# Choline PET: Where Should We Start from

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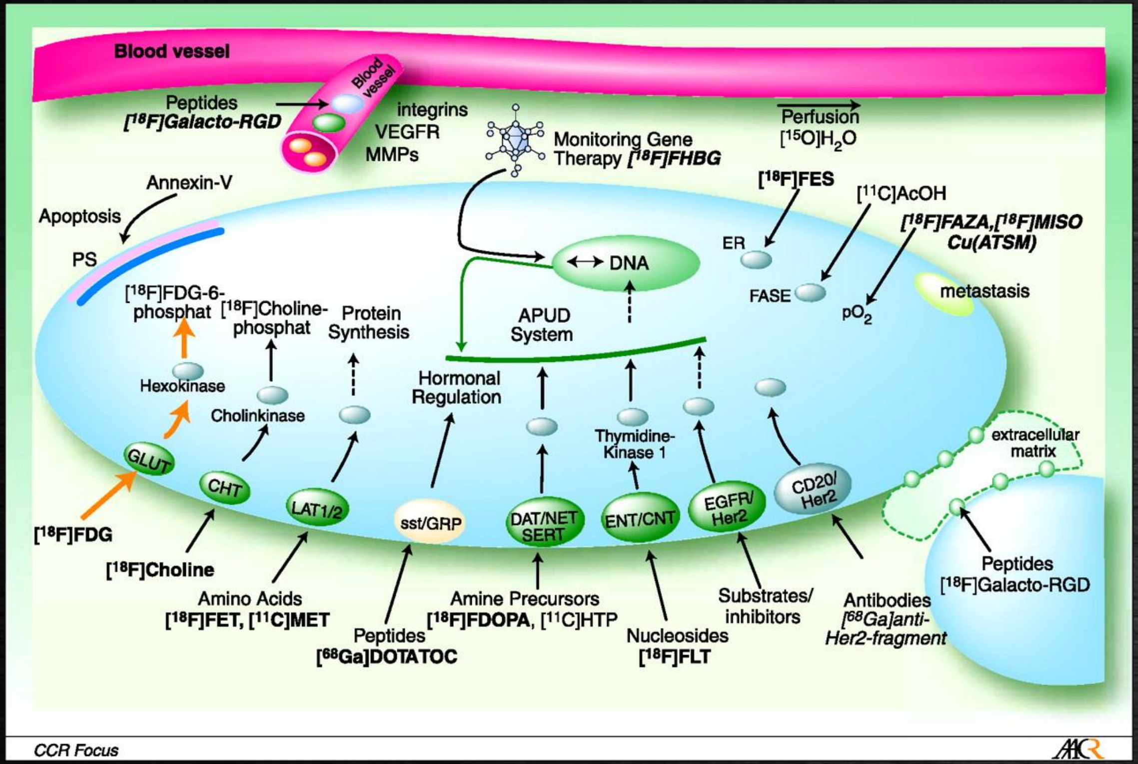
# Conventional Imaging in Detecting Prostate Cancer (PCa)

- Morphological
  - Computed tomography (CT)
  - Magnetic resonance imaging (MRI)
- Functional
  - Bone scintigraphy (BS)
  - Multiparametric MRI (mpMRI)
- Clinical settings
  - Primary staging, biochemical recurrence (BCR), treatment plan
  - Risk stratification

# Limitations of Traditional Weapons

- CT/MRI: based on size and shape
  - Small tumor disease, low Gleason score
  - Subjective interpretation
- BS
  - >80% bone metastasis is osteoblastic nature
  - Various sensitivity (62-89%), low specificity
  - Single photon emission tomography (SPECT)

# PET tracer for PCa

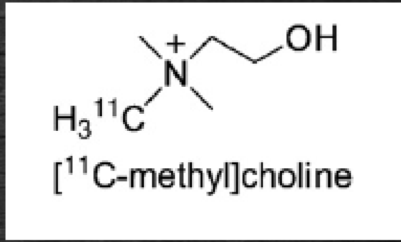


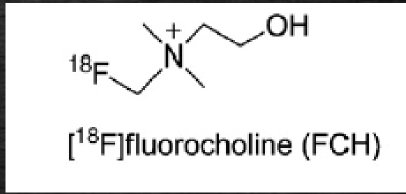

Clin Cancer Res. 2007 Jun 15;13(12):3470-81

- Glucose: $^{18}$F-Fluoro-2-Deoxyglucose (FDG)
- Sodium fluoride (NaF)
- Choline (labelled with C-11 or F-18)
- Amino acid: $^{18}$F-Fluciclovine ($^{18}$F-FACBC)
- Fatty acid: $^{11}$C-Acetate
- Prostate-specific membrane antigen (PSMA)

# Choline PET

- FDA approval in Sep 2012
- Overexpression of choline kinase in PCa
  - Phosphatidylcholine, a component of cell membrane
  - Choline is the substrate of choline kinase
- $^{11}$C-Choline
  - Chemically identical to endogenous choline
  - Short half-life
- $^{18}$F-Choline
  - Chemically different to endogenous choline
  - Higher urinary excretion
- Similar performance

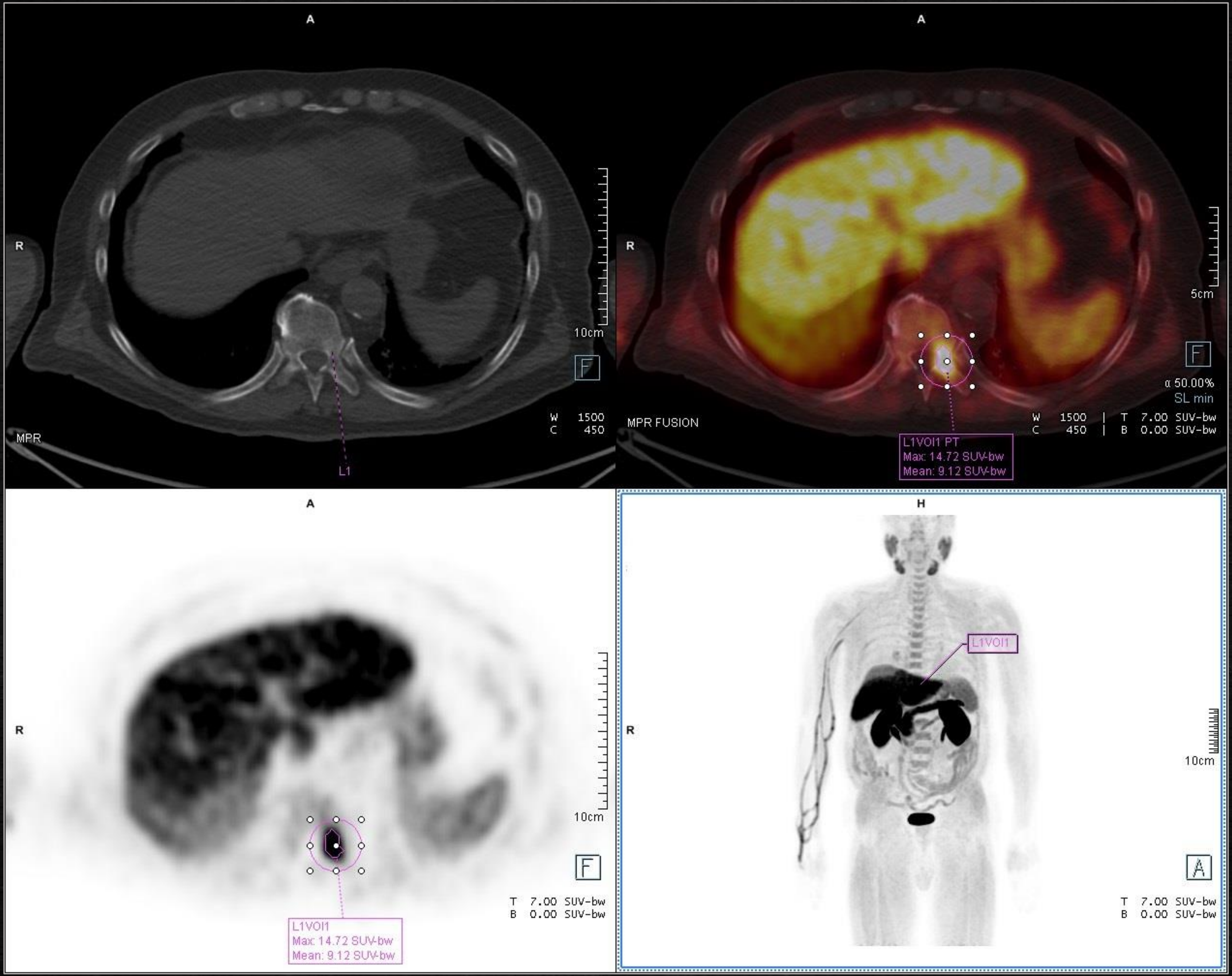



Eur J Nucl Med Mol Imaging. 2006 Dec;33(12):1387-98
J Nucl Med. 2006 Feb;47(2):262-9
J Nucl Med. 2011 Jan;52(1):81-9

# Case 1

- 75-year-old male, prostate cancer diagnosed in 2014/5
  - cT3bN0M0, iPSA 20.033, Gleason score 5+5
  - Status post ADT + RT (prostate bed), nadir iPSA <0.008
- Biochemical failure in 2019/3 with iPSA 2.212
  - Negative MRI and bone scan
- F-choline PET for restaging


A
R
10cm
MPR
W 1500
C 450
L1
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5cm
α 50.00%
SL min
MPR FUSION
W 1500 | T 7.00 SUV-bw
C 450 | B 0.00 SUV-bw
L1VOI1 PT
Max: 14.72 SUV-bw
Mean: 9.12 SUV-bw
A
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10cm
T 7.00 SUV-bw
B 0.00 SUV-bw
L1VOI1
Max: 14.72 SUV-bw
Mean: 9.12 SUV-bw
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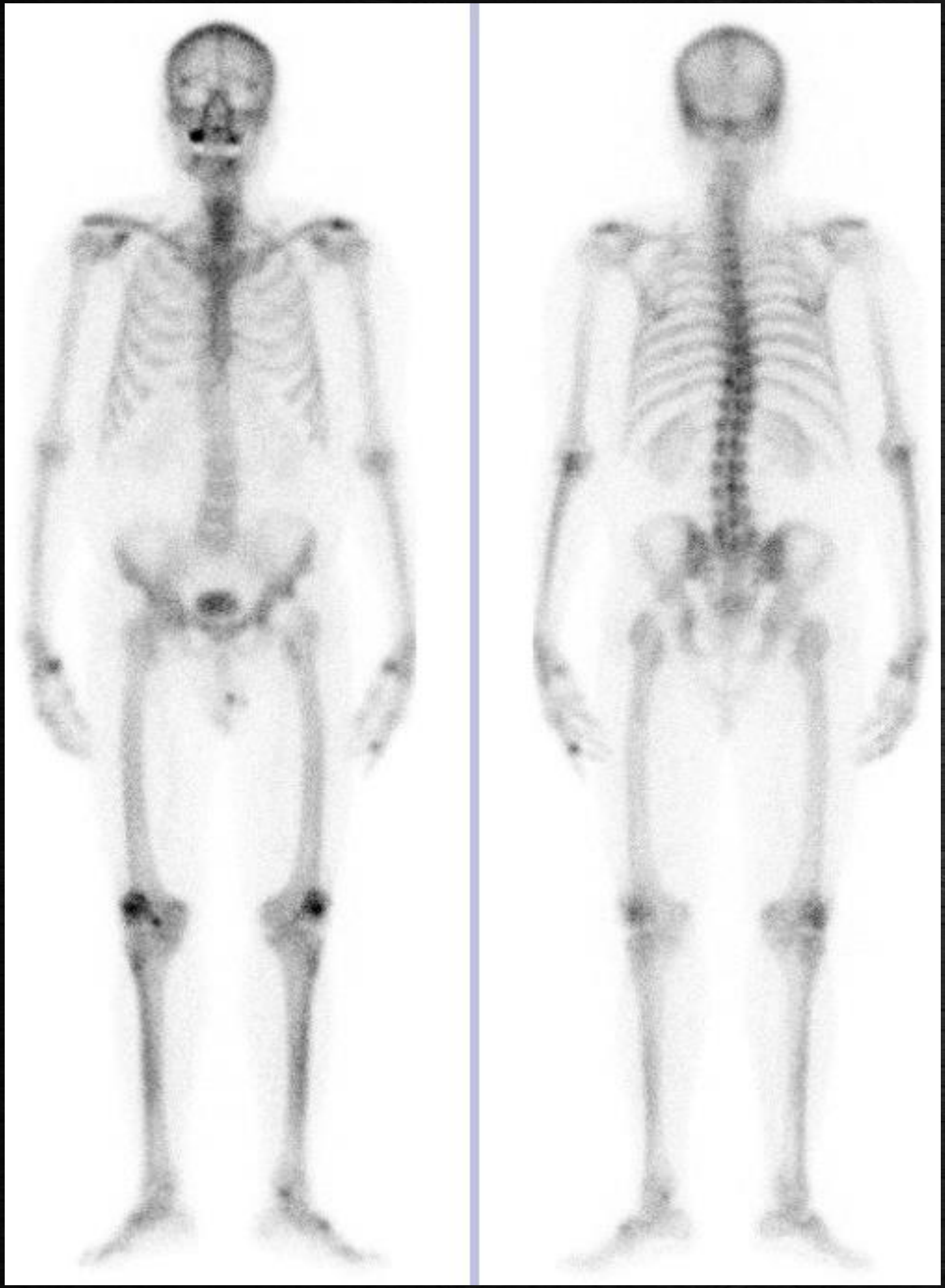
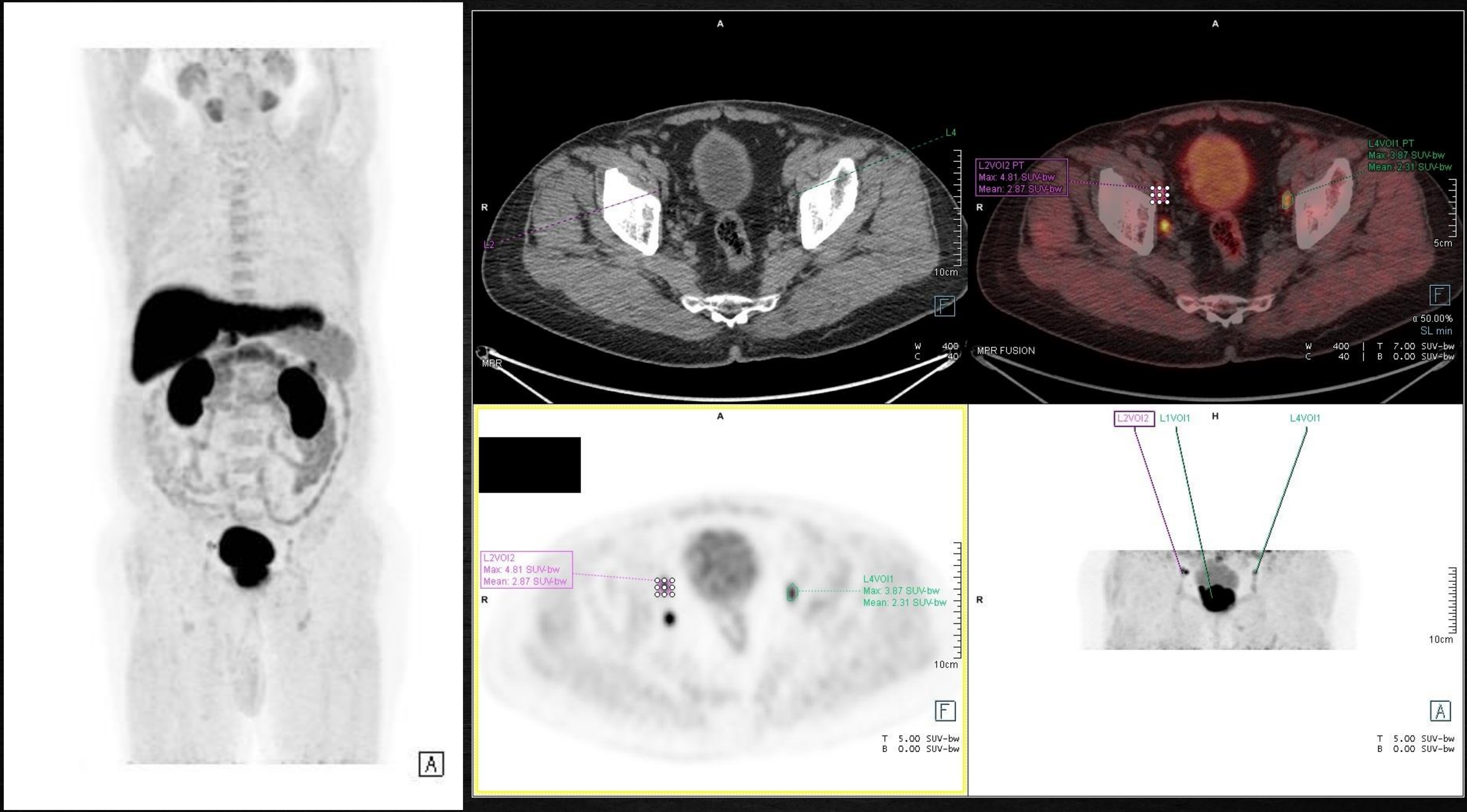
B 0.00 SUV-bw



- Status post salvage ADT with Zoladex
- Radiation therapy to single bone metastasis at T10 spine
- iPSA gradually decreased after therapy

# Case 2

- 71-year-old male, prostate cancer, diagnosed in 2019/3
- cT3aN0Mx, iPSA 106, Gleason score 4+4
- Bone scan was arranged due to high risk


A
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Max: 4.81 SUV-bw
Mean: 2.87 SUV-bw
L4VOI1 PT
Max: 3.87 SUV-bw
Mean: 2.31 SUV-bw
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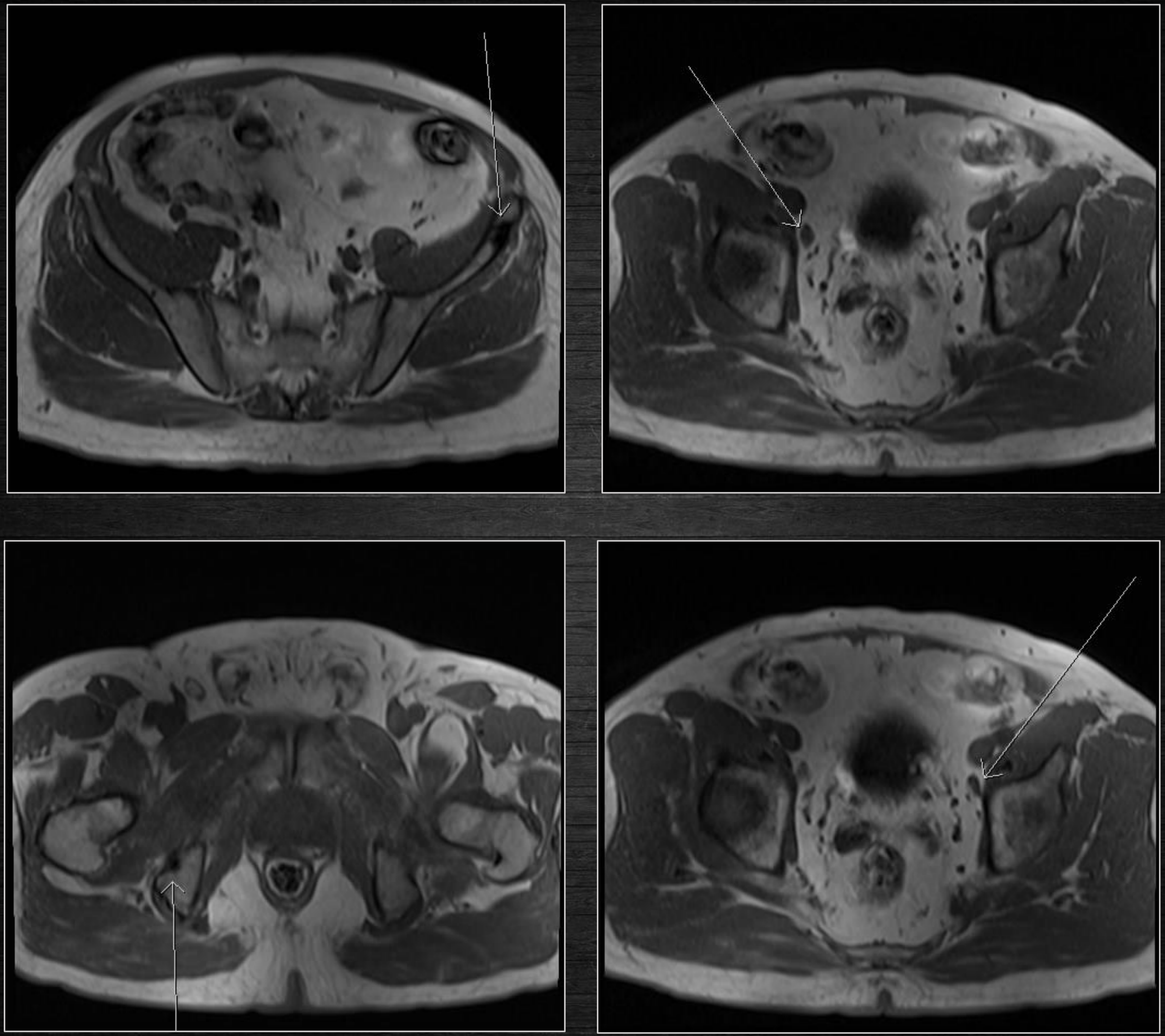
C 40 | B 0.00 SUV-bw
L2VOI2
Max: 4.81 SUV-bw
Mean: 2.87 SUV-bw
L4VOI1
Max: 3.87 SUV-bw
Mean: 2.31 SUV-bw
T 5.00 SUV-bw
B 0.00 SUV-bw
L2VOI2
L1VOI1
H
L4VOI1
10cm
T 5.00 SUV-bw
B 0.00 SUV-bw

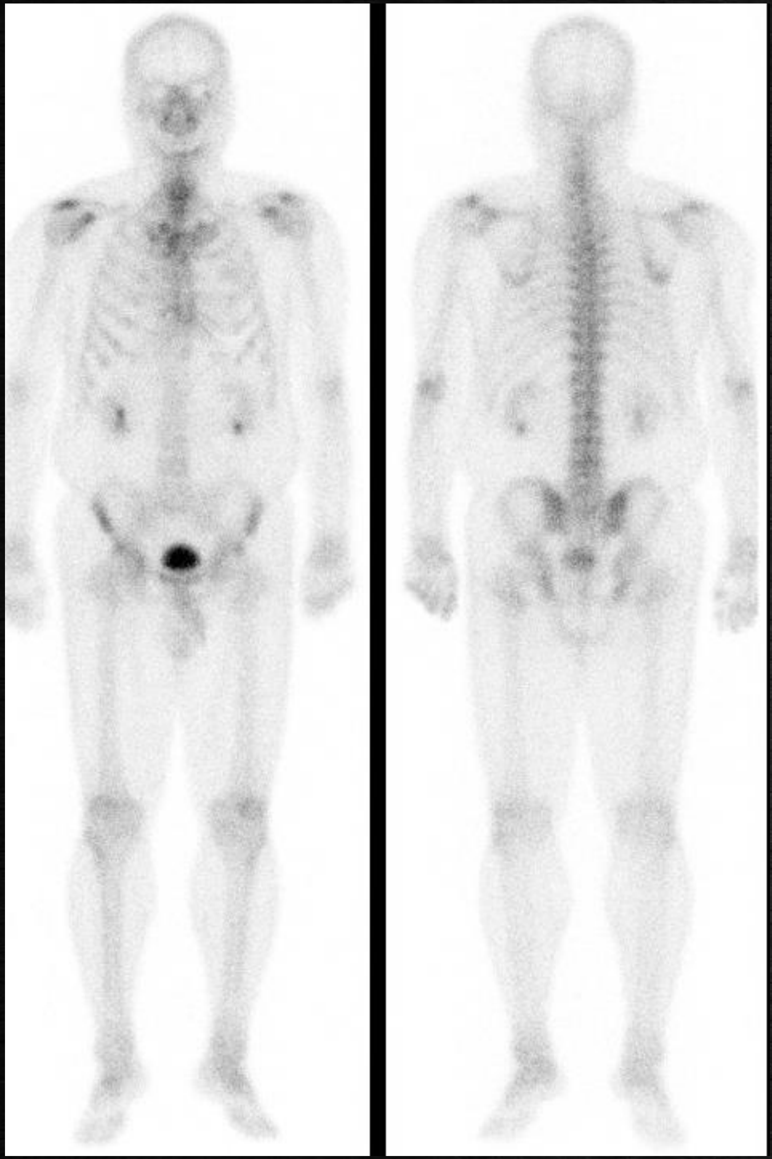
# Clinical course

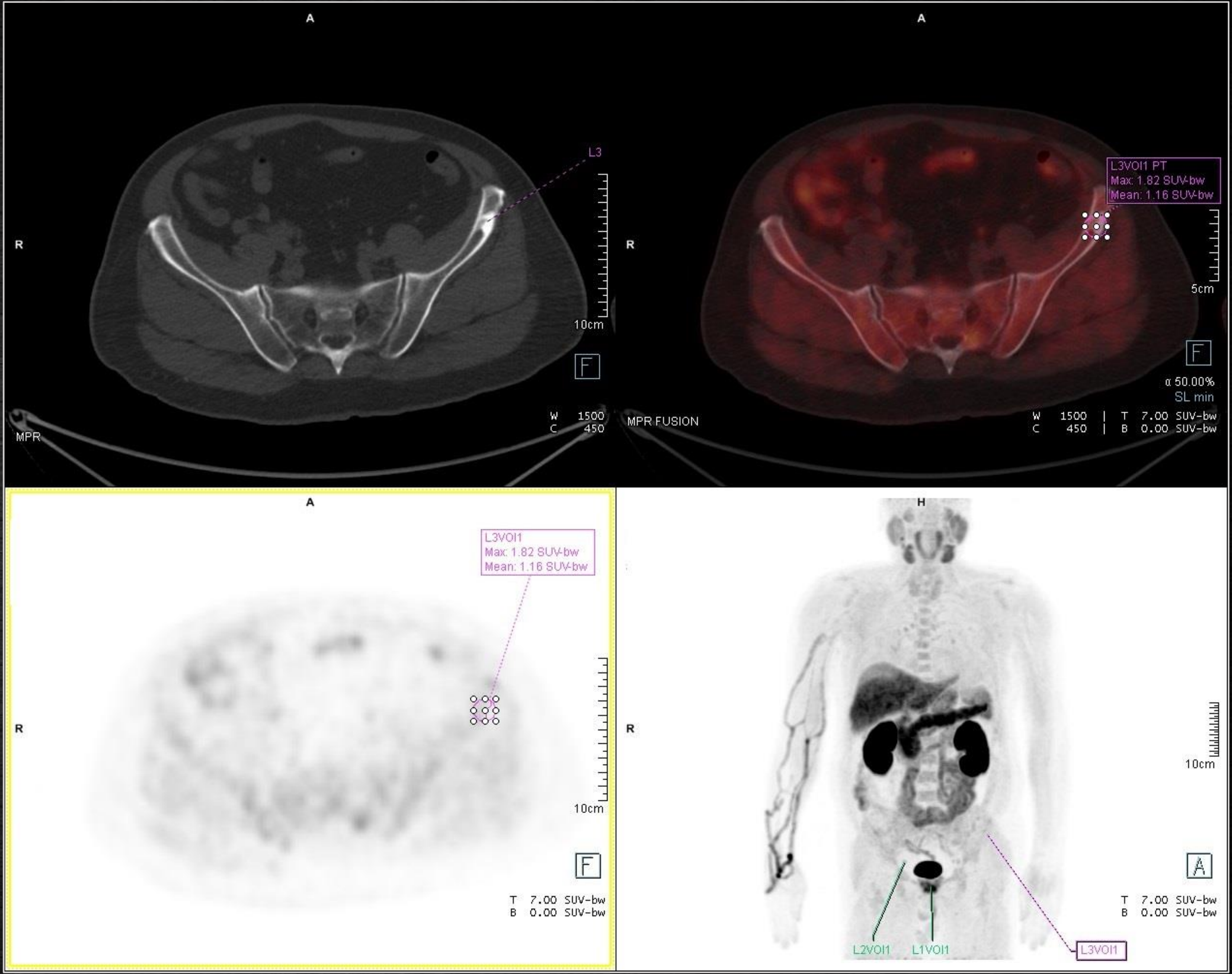
- N1 disease by FCH PET
- Status post neoadjuvant ADT then radiation therapy to prostate bed and pelvis LAPs
- iPSA significantly decreased to 0.607 soon after therapy

# Case 3

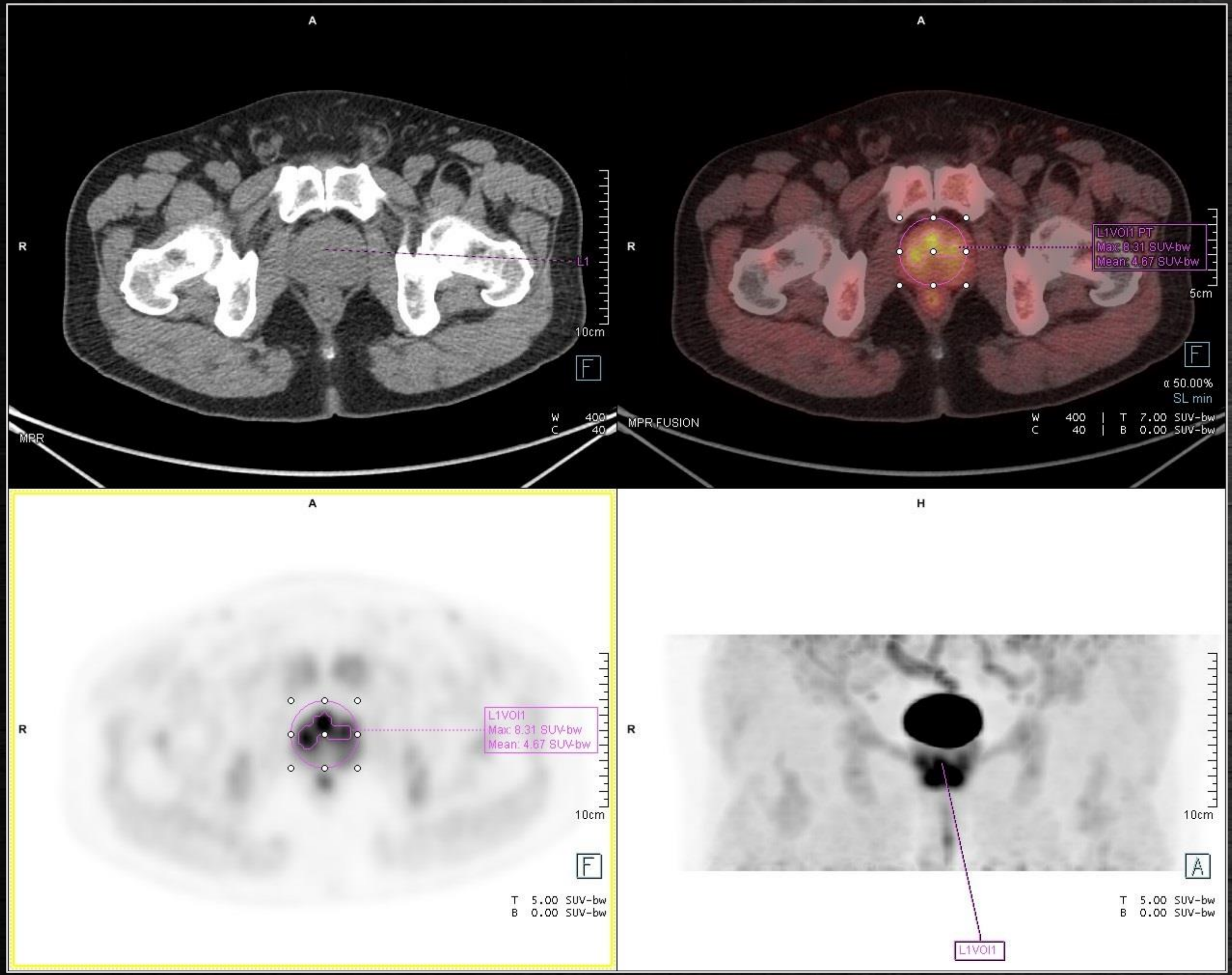
- 68-year-old male, prostate cancer, diagnosed in 2019/1
- cT1cN1M?, iPSA 17.3, Gleason score 3+4
  - N1: bilateral external iliac nodes by MRI
  - M?: sclerotic iliac bone lesion by MRI
- Negative bone scan
- FCH PET for primary staging

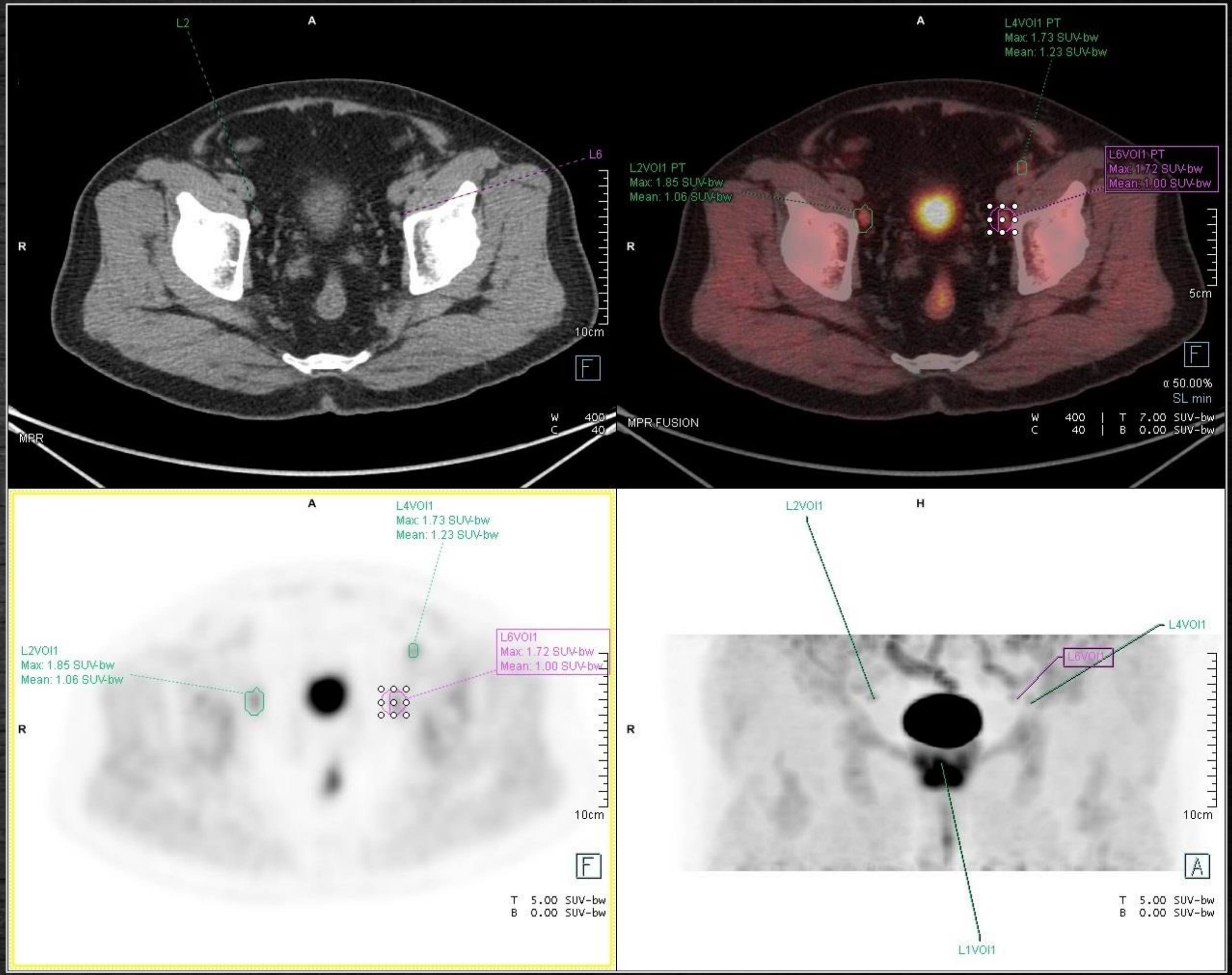






A
L3
R
10cm
MPR
W 1500
C 450
L3VOI1 PT
Max: 1.82 SUV-bw
Mean: 1.16 SUV-bw
5cm
α 50.00%
SL min
MPR FUSION
W 1500 | T 7.00 SUV-bw
C 450 | B 0.00 SUV-bw
L3VOI1
Max: 1.82 SUV-bw
Mean: 1.16 SUV-bw
T 7.00 SUV-bw
B 0.00 SUV-bw
H
L2VOI1
L1VOI1
L3VOI1


L1
L1VOI1 PT
Max: 8.31 SUV-bw
Mean: 4.67 SUV-bw
MPR
MPR FUSION
L1VOI1
Max: 8.31 SUV-bw
Mean: 4.67 SUV-bw
L1VOI1


L2
L6
L4VOI1 PT
Max: 1.73 SUV-bw
Mean: 1.23 SUV-bw
L2VOI1 PT
Max: 1.85 SUV-bw
Mean: 1.06 SUV-bw
L6VOI1 PT
Max: 1.72 SUV-bw
Mean: 1.00 SUV-bw
MPR
MPR FUSION
L4VOI1
Max: 1.73 SUV-bw
Mean: 1.23 SUV-bw
L2VOI1
Max: 1.85 SUV-bw
Mean: 1.06 SUV-bw
L6VOI1
Max: 1.72 SUV-bw
Mean: 1.00 SUV-bw
L2VOI1
L4VOI1
L6VOI1
L1VOI1

# Clinical course

- Treated as N1M0 disease (patient asked for aggressive treatment)
  - Neoadjuvant ADT then radiation therapy to prostate bed and pelvic LAPs
  - Bone biopsy if necessary
- iPSA decreased 0.089 after therapy
- Bone biopsy was hold due to good therapy response

# Advantages

- Outperformed than conventional imaging (CT/MRI/BS)
- Meta-analysis (Fanti et al. 2016) for $^{11}C$-Choline
  - 2126 BCR patients in 18 studies, detection rate 62%
  - 1270 patients in 12 studies reported sensitivity and specificity
    - Sensitivity 89%, specificity 89%
- Meta-analysis (Evangelista et al. 2013) for $^{18}F$-Choline PET
  - 441 primary staging patients in 10 studies
  - LN detection in primary staging: sensitivity/specificity = 49%/95%


Eur J Nucl Med Mol Imaging. 2011 Jan;38(1):14-22
Eur J Nucl Med Mol Imaging. 2016 Jan;43(1):55-69
Eur Urol. 2013 Jun;63(6):1040-8

# PSA stratification

| PSA | Detection rate |
|---|---|
| <1 | 36% |
| 1-2 | 43% |
| 2-3 | 63% |
| >3 | 73% |

Krause et al. 2008
63 patients

| PSA | Detection rate |
|---|---|
| 0.2-1 | 19% |
| 1-3 | 46% |
| >3 | 82% |

Giovacchini et al. 2010
2124 patients
Best cutoff: 1.4

- Evangelista et al. 2016
  - 3203 patients
  - Detection rate 45%
  - Optimal cutoff 1.16
- Change of management: 50%
- EAU guideline suggestion
  - PSA>1
  - Preferably 1-2


Eur J Nucl Med Mol Imaging. 2008 Jan;35(1):18-23
Eur J Nucl Med Mol Imaging. 2010 Feb;37(2):301-9
Eur J Nucl Med Mol Imaging. 2016 Oct;43(11):1971-9
Am J Clin Oncol. 2017 Jun;40(3):256-259
Eur Urol. 2014 Feb;65(2):467-79

European Association of Urology

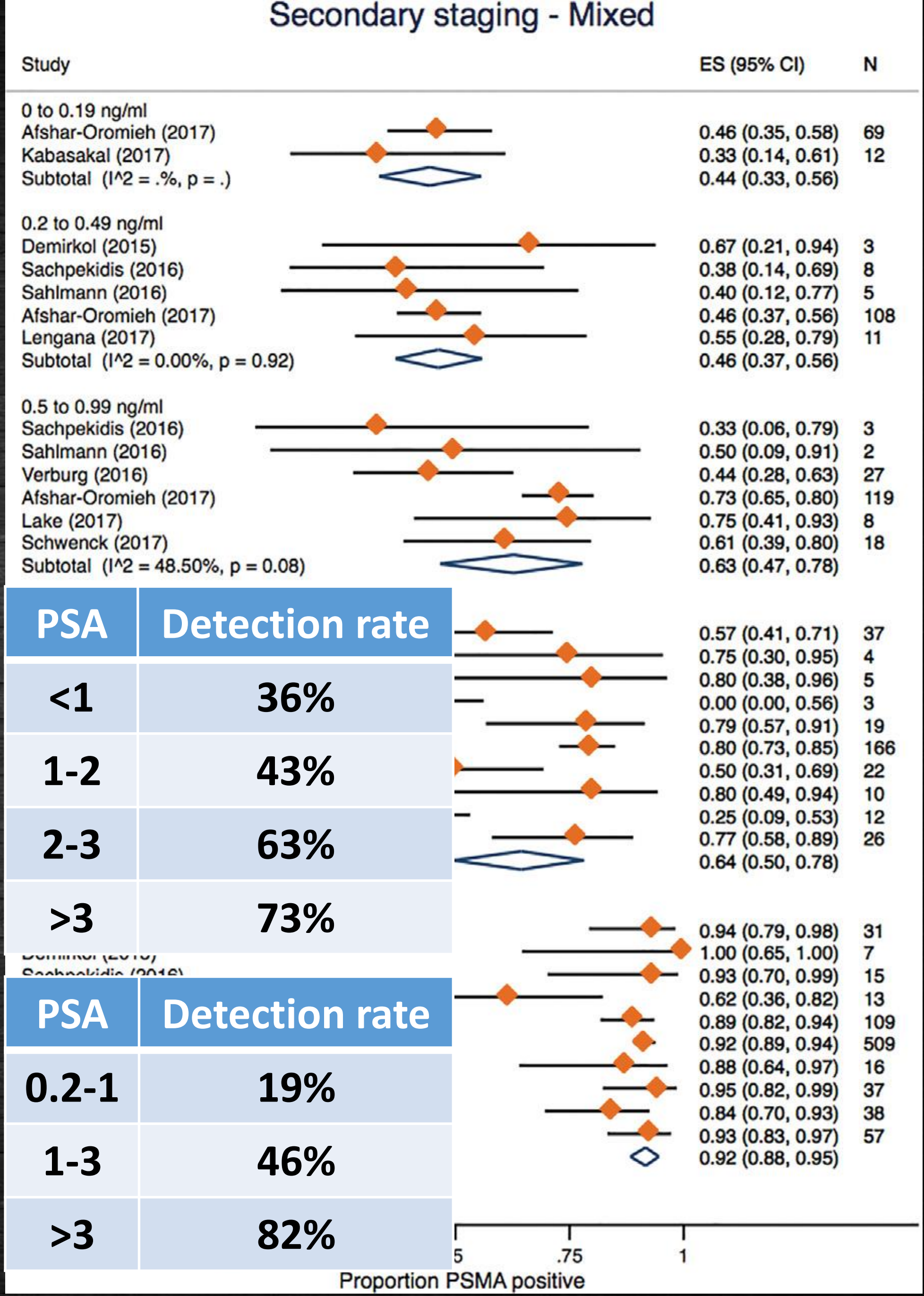
Platinum Priority – Review – Prostate Cancer
*Editorial by XXX on pp. x–y of this issue*

# Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer—Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis

*Marlon Perera [a,b,c,*], Nathan Papa [a], Matthew Roberts [b,c], Michael Williams [b], Cristian Udovicich [d], Ian Vela [b,e], Daniel Christidis [a], Damien Bolton [a,f], Michael S. Hofman [g], Nathan Lawrentschuk [a,f,h,i], Declan G. Murphy [h,i]*

**4970 patients 37 studies**

| PSA | Detection Rate (%) |
|---|---|
| <0.2 | 33 |
| 0.2-0.49 | 45 |
| 0.5-0.99 | 59 |
| 1-1.99 | 75 |
| ≥2 | 95 |




| PSA | Detection rate |
|---|---|
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| PSA | Detection rate |
|---|---|
| 0.2-1 | 19% |
| 1-3 | 46% |
| >3 | 82% |

Eur Urol. 2019 Feb 14, Epub

## Detection of recurrent prostate cancer lesions before salvage lymphadenectomy is more accurate with $^{68}$Ga-PSMA-HBED-CC than with $^{18}$F-Fluoroethylcholine PET/CT

David Pfister[1,4] • Daniel Porres[1,4] • Axel Heidenreich[1,4] • Isabel Heidegger[1] • Ruth Knuechel[2] • Florian Steib[2] • Florian F. Behrendt[3] • Frederik A. Verburg[3]

Eur J Nucl Med Mol Imaging. 2016 Jul;43(8):1410-7

## Comparison of $^{68}$Ga-labelled PSMA-11 and $^{11}$C-choline in the detection of prostate cancer metastases by PET/CT

Johannes Schwenck[1,3] • Hansjoerg Rempp[2] • Gerald Reischl[3] • Stephan Kruck[4] • Arnulf Stenzl[4] • Konstantin Nikolaou[2] • Christina Pfannenberg[2] • Christian la Fougère[1,5]

Eur J Nucl Med Mol Imaging. 2017 Jan;44(1):92-101

## Detection Rate of $^{18}$F-Choline PET/CT and $^{68}$Ga-PSMA-HBED-CC PET/CT for Prostate Cancer Lymph Node Metastases with Direct Link from PET to Histopathology: Dependence on the Size of Tumor Deposits in Lymph Nodes

Cordula A. Jilg[1], Vanessa Drendel[2], H. Christian Rischke[3,4], Teresa I. Beck[4], Kathrin Reichel[1], Malte Krönig[1], Ulrich Wetterauer[1], Wolfgang Schultze-Seemann[1], Philipp T. Meyer[4,5], and Werner Vach[6,7]

J Nucl Med. 2019 Jul;60(7):971-977

## Comparison of PSMA-PET/CT, choline-PET/CT, NaF-PET/CT, MRI, and bone scintigraphy in the diagnosis of bone metastases in patients with prostate cancer: a systematic review and meta-analysis

Skeletal Radiol. 2019 Dec;48(12):1915-1924

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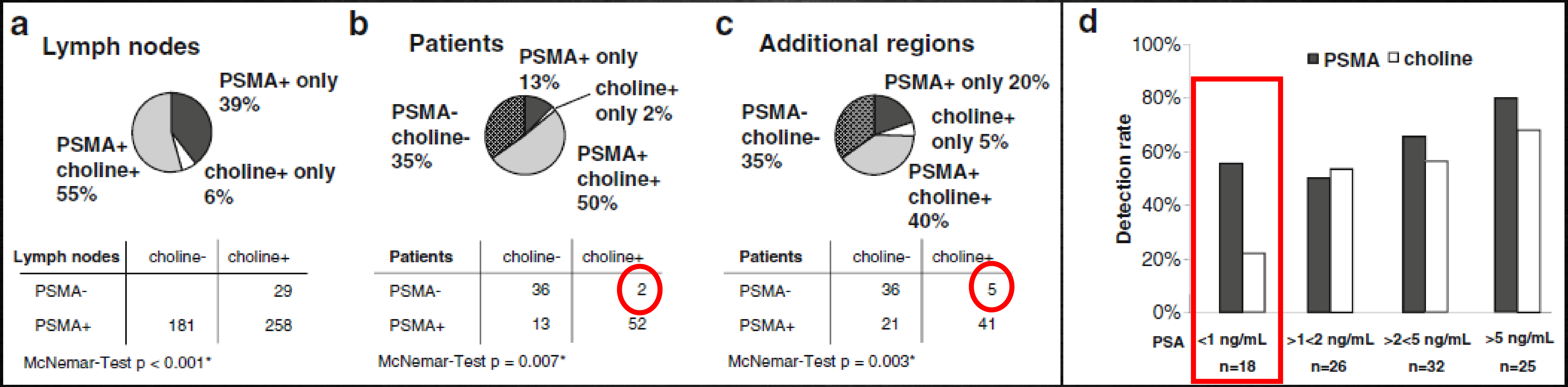
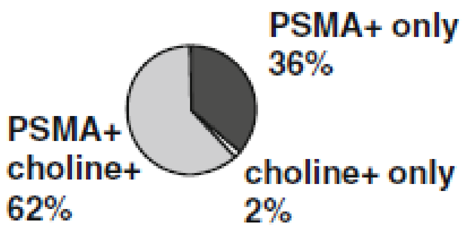
103 patients for restaging, median PSA 2.7



a

## Bone lesions (380 bone lesions)

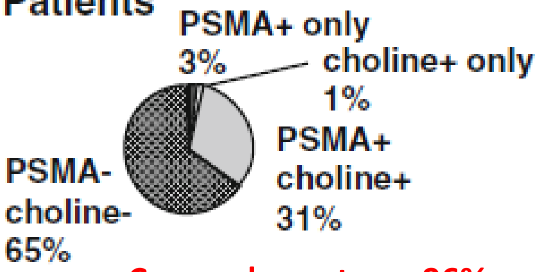



| Bone lesions | choline- | choline+ |
|---|---|---|
| PSMA- | | 8 |
| PSMA+ | 138 | 234 |

McNemar-Test $p < 0.001^{*}$

b

## Patients



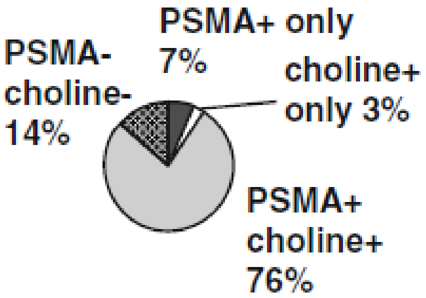

Concordance tae = 96%

| Patients | choline- | choline+ |
|---|---|---|
| PSMA- | 67 | 1 |
| PSMA+ | 3 | 32 |

McNemar-Test $p = 0.625$

a

## Patients

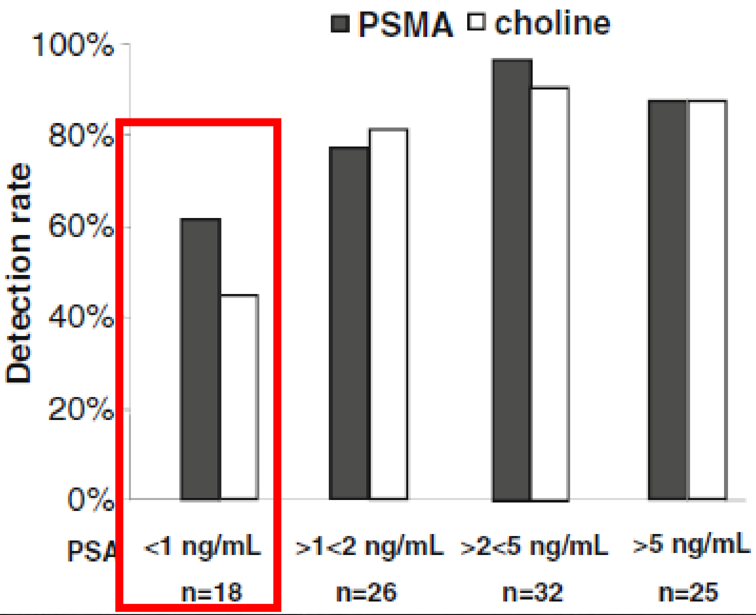


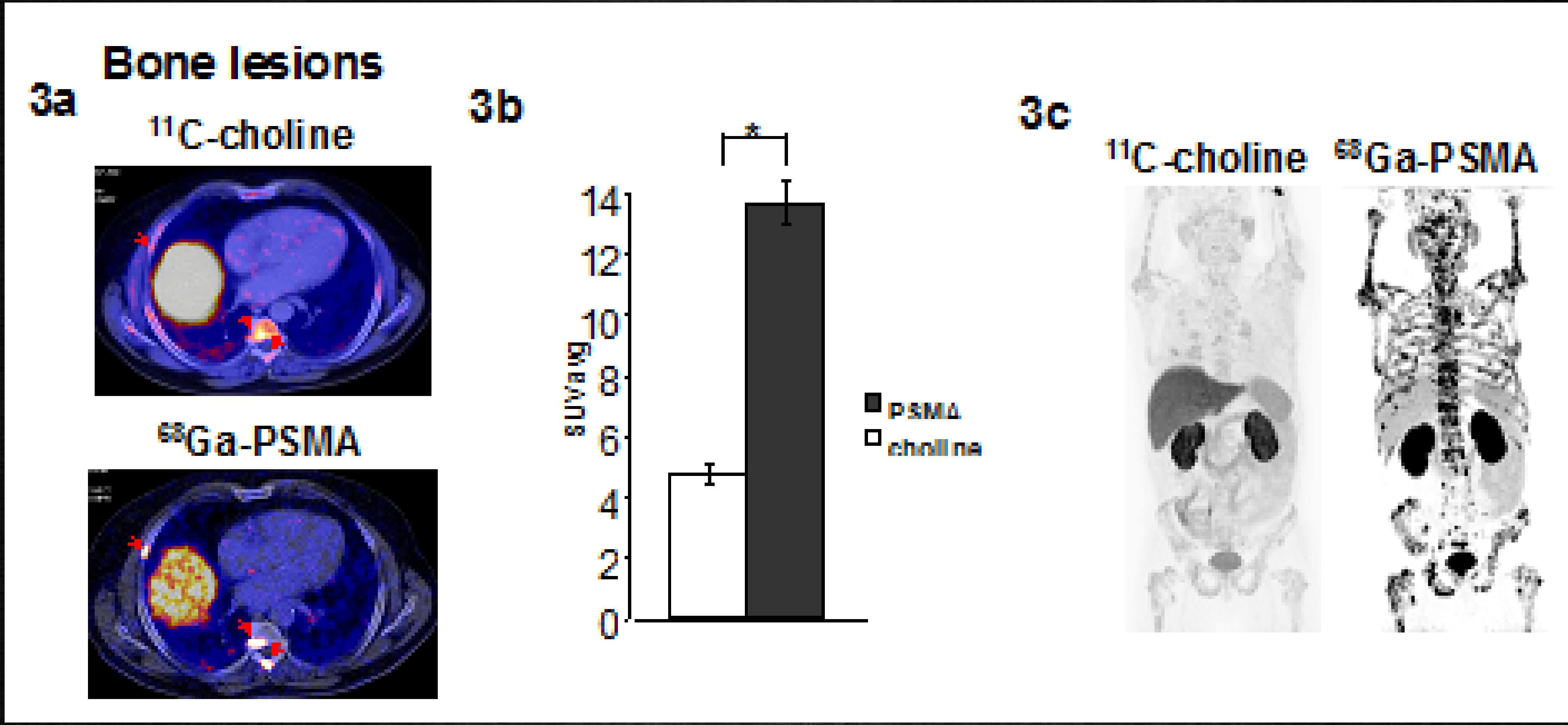

Concordance tae = 90%

| Patients | choline- | choline+ |
|---|---|---|
| PSMA- | 14 | 3 |
| PSMA+ | 7 | 79 |

McNemar-Test $p = 0.344$

b




Bone lesions
3a
11C-choline
68Ga-PSMA
3b
*
14
12
10
8
6
4
2
0
SUVavg
PSMA
choline
3c
11C-choline
68Ga-PSMA

# Comparing the Staging/Restaging Performance of $^{68}$Ga-Labeled Prostate-Specific Membrane Antigen and $^{18}$F-Choline PET/CT in Prostate Cancer

## *A Systematic Review and Meta-analysis*

*Chun-Yi Lin, MD, DrPH,*† Ming-Tsung Lee, PhD,‡*
*Cheng-Li Lin, MSc,§|| and Chia-Hung Kao, MD¶**††*

**TABLE 3.** Pooled Analysis of the Diagnostic Performance for $^{68}$Ga-PSMA PET/CT and $^{18}$F-Choline PET/CT on a Per-Patient and a Per-Lesion Basis

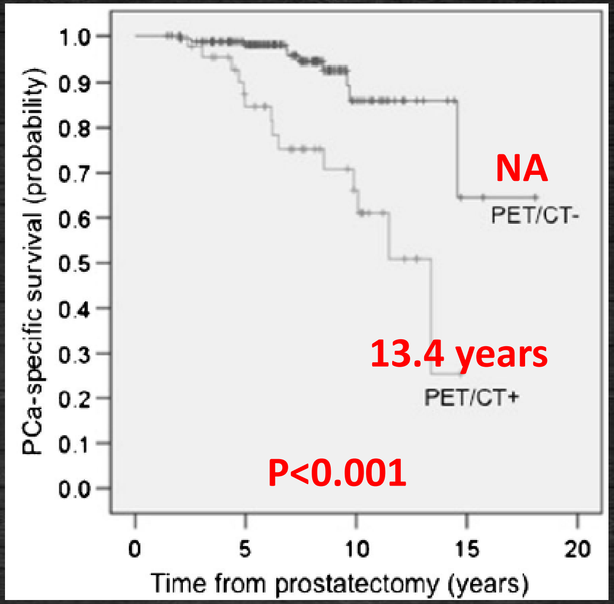
| Data Type | No. Studies | No. Patients (Lesions) | Sensitivity (95% CI) | Specificity (95% CI) | PLR (95% CI) | NLR (95% CI) | DOR (95% CI) | AUC |
|---|---|---|---|---|---|---|---|---|
| $^{68}$Ga-PSMA | | | | | | | | |
| Patient based | 13 | 652 | 0.92 (0.89–0.94) | 0.94 (0.90–0.97) | 7.91 (3.50–17.91) | 0.14 (0.06–0.30) | 79.04 (24.17–258.53) | 0.958 |
| Lesion based | 9 | 1951 | 0.83 (0.80–0.85) | 0.95 (0.94–0.97) | 23.30 (7.56–71.80) | 0.17 (0.12–0.26) | 153.58 (42.30–557.53) | 0.937 |
| $^{18}$F-choline | | | | | | | | |
| Patient based | 16 | 2122 | 0.93 (0.91–0.94) | 0.83 (0.80–0.85) | 4.98 (2.96–8.37) | 0.10 (0.04–0.23) | 68.27 (28.22–165.20) | 0.951 |
| Lesion based | 4 | 1039 | 0.81 (0.77–0.84) | 0.92 (0.89–0.94) | 8.59 (3.91–18.92) | 0.20 (0.06–0.69) | 44.82 (8.22–244.29) | 0.984 |

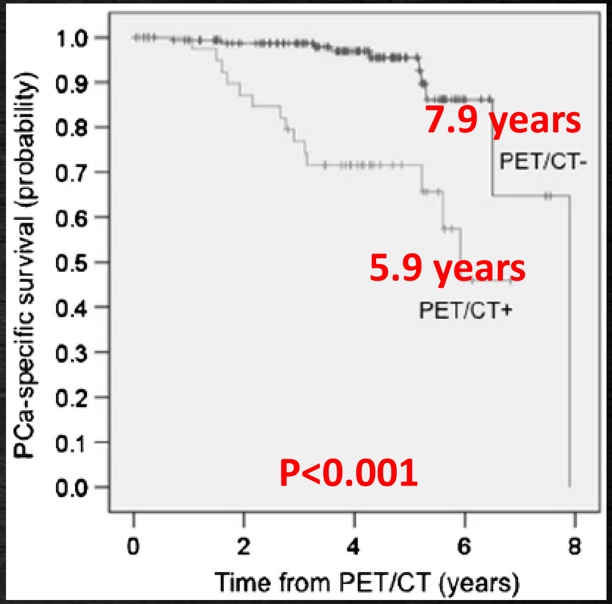
- Patient-based accuracy, sensitivity, specificity, DOR (p): 0.151, 0.521, 0.062, 0.772
- Lesion-based accuracy, sensitivity, specificity, DOR (p): 0.384, 0.481, 0.170, 0.386

Clin Nucl Med. 2019 May;44(5):365-376

# Prognostic value

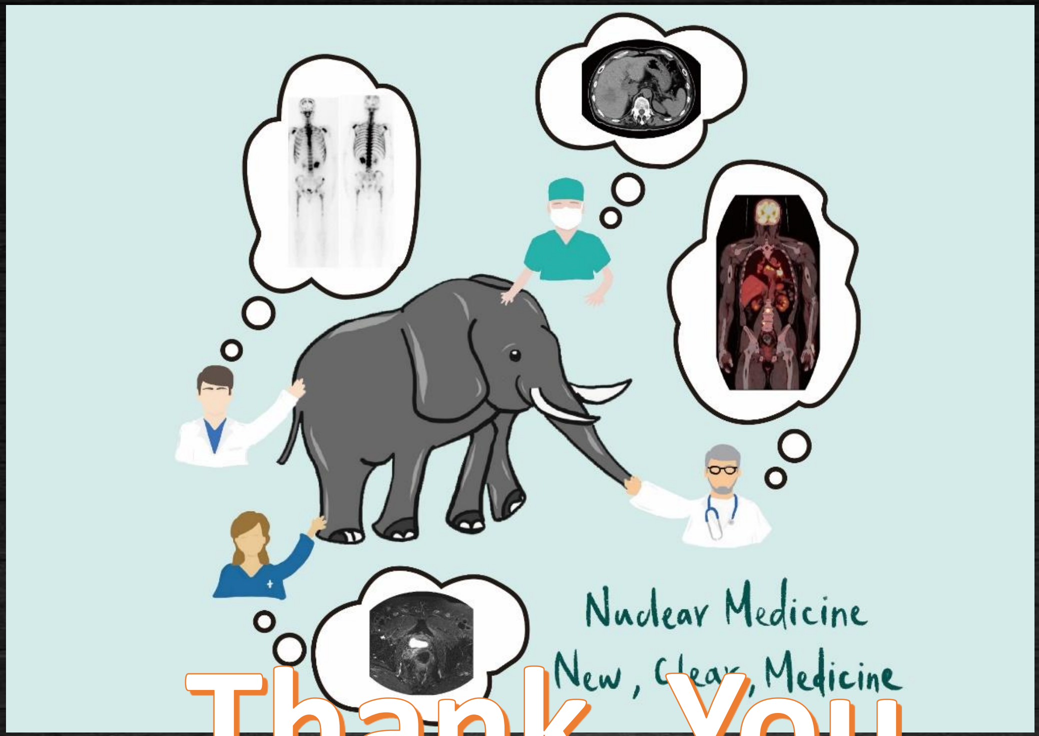
- 210 PCa patients having prostatectomy, CCH PET due to BCR
- Median PSA 0.54
- Median follow up: 6.9 years (95%CI, 2.0-14.5 year)




| | Whole group ($n = 210$) | PET/CT − ($n = 124$) | PET/CT + ($n = 86$) |
|---|---|---|---|
| 5-year | 95.2% (93.6%–96.8%) | 98.0% (96.9%–99.1%) | 84.7% (78.9%–90.5%) |
| 10-year | 80.3% (75.8%–84.8%) | 86.0% (80.7%–91.3%) | 63.6% (54.5%–72.7%) |
| 15-year | 52.3% (38.0%–66.6%) | 64.5% (45.5%–83.5%) | 25.4% (6.4%–44.4%) |

Eur J Nucl Med Mol Imaging. 2019 Apr;46(4):921-929




# Thank You

*No need to be frustrated*

*Polymorphic tumor nature raises the need of multimodality imaging*

*Appropriate approach depends on the clinical setting, purpose, and real world status*