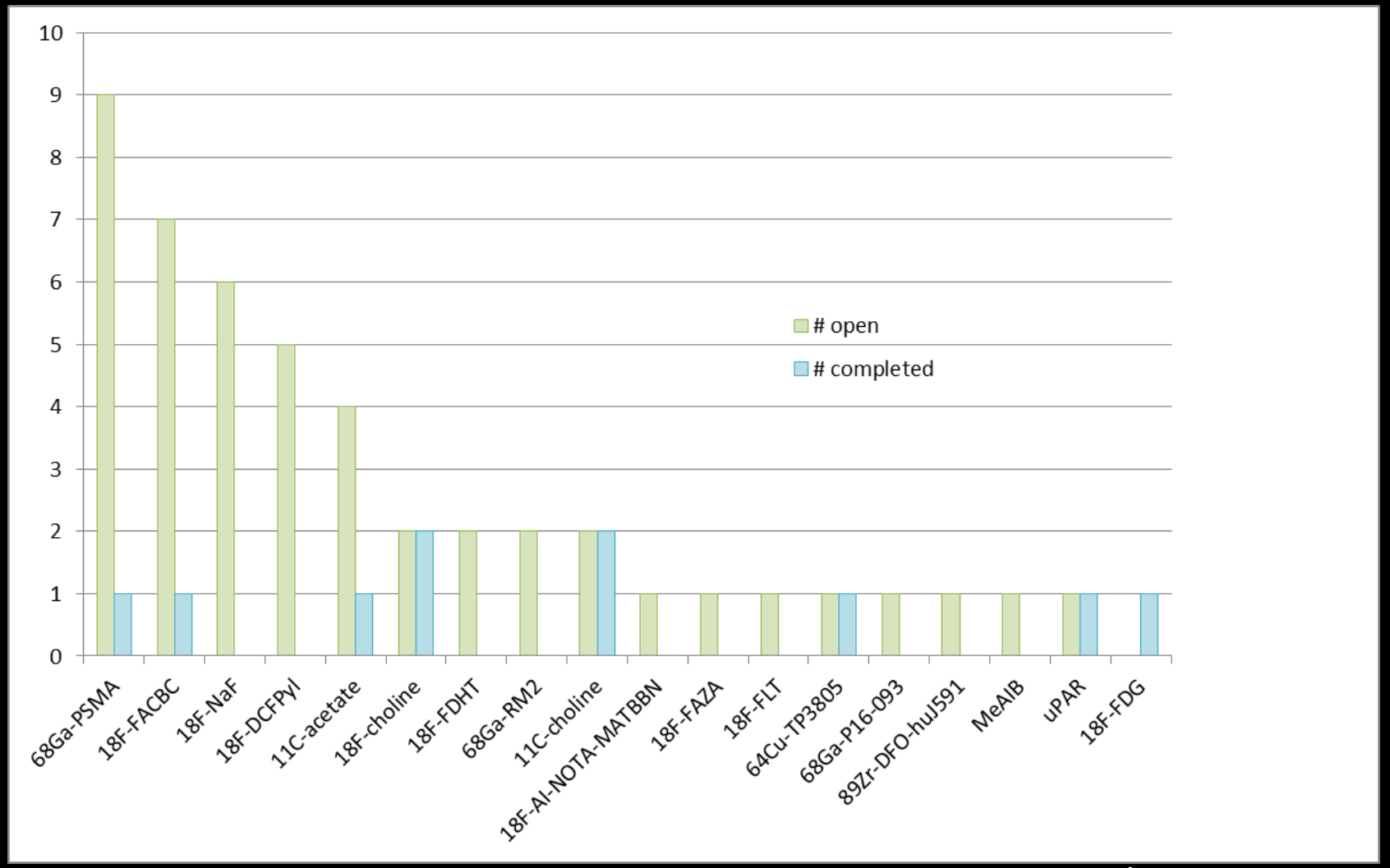
Androgen-indifferent, AR$^{+/-}$
After treatment with an AR antagonist, cells with altered *RB1* and *TP53* are selected. Factors including SOX2 and EZH2 contribute to dedifferentiation and plasticity.

Androgen-independent, AR^{-}
Cells established are most often reprogrammed to the neuroendocrine lineage that is resistant to enzalutamide.

Neuroendocrine Prostate + GaDOTATATE study



Current and Recently Completed Prostate PET Clinical Trials by Tracer



courtesy: Christine Lorenz Siemens

www.clinicaltrials.gov

Current Prostate PET Clinical Trials

Locations for Top 5 Tracers in Evaluation

68Ga-PSMA

- USA, Canada, Austria, Belgium

18F-FACBC

- USA, Norway, UK

18F-NaF

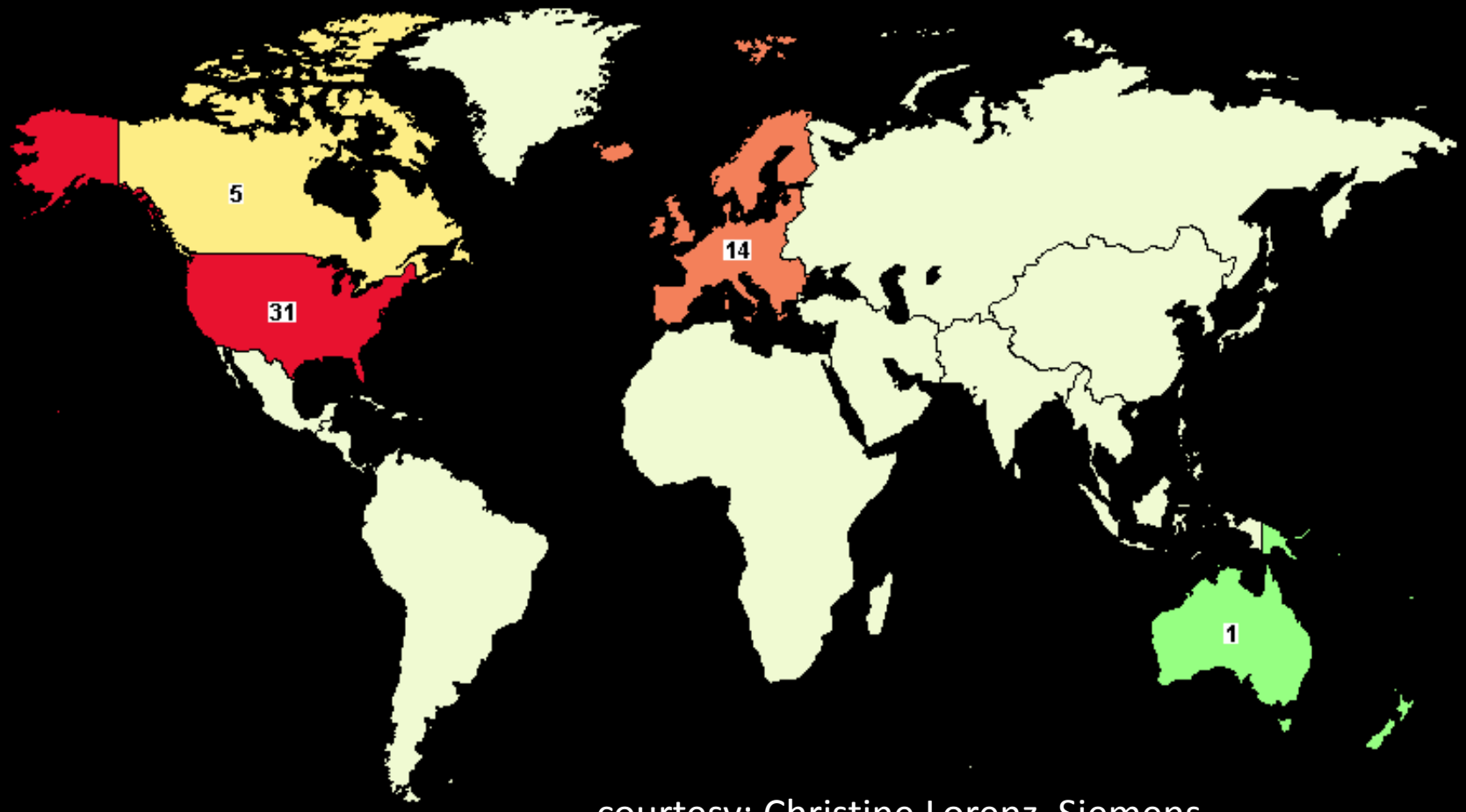
- Switzerland, USA, Canada

18F-DCFPyl

- Canada, USA

11C-acetate

- USA



courtesy: Christine Lorenz Siemens

: www.clinicaltrials.gov

Clinical Uses of PSMA PET

- Localized prostate cancer:
  - Lesion detection
  - TNM staging
- Biochemical recurrence after prostatectomy, xRT, brachytherapy
- Metastatic disease
  - Determining the tumor burden
  - Understand ADT response status?

Integrating MRI into PSMA PET

- MRI is very helpful in localizing PSMA uptake in primary tumors
  - Informs regarding EPE, SVI
  - Localization of local node and bone disease
- MRI is critical for localizing regional recurrence positive on PSMA
  - Localizing periurethral recurrence
  - Localizing residual SVI and node/bone disease
- MRI is helpful in verifying structural abnormalities in sites of PSMA uptake in metastatic diseased

Thank you…