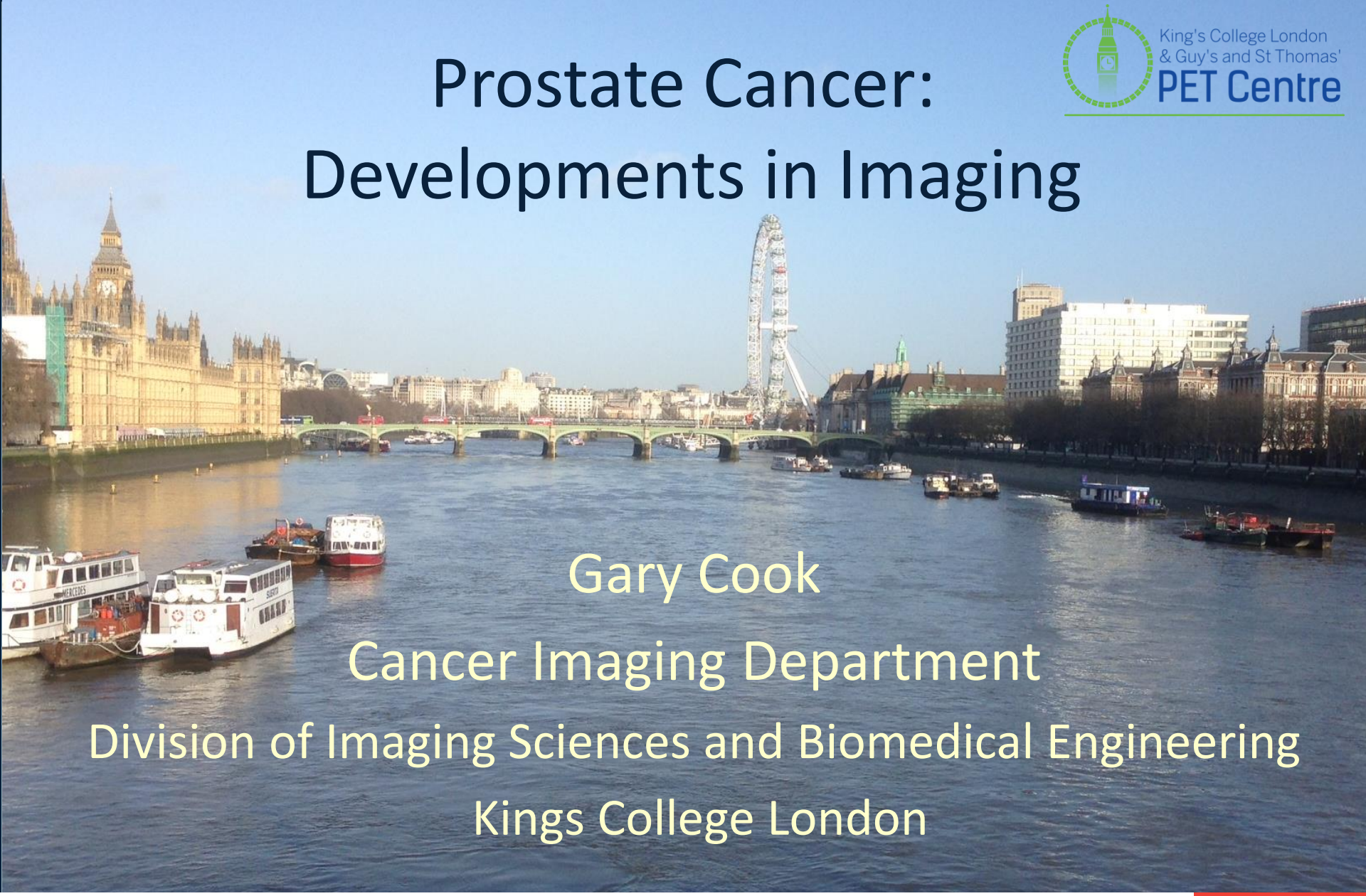
# Prostate Cancer: Developments in Imaging




Gary Cook

Cancer Imaging Department

Division of Imaging Sciences and Biomedical Engineering

Kings College London


King's College London & Guy's and St Thomas' PET Centre

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# Summary

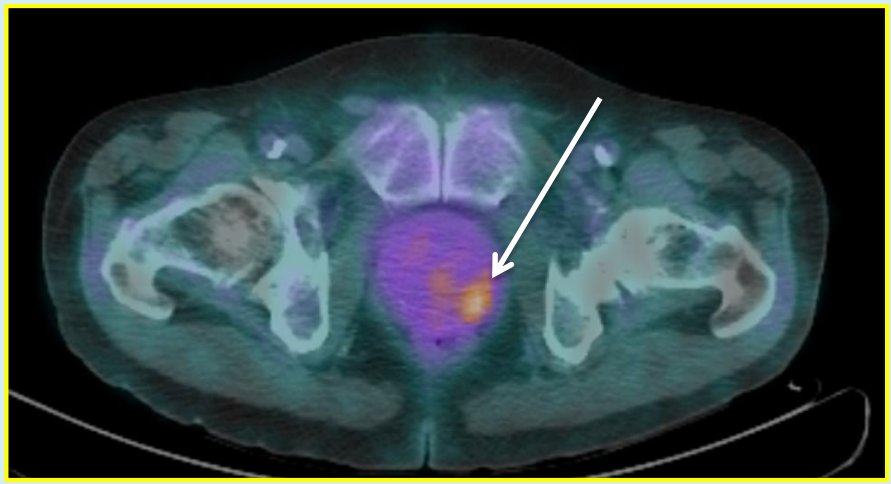
- **Current PET**
- Metabolism: $^{18}$FDG, Choline ($^{11}$C / $^{18}$F-choline)
- Bone metastases: $^{18}$F-fluoride

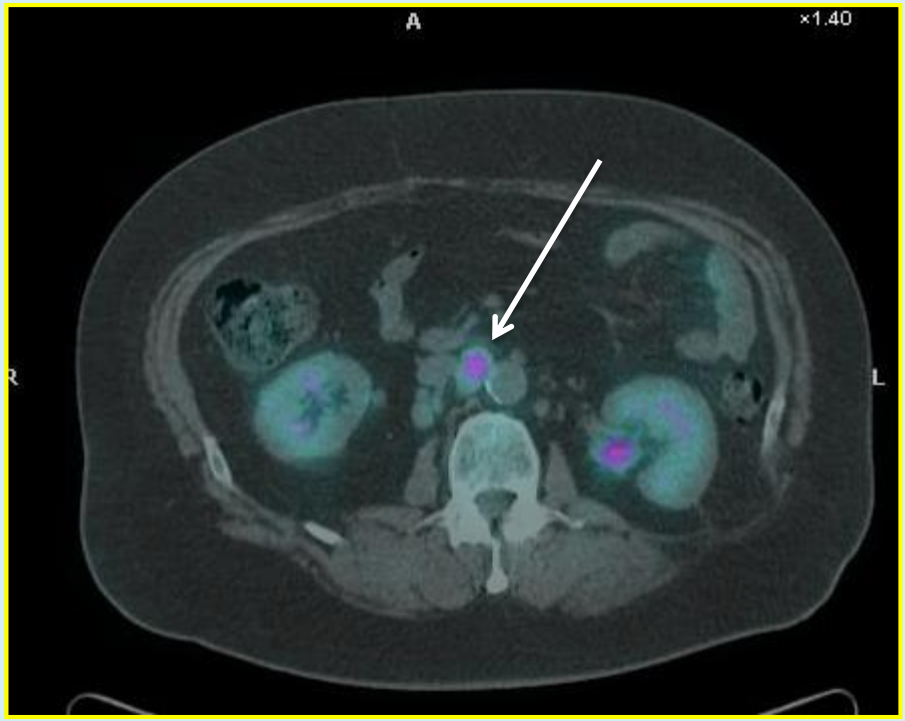
- **Novel agents**
- Prostate-specific membrane antigen (PSMA)
- Amino acids ($^{18}$F-FACBC)
- Fatty acid metabolism ($^{11}$C-Acetate)
- Androgen receptor ($^{18}$F-FDHT)
- Bombesin (GRPR expression)

- **Imaging hardware**
- PET-MRI

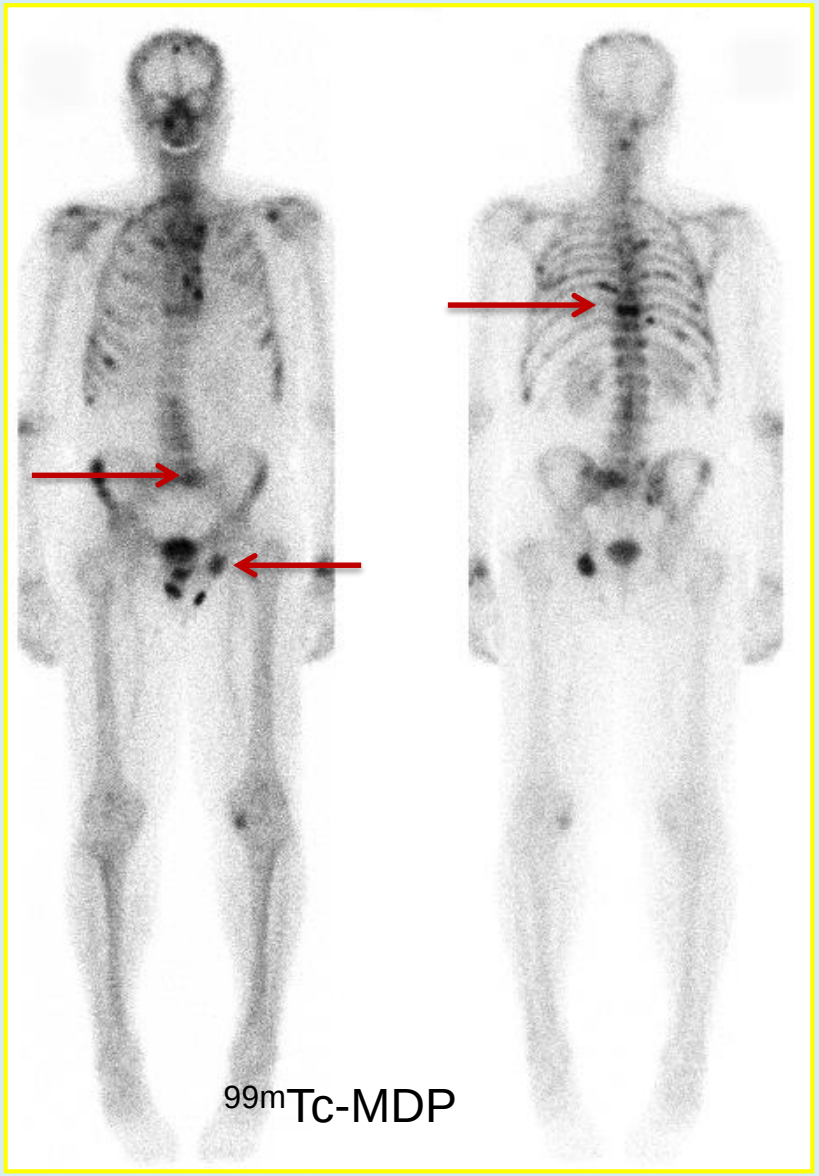
# $^{18}$F-FDG

- Poor sensitivity except in aggressive or dedifferentiated tumours
- Urinary excretion
- 28/91 patients detected with PSA relapse following prostatecomy *(Schoder Clin Cancer Res 2007)*
- 65% of bone metastases (PPV=98%) *(Shreve Radiol 1996)*





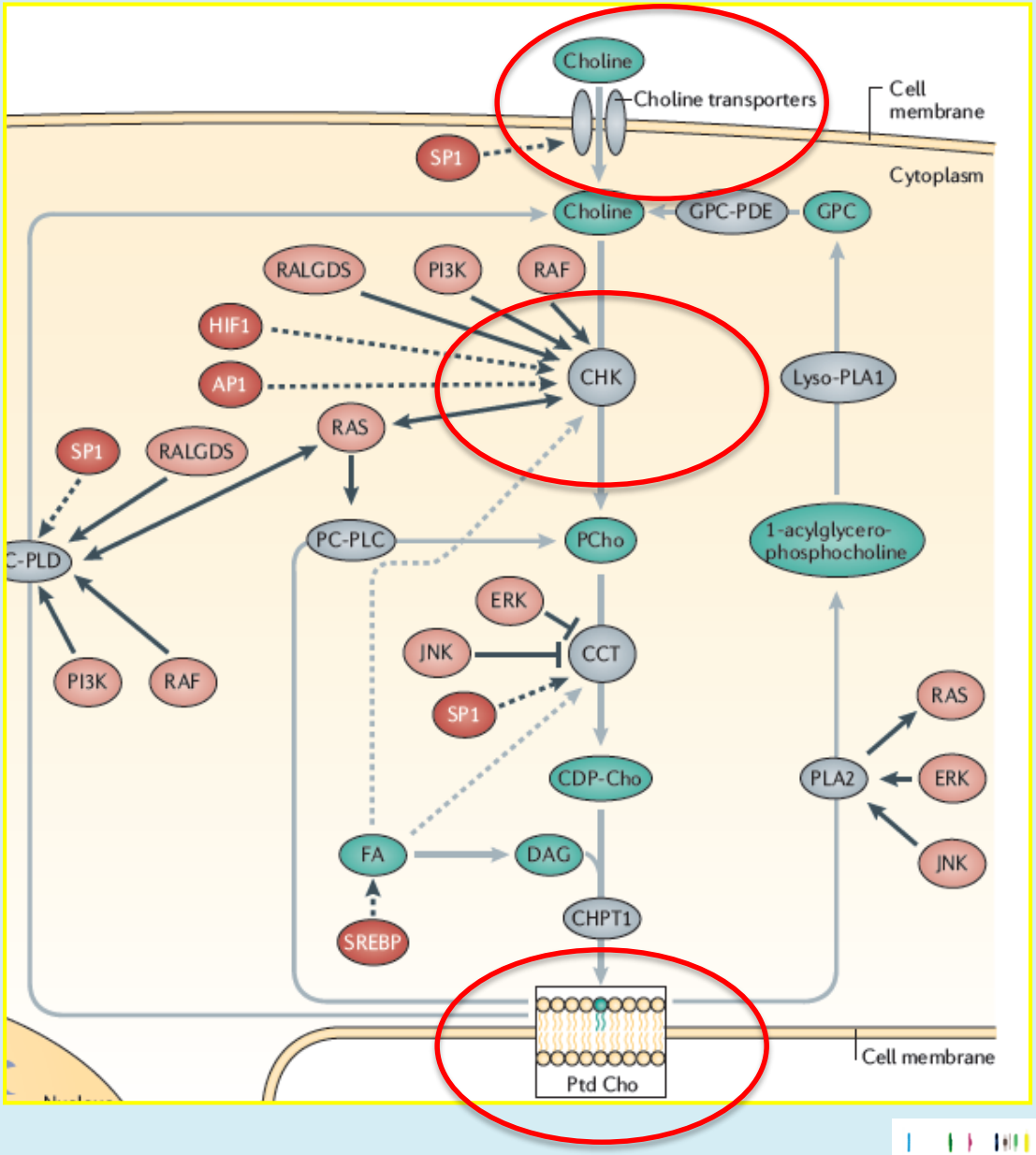

$^{18}$FDG



$^{99m}$Tc-MDP

$^{18}$FDG

# Choline mechanisms



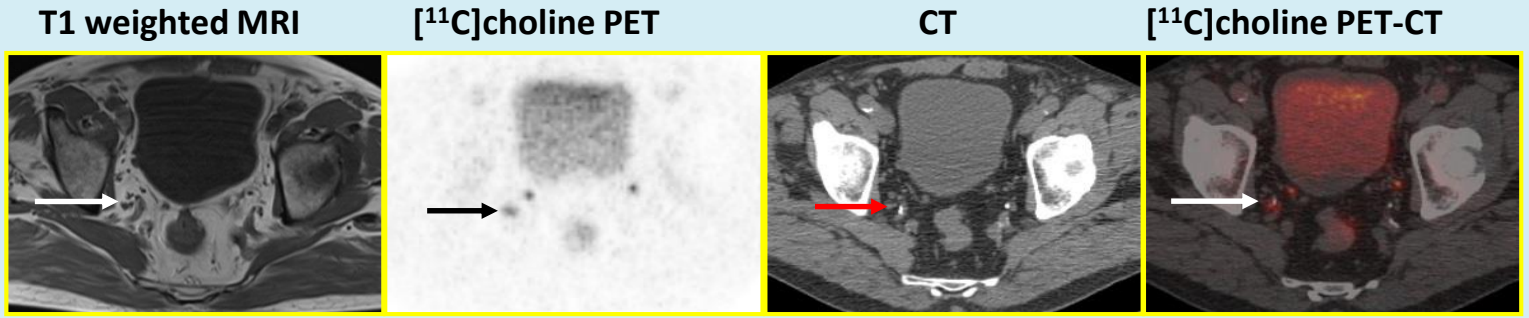
# Choline PET

Diagnostic efficacy of $^{18}$F- and $^{11}$C-choline PET and PET/CT in patients with primary prostate cancer

| Tracer | Ref. | Author | Year | Modus | Pts. (*n*) | Local tumor | | Lymph nodes | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) |
| $^{18}$F-FCH | [26] | Kwee | 2005 | PET | 17 | 100 | — | — | — |
| | [31] | Schmid | 2005 | PET/CT | 19 | 100 | — | — | — |
| | [27] | Kwee | 2006 | PET | 26 | 100 | — | — | — |
| | [54] | Husarik | 2008 | PET/CT | 43 | 98 | — | 33 | 100 |
| $^{11}$C-Cho | [6] | Kotzerke | 2000 | PET | 23 | 100 | — | 50 | 90 |
| | [23] | de Jong | 2002 | PET | 25 | 100 | — | 80 | 95 |
| | [35] | de Jong | 2003 | PET | 67 | — | — | 80 | 96 |
| | [32] | Sutinen | 2004 | PET | 14 | 100 | — | — | — |
| | [33] | Yamaguchi | 2005 | PET | 20 | 100 | — | — | — |
| | [34] | Yoshida | 2005 | PET | 13 | — | — | — | — |
| | [24] | Farsad* | 2005 | PET/CT | 36 | 66 | 81 | — | — |
| | [29] | Reske* | 2006 | PET/CT | 26 | 100 | — | — | — |
| | [30] | Scher | 2007 | PET/CT | 58 | 86 | 70 | — | — |
| | [28] | Martorana* | 2006 | PET/CT | 43 | 66 | 84 | — | — |
| | [25] | Giovacchini* | 2008 | PET/CT | 19 | 72 | 43 | — | — |
| | [36] | Schiavina | 2008 | PET/CT | 57 | — | — | 60 | 98 |
| | [66] | Li† | 2008 | PET/CT | 49 | 90 | 86 | — | — |
| Sum | | | | | 555 | | | | |
| Mean | | | | | | 91 | 73 | 61 | 96 |
| Median | | | | | | 100 | 81 | 60 | 96 |

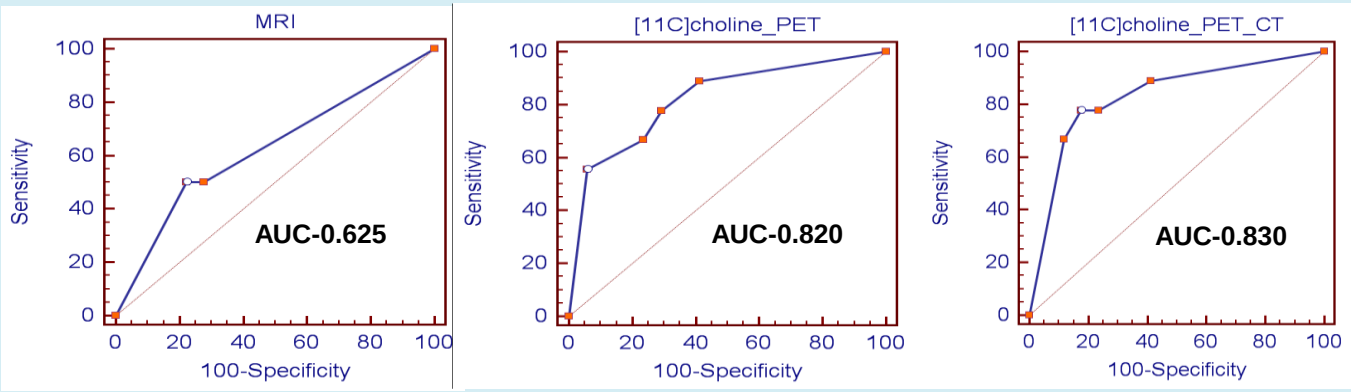
*Krause BJ et al. Urol Oncol. 2011*

# [$^{11}$C]Choline PET-CT in staging high risk Prostate Cancer




Arrow denotes a 4mm obturator node

**ROC curves – per patient basis**




**Sensitivity – 50%**
**Specificity – 72.2%**

**Sensitivity – 66.7%**
**Specificity – 76.4%**

**Sensitivity – 77.8%**
**Specificity – 82.4%**

*Contractor, Challapalli et al: Clin Cancer Res, 2011*

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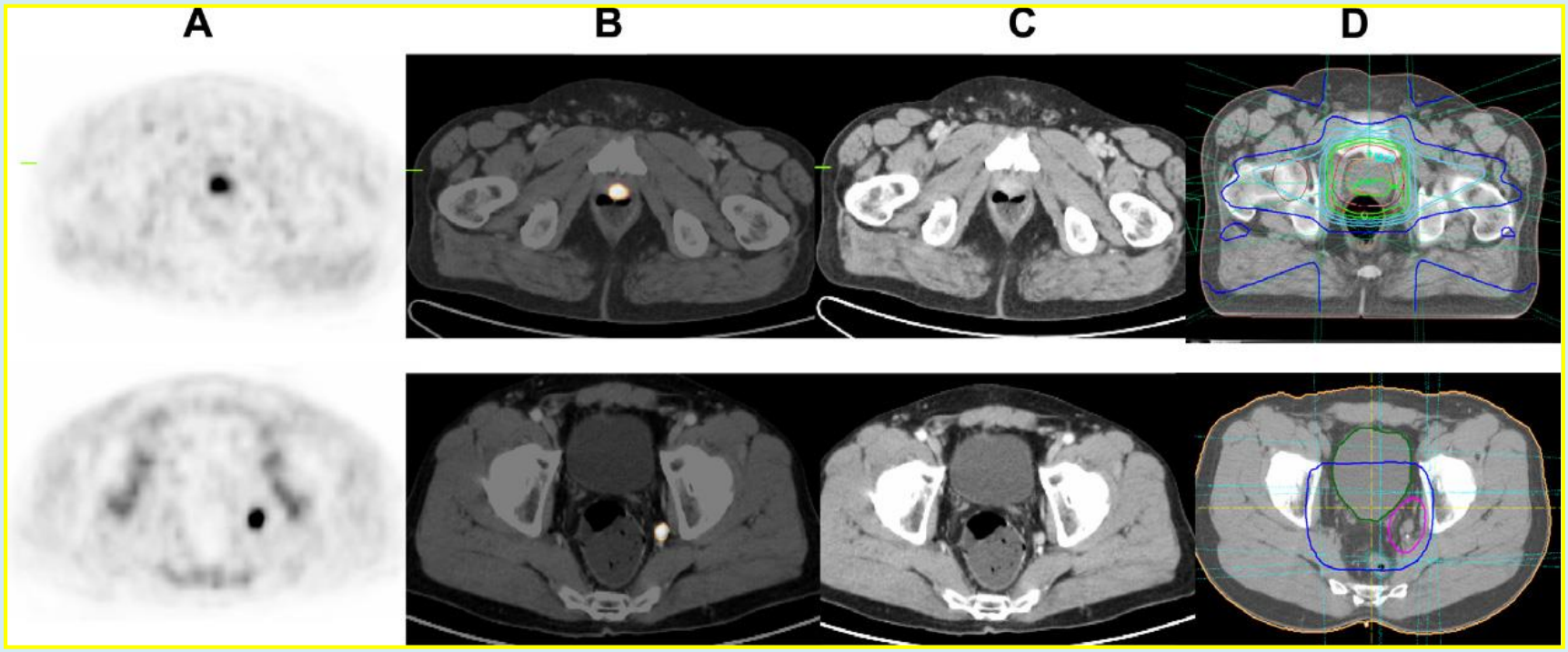
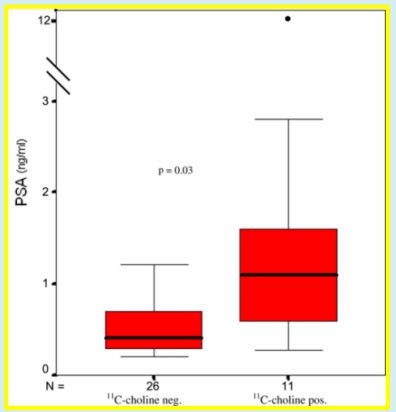



*Souvatzoglou et al. Radiotherapy and Oncology 99 (2011) 193–200*




5/37 for salvage RT to prostate bed had +ve iliac nodes affecting the PTV

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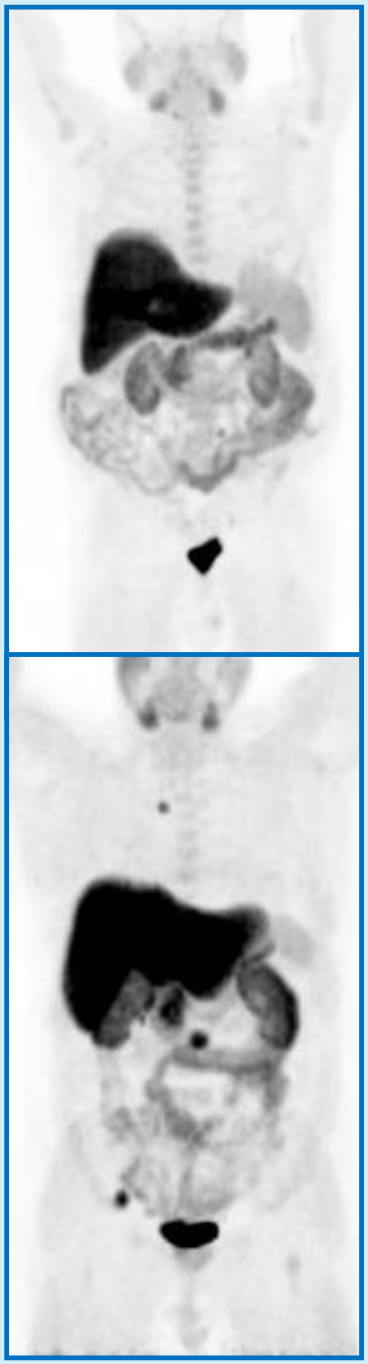
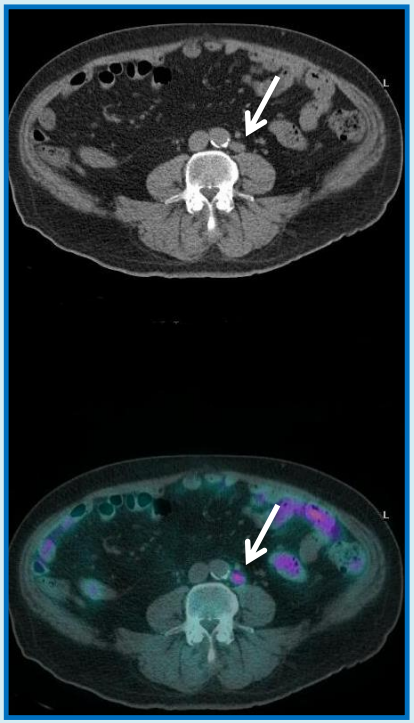
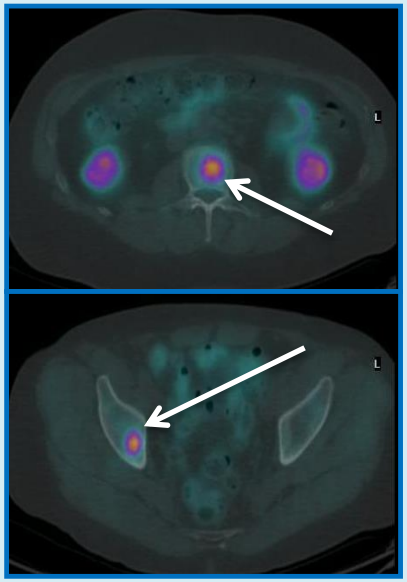




66y male. Rising PSA 2.3 after radical prostatectomy

A small 0.6cm left PA choline-avid lymph node is shown

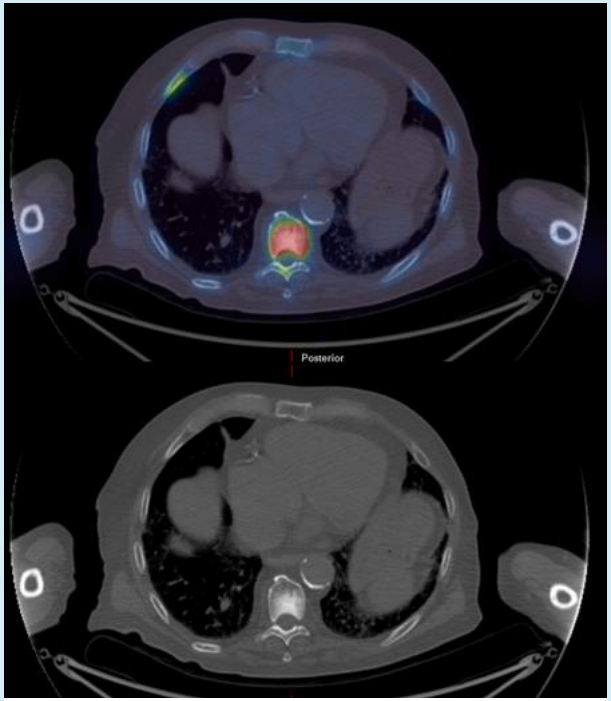


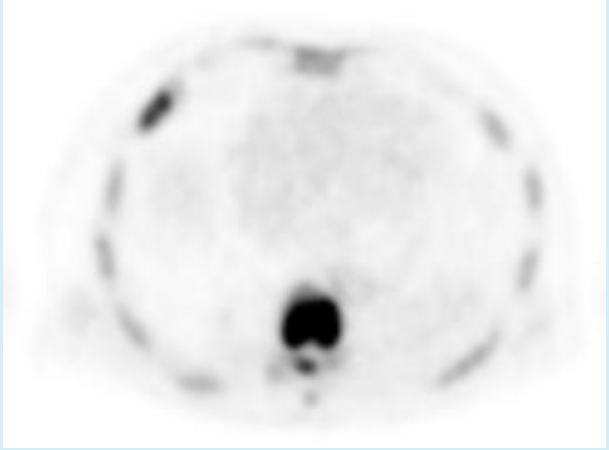
A 64y male. New diagnosis PSA 134 GI 4+4.

Equivocal bone scan with rib hot spot only

Primary tumour uptake

Bone metastases



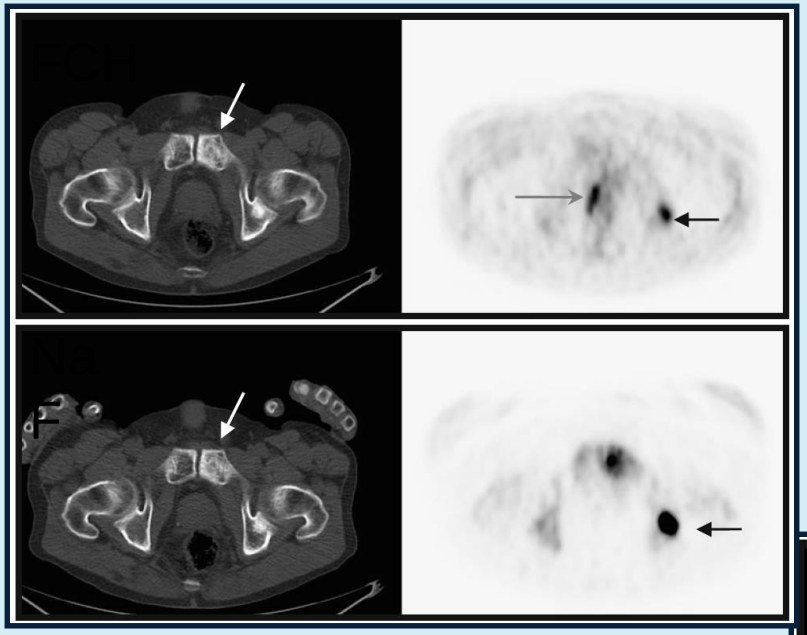




**$^{18}$F-fluoride PET/CT**
**Metastatic prostate cancer**

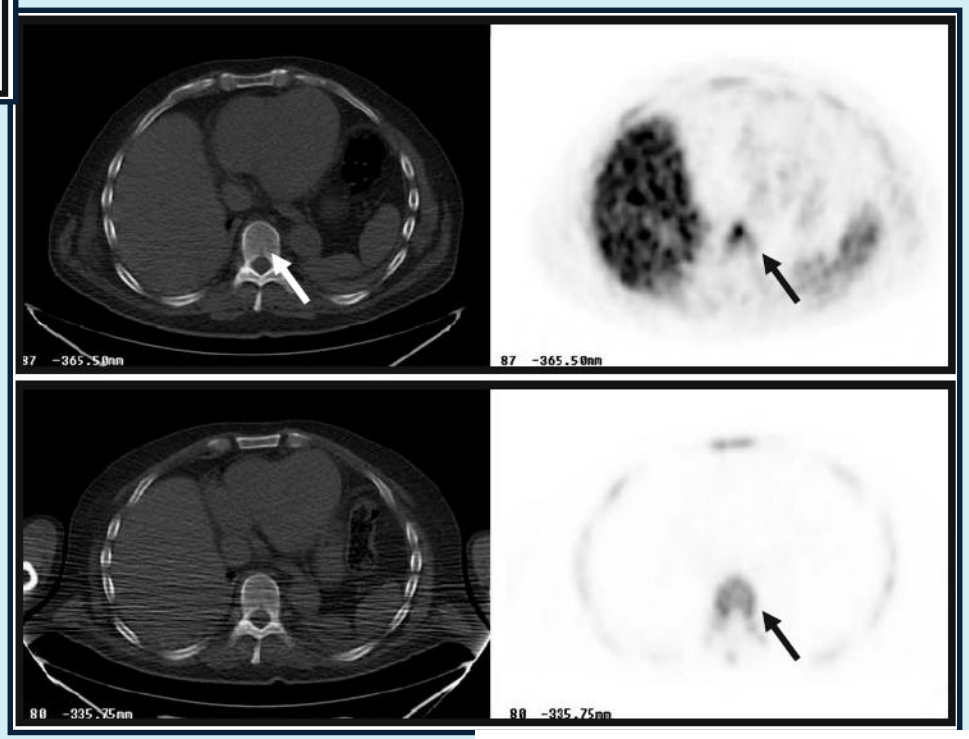
# $^{18}$F-fluoride PET/CT

- *Even-Sapir et al. JNM 2006;47:287*
- **Ca prostate – high risk, n=44**
- **MDP +/- SPECT, F18 +/- CT**
- **F18 PET/CT > F18 PET specificity**
- **F18 PET/CT > planar and SPECT sensitivity and specificity**

# Prostate Cancer




*Beheshti et al. EJNM&MI 2008;35:1766*



Ca prostate (n=38)
$^{18}$F-fluoride: Se 81% Sp 93%  Acc 86%
$^{18}$F-choline:  Se 74% Sp 99%* Acc 85%
Management change in 2/38 due to detection of early marrow metastases

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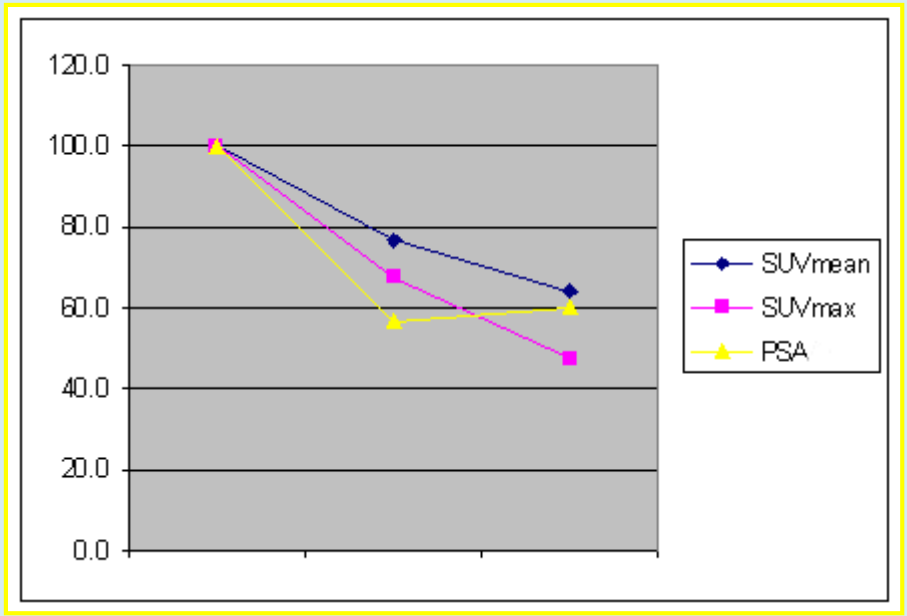
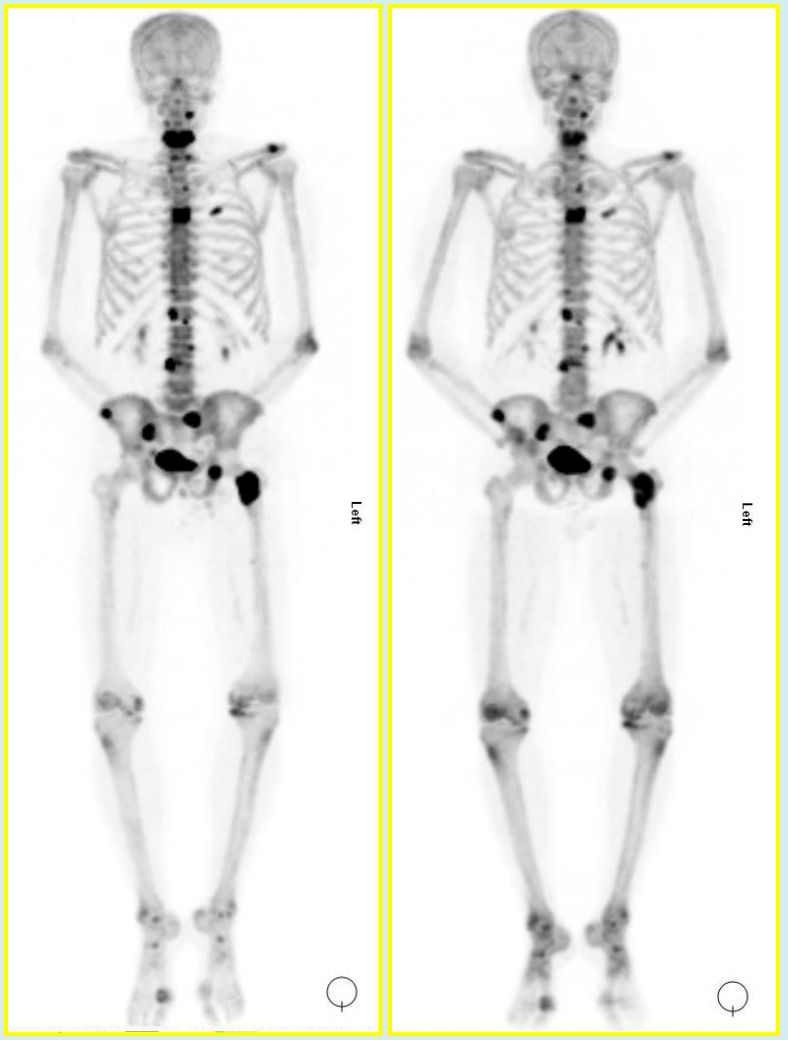
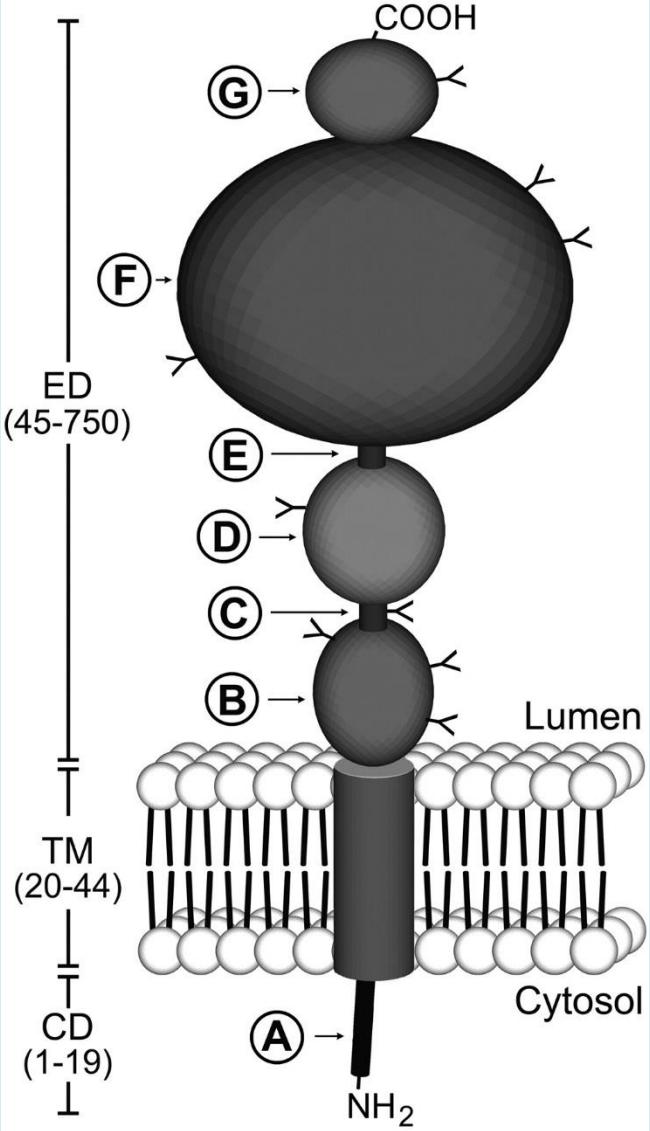



0 and 12 weeks

# PSMA

- Transmembrane glycoprotein expressed by most prostate cancer cells.
- Increased expression in high-grade, metastatic and CRPC.
- Expressed on tumour neovasculature
- Poor results with $^{111}$In-capromab (internal epitope).
- 2nd generation extracellular domain binding
- $^{99m}$Tc-MIP-1404/5 , $^{89}$Zr-J591, $^{18}$F-DCFBC, $^{68}$Ga-PSMA




Rajasekaran A K et al. Am J Physiol Cell Physiol 2005;288:C975-C981

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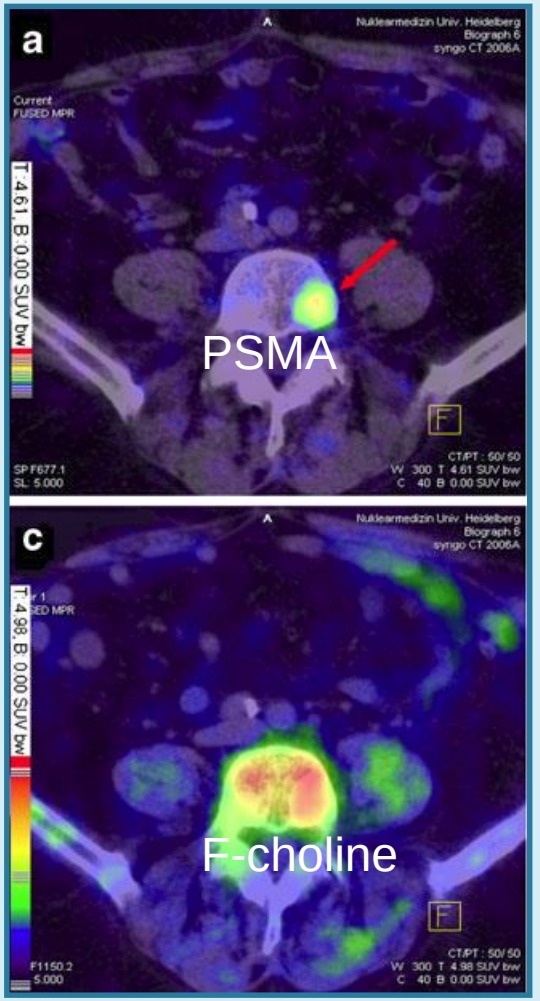
Eur J Nucl Med Mol Imaging (2014) 41:11–20
DOI 10.1007/s00259-013-2525-5

ORIGINAL ARTICLE

# Comparison of PET imaging with a $^{68}$Ga-labelled PSMA ligand and $^{18}$F-choline-based PET/CT for the diagnosis of recurrent prostate cancer

Ali Afshar-Oromieh · Christian M. Zechmann · Anna Malcher · Matthias Eder · Michael Eisenhut · Heinz G. Linhart · Tim Holland-Letz · Boris A. Hadaschik · Frederik L. Giesel · Jürgen Debus · Uwe Haberkorn




- n=37, $^{18}$F-choline, $^{68}$Ga-PSMA, b/c recurrence
- 78 (32) PSMA vs 56 (26) Choline (p = 0.04)
- T:B > 10% higher with PSMA in 94% of lesions

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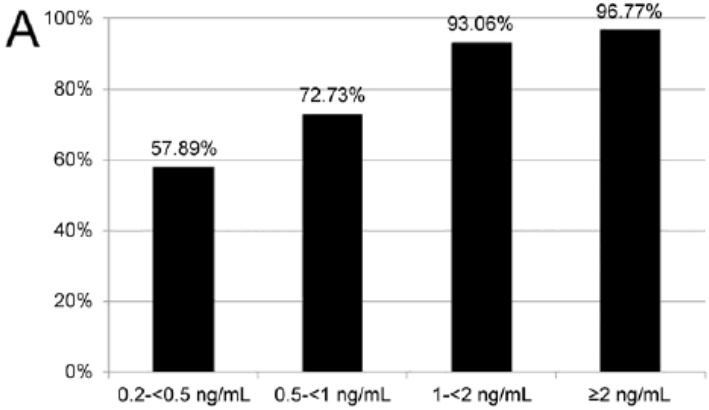
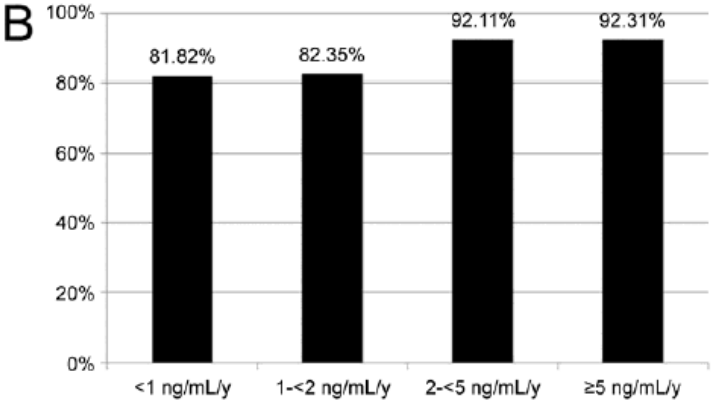
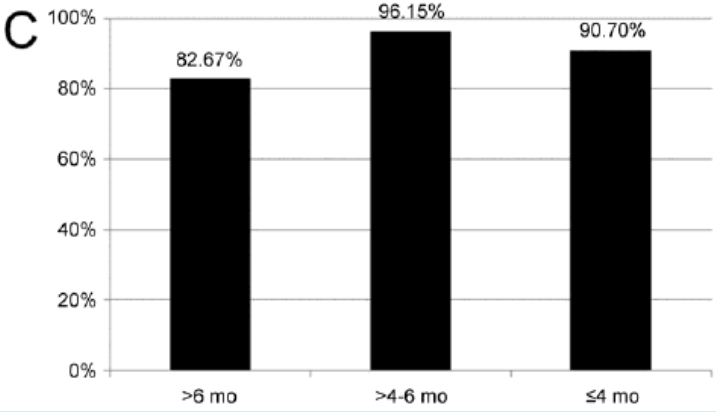
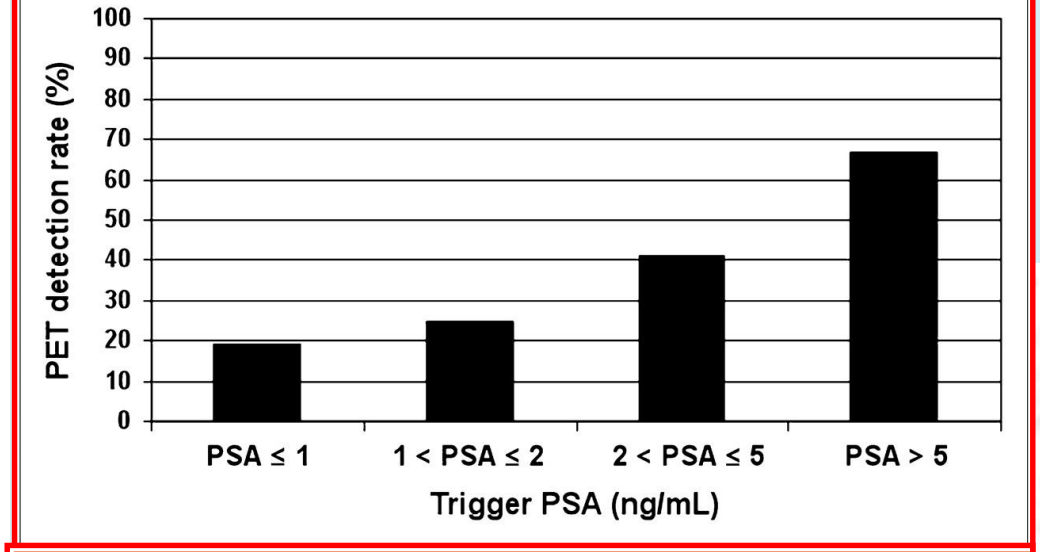


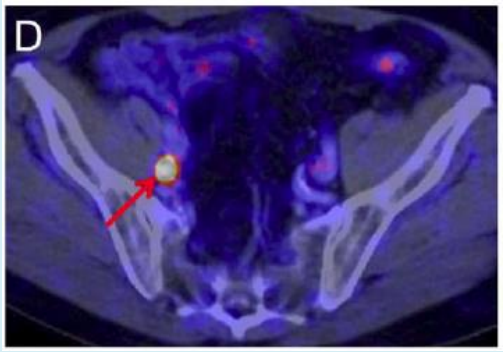



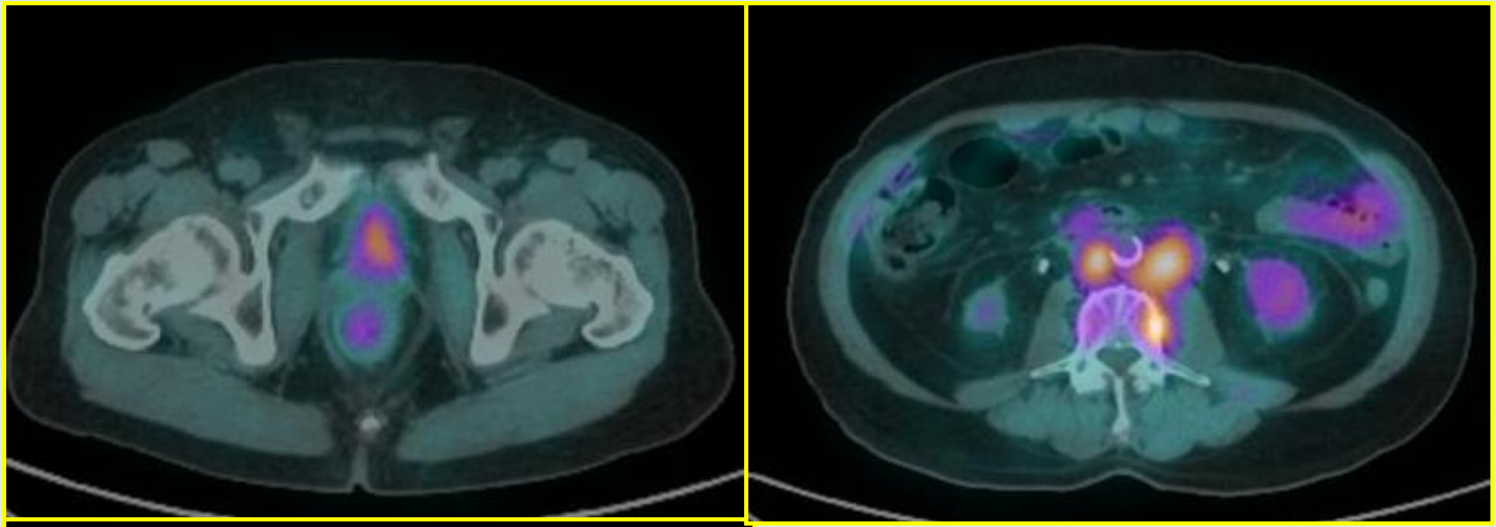

# Influence of Trigger PSA and PSA Kinetics on $^{11}$C-Choline PET/CT Detection Rate in Patients with Biochemical Relapse After Radical Prostatectomy

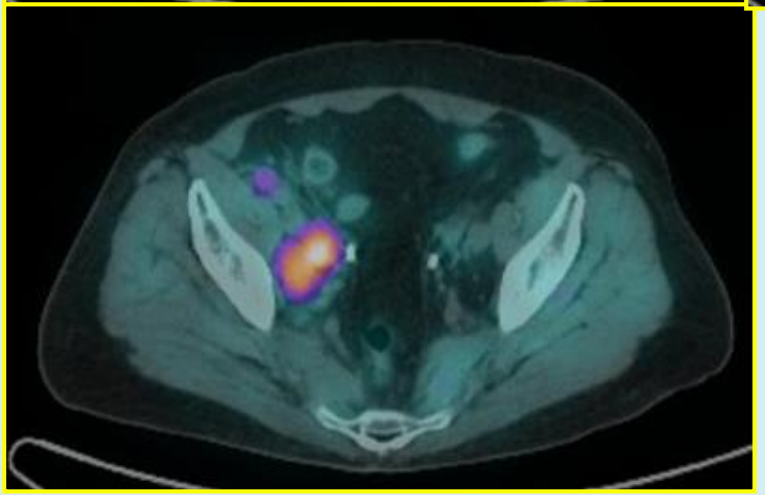
Paolo Castellucci[1], Chiara Fuccio[1], Cristina Nanni[1], Ivan Santi[1], Anna Rizzello[1], Filippo Lodi[1], Alessandro Franceschelli[2], Giuseppe Martorana[2], Fabio Manferrari[2], and Stefano Fanti[1]

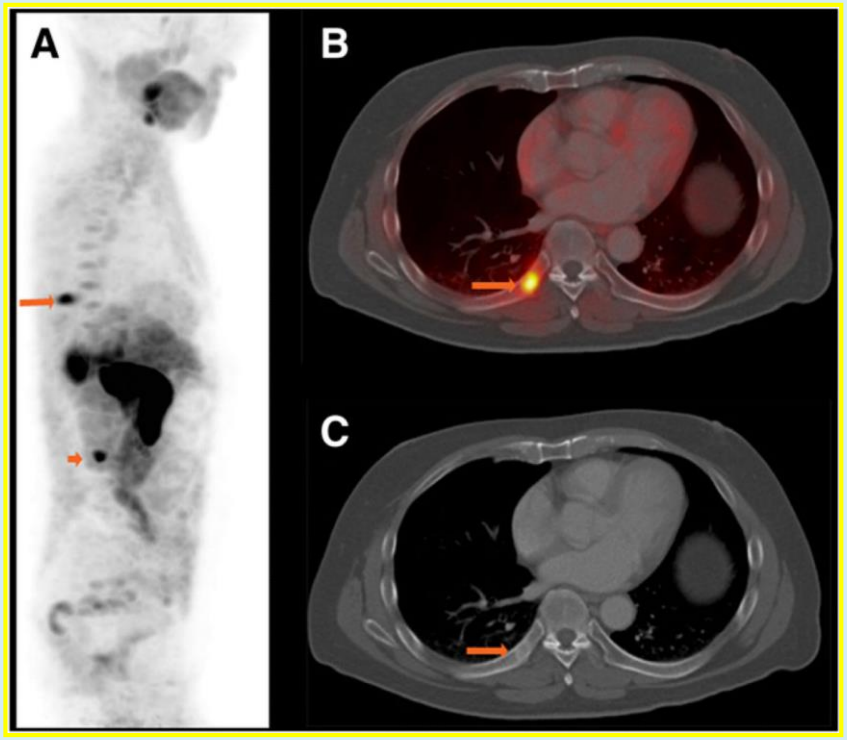



# Other Tracers

- $^{11}$C-acetate: fatty acid synthesis (FA synthase)
- $^{18}$F-FDHT: androgen receptor imaging
- Bombesin analogues: GRPR imaging
- $\alpha_v\beta_3$ integrin imaging: angiogenesis / osteoclasts








$^{11}$C-acetate

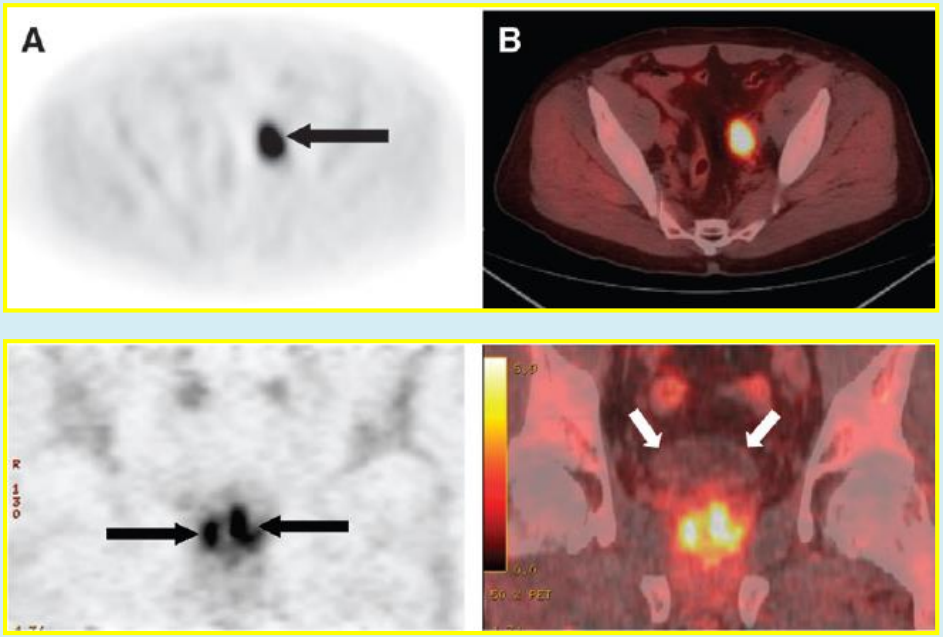
*Jadvar M. JNM 2011;52:81*

# $^{18}$F-FACBC

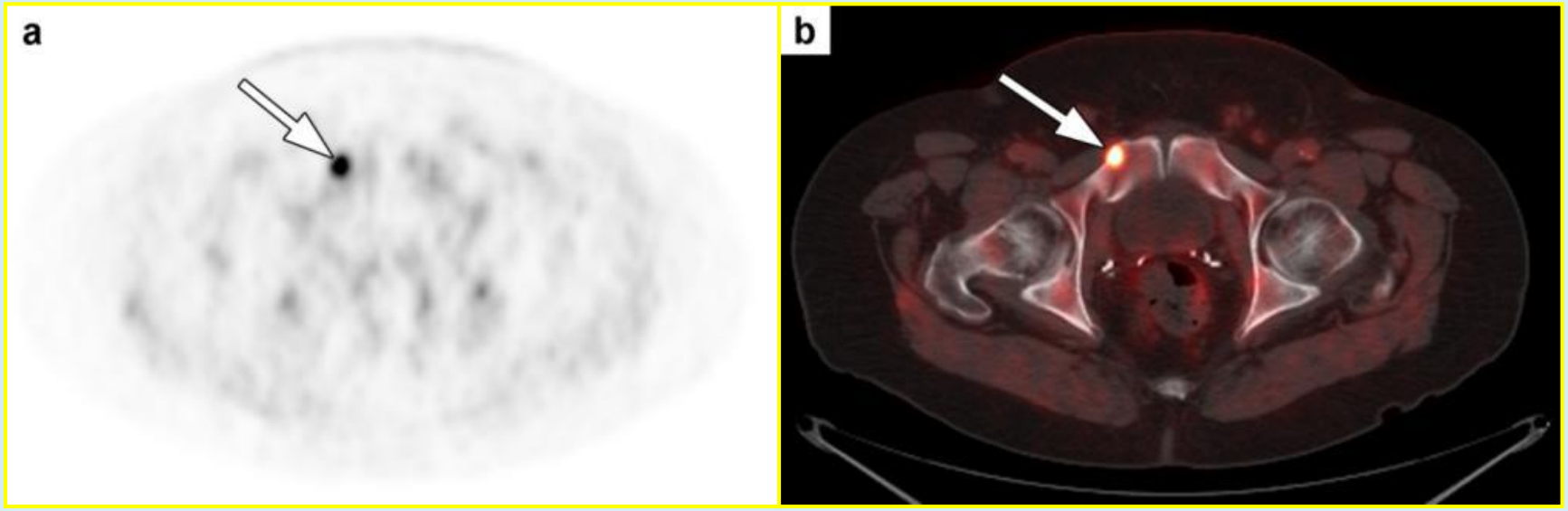
- Synthetic L-leucine analogue
- Amino acid transport system
- Little renal excretion
- 40/48 prostate sextants
- Nodal status 7/9

- UK FALCON (TSB/BED)
- n=140, BCR

*Schuster JNM 2007*

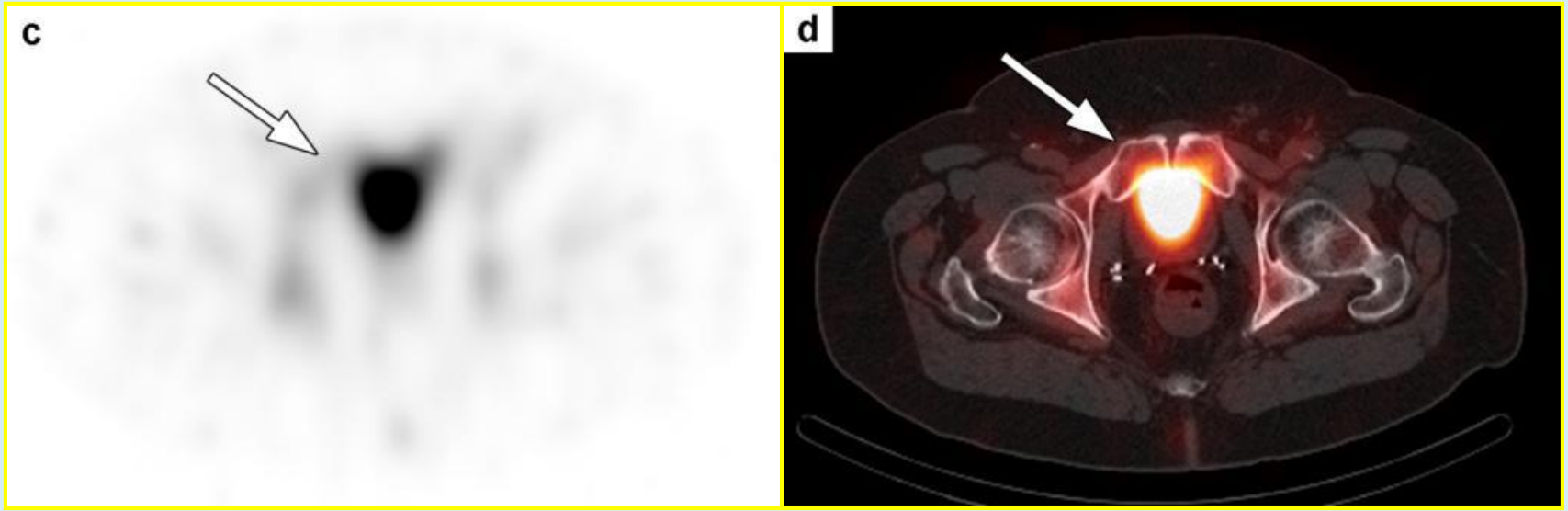


$^{18}$F-FACBC




PSA = 2.9

ProstaScint




*Schuster D et al. Radiology 2011*

VOLUME 31 · NUMBER 28 · OCTOBER 1 2013

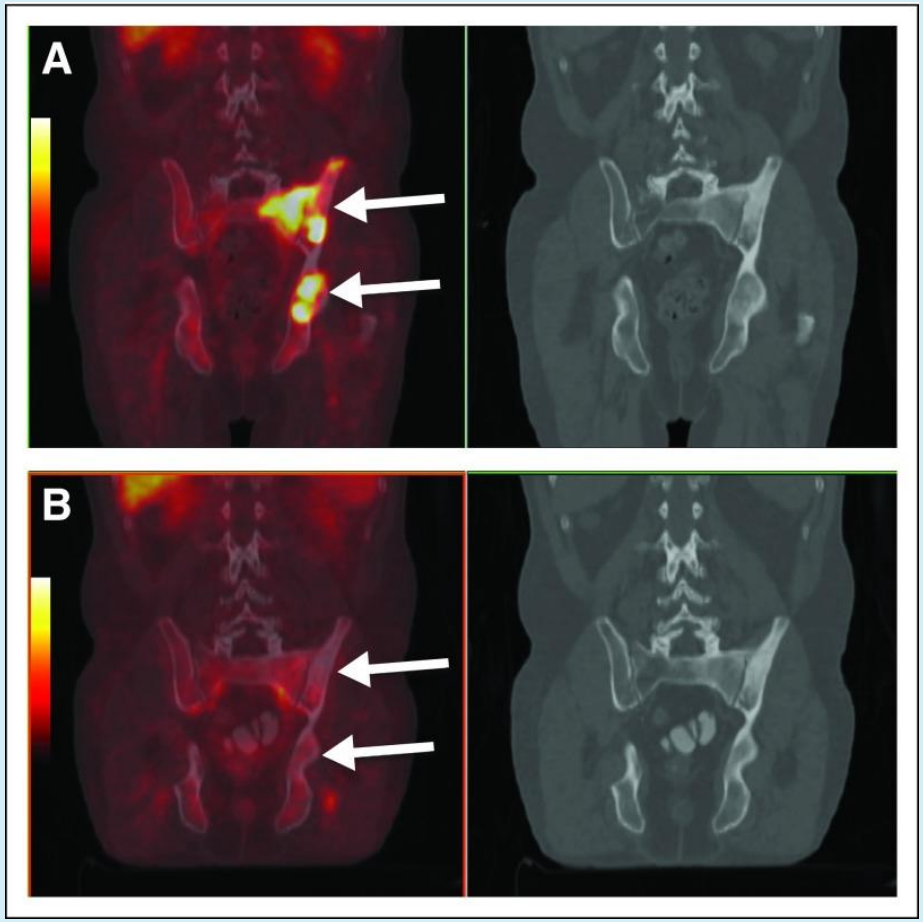
JOURNAL OF CLINICAL ONCOLOGY

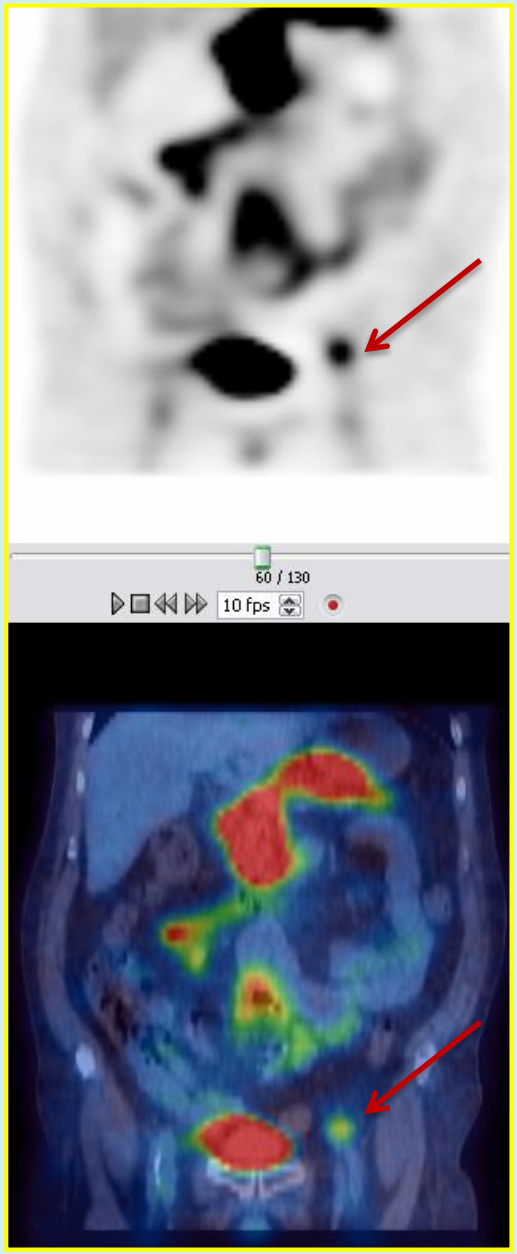
ORIGINAL REPORT

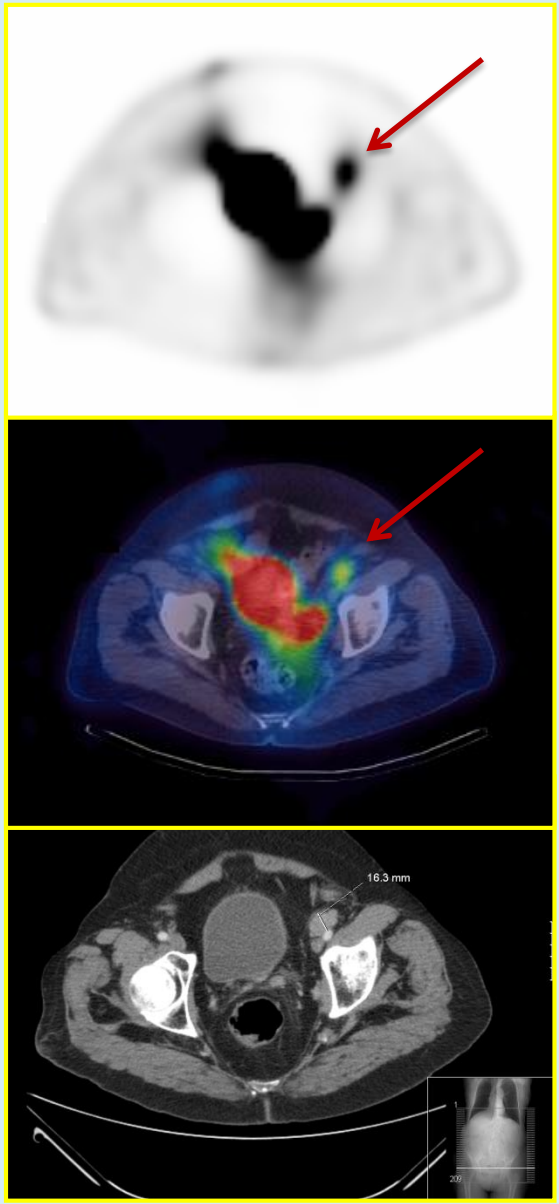
# Phase I Study of ARN-509, a Novel Antiandrogen, in the Treatment of Castration-Resistant Prostate Cancer

*Dana E. Rathkopf, Michael J. Morris, Josef J. Fox, Daniel C. Danila, Susan F. Slovin, Jeffrey H. Hager, Peter J. Rix, Edna Chow Maneval, Isan Chen, Mithat Gönen, Martin Fleisher, Steven M. Larson, Charles L. Sawyers, and Howard I. Scher*

**$^{18}$F-FDHT**





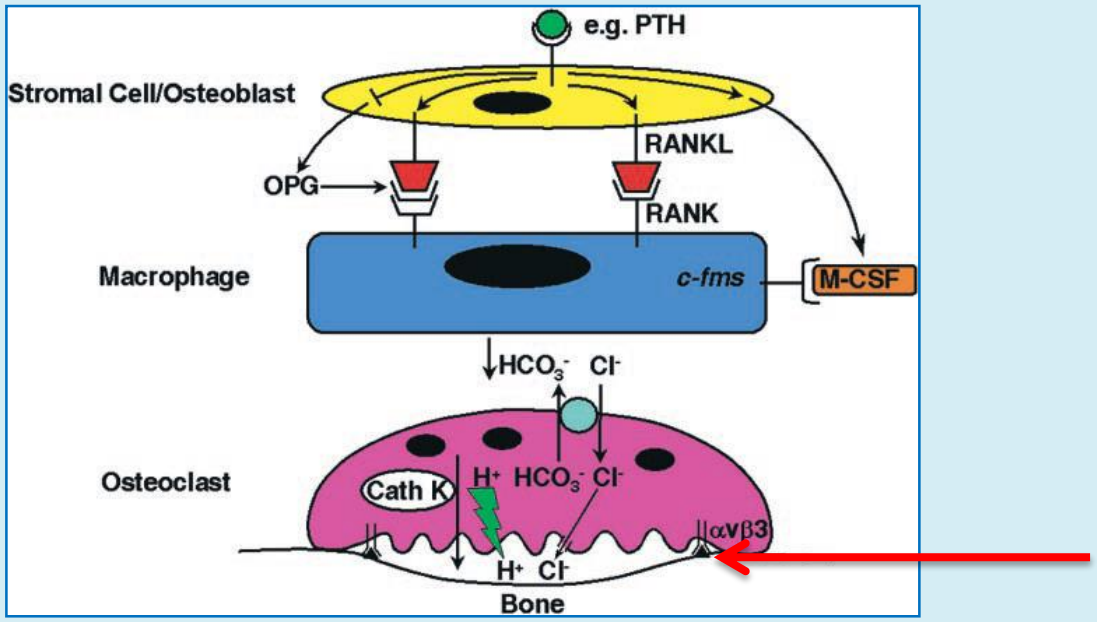

Courtesy: Prof N Avril
St Barts, London

$^{99m}$Tc Demobesin-4

Gastrin Releasing Peptide Receptor imaging

# $\alpha_v\beta_3$ integrin

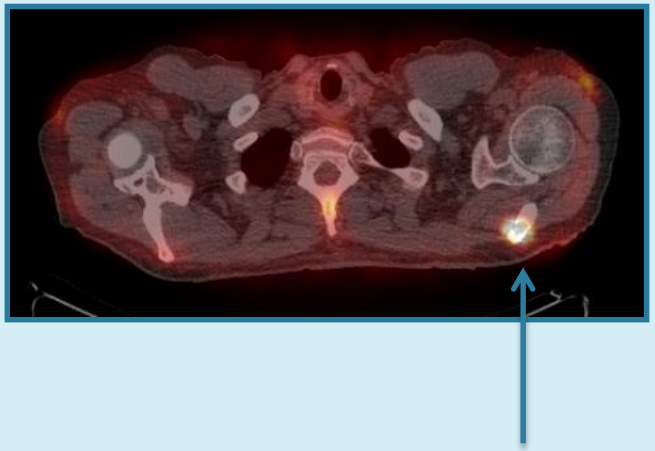
- $\alpha_v\beta_3$ integrin is implicated in the pathogenesis of benign and malignant bone disease where there is increased bone resorption mediated by osteoclasts
- Osteoclasts express the highest levels of $\alpha_v\beta_3$ of any cell in the body.



# Integrin expression

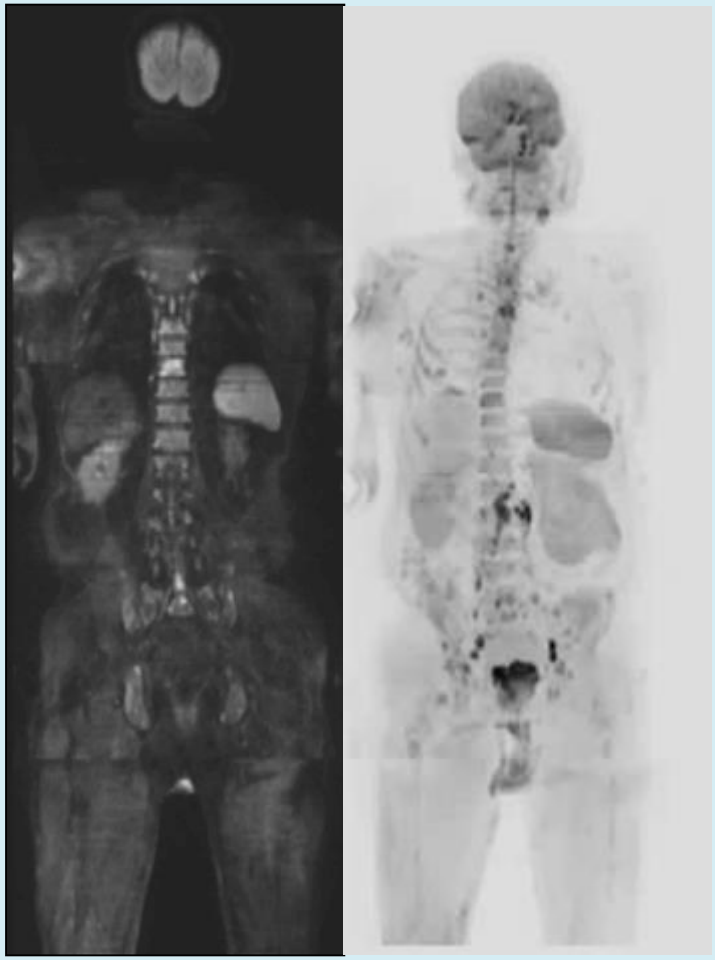
$^{99m}$Tc MDP

$^{99m}$Tc-maraciclatide



Prostate Cancer: Bone metastases

# DW-MRI & cancer



b800 MPR Inverted MIP

**Metastatic Prostate Cancer**

- **<u>High signal intensity on high b-value DWI with cancer reflects its microstructure:</u>**
- Cell density ↑
- Cell size ↓
- Cell membrane integrity ↑
- Extracellular extravascular space ↓
- Macromolecular content ↑
- Glandular tissue ↑
- Necrosis ↑

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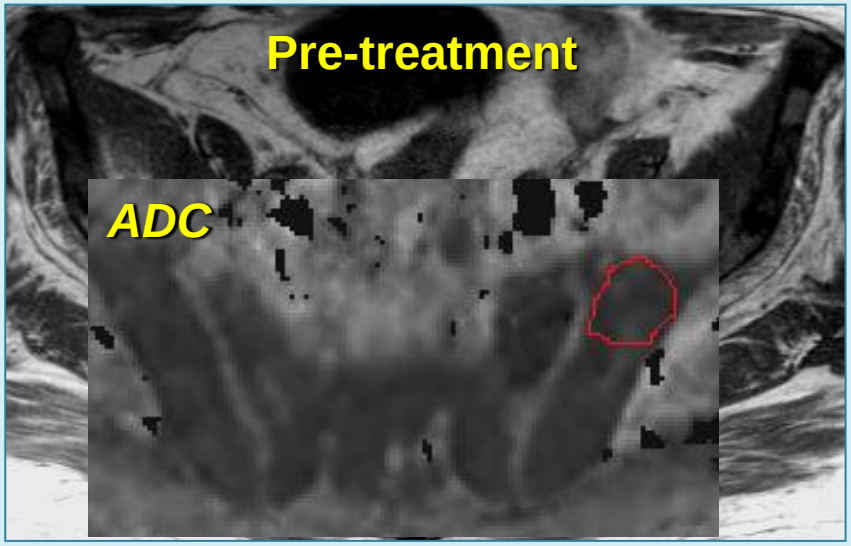
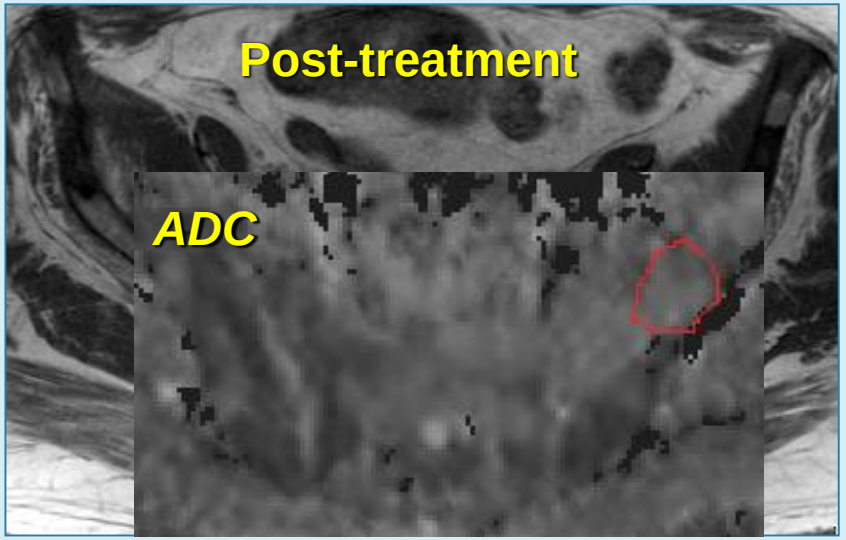
# Treatment Response – DW MRI

## *Bone Metastases*

Courtesy Dr M Koh



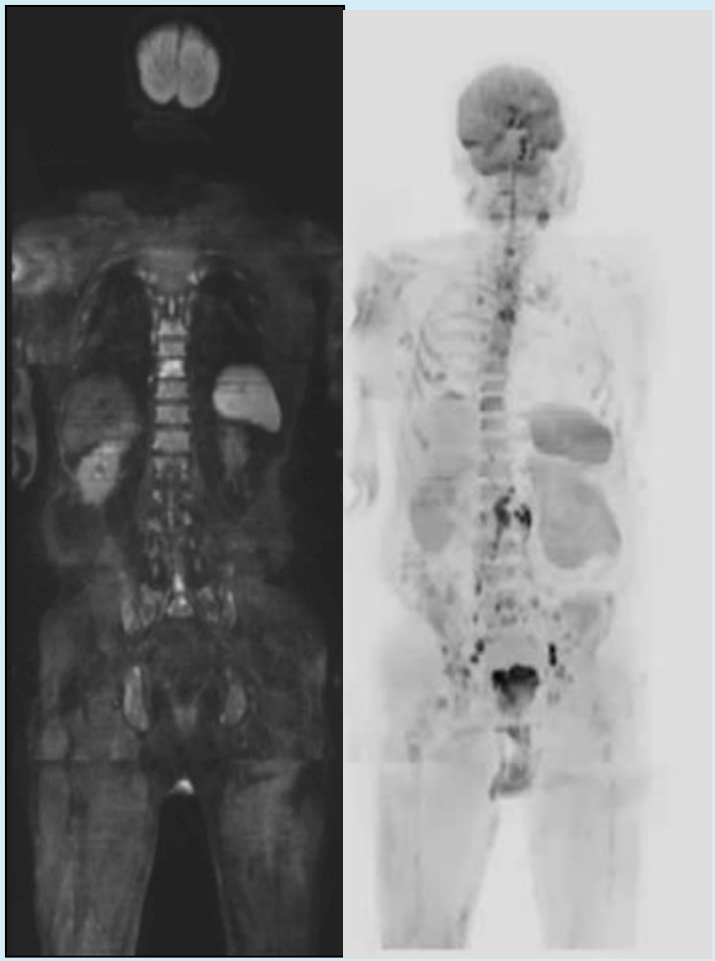

***Median ADC***

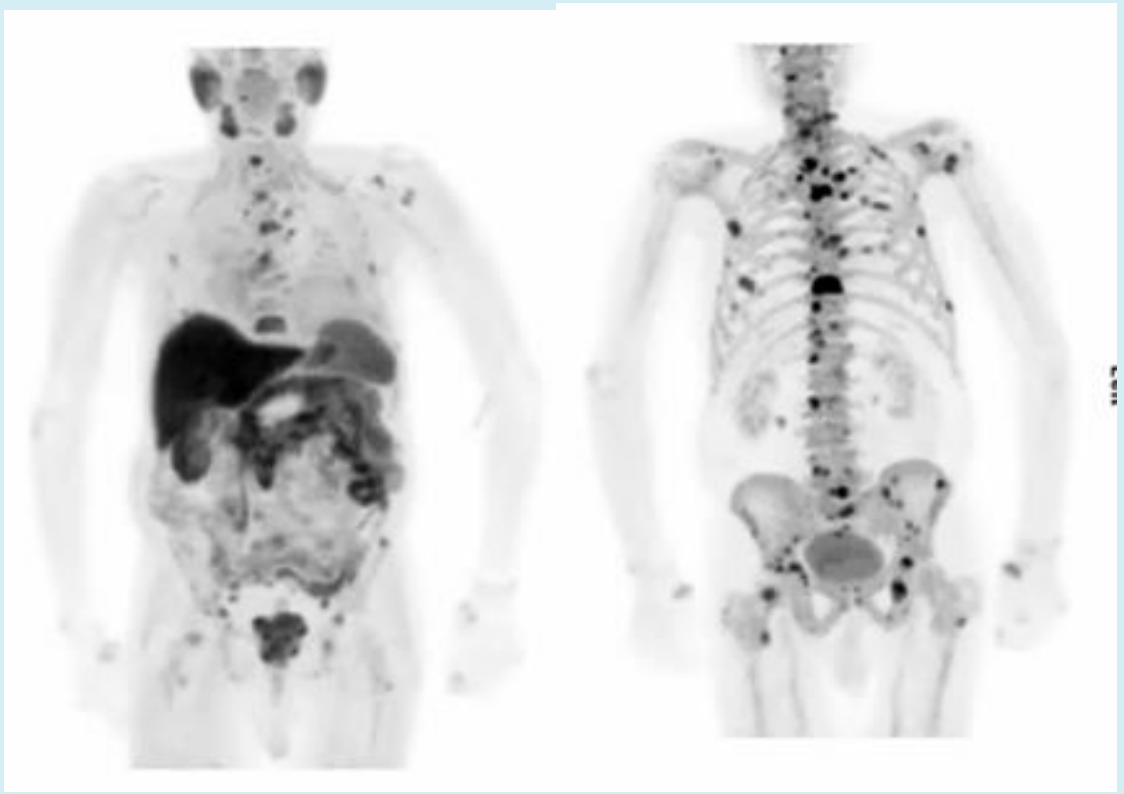
***0.69 x 10-3 mm2/s***

***Median ADC***

***1.56 x 10-3 mm2/s***

# PET/MRI





b800 DW-MRI

18F-choline

18F-fluoride

*Clinical Study*

# Value of Fused $^{18}$F-Choline-PET/MRI to Evaluate Prostate Cancer Relapse in Patients Showing Biochemical Recurrence after EBRT: Preliminary Results

**Arnoldo Piccardo,[1] Francesco Paparo,[2] Riccardo Picazzo,[2] Mehrdad Naseri,[1] Paolo Ricci,[3] Andrea Marziano,[2] Lorenzo Bacigalupo,[2] Ennio Biscaldi,[2] Gian Andrea Rollandi,[2] Filippo Grillo-Ruggieri,[3] and Mohsen Farsad[4]**

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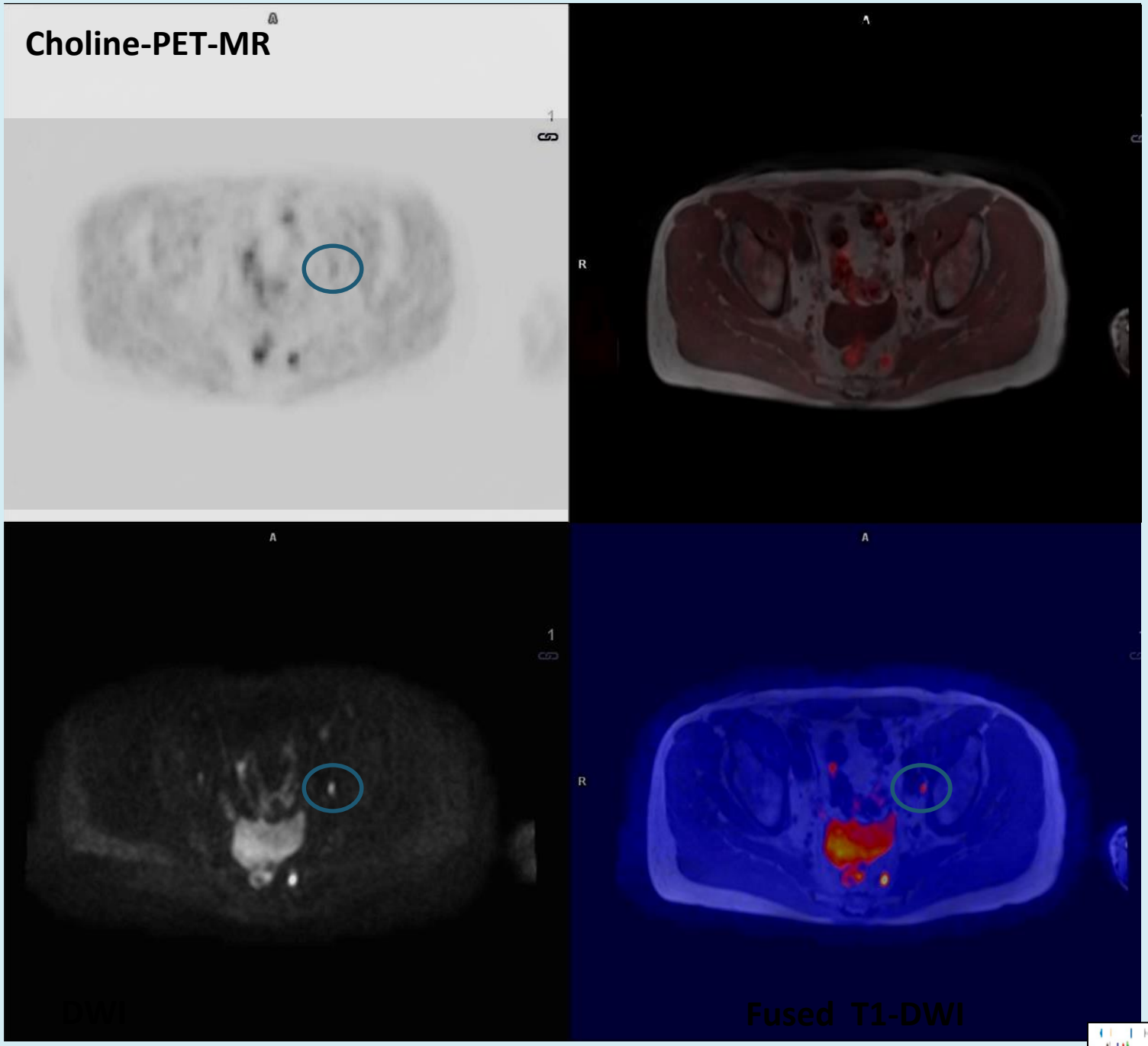
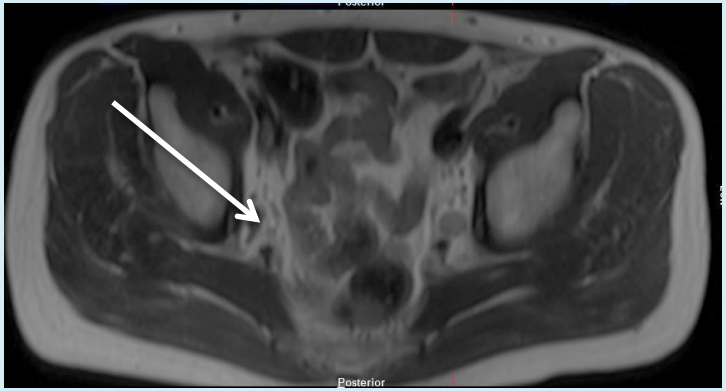
TABLE 3: Lesion-based analysis and sensitivity in lesion detection according to different sites of recurrence/metastases (i.e., local recurrence, lymph nodes, and bone) obtained by mMRI, $^{18}$F-Choline PET/MRI, CeCT, and $^{18}$F-Choline PET/CT.

| | mMRI | $^{18}$F-Choline-PET/MRI | CeCT | $^{18}$F-Choline-PET/CT |
|---|---|---|---|---|
| Prostate gland | | | | |
| Sensitivity | 6/6 (100%) | 6/6 (100%) | 1/6 (17%) | 4/6 (67%) |
| Specificity | 14/15 (93%) | 15/15 (100%) | 15/15 (100%) | 15/15 (100%) |
| Accuracy | 20/21 (95%) | 21/21 (100%) | 16/21 (76%) | 19/21 (90%) |
| Lymph nodes | | | | |
| Sensitivity | 27/40 (67%) | 40/40 (100%) | 23/40 (57%) | 40/40 (100%) |
| Specificity | 15/15 (100%) | 15/15 (100%) | 15/15 (100%) | 15/15 (100%) |
| Accuracy | 42/55 (76%) | 55/55 (100%) | 38/55 (69%) | 55/55 (100%) |
| Bone | | | | |
| Sensitivity | 14/14 (100%) | 14/14 (100%) | 6/14 (43%) | 13/14 (93%) |
| Specificity | 11/12 (92%) | 11/12 (92%) | 12/12 (100%) | 11/12 (92%) |
| Accuracy | 25/26 (96%) | 25/26 (96%) | 18/26 (69%) | 25/26 (96%) |

# Choline-PET-MR

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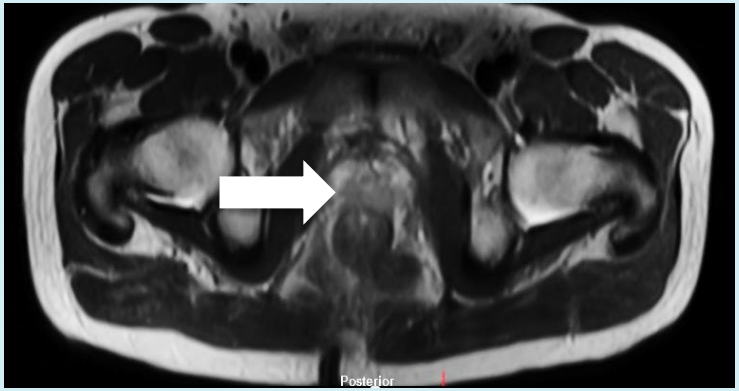
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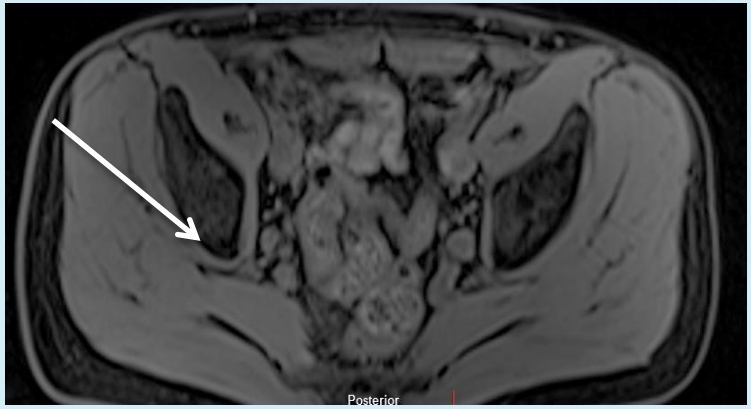
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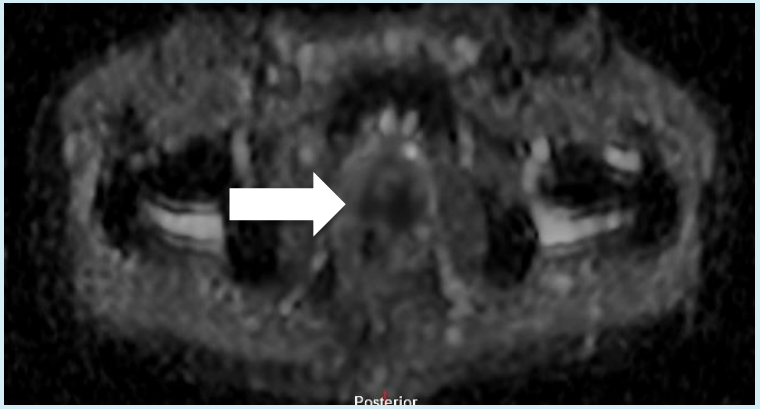
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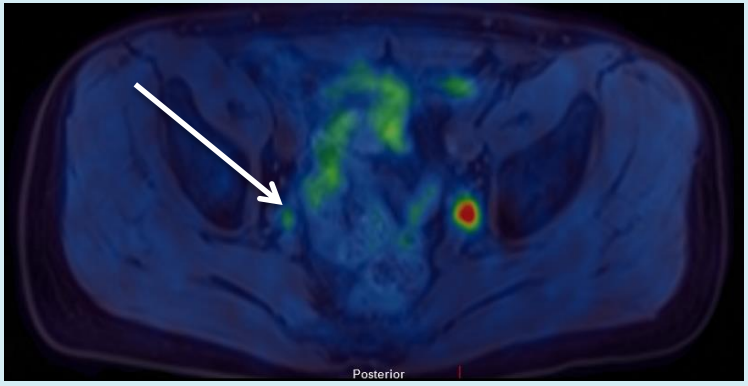
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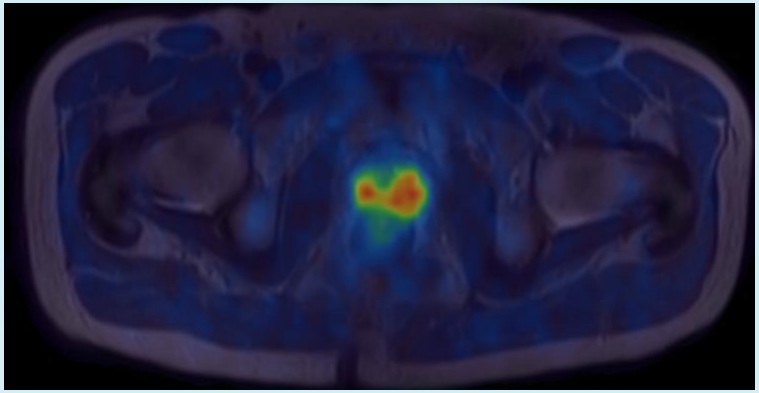

# Conclusions

- Skeletal staging: Choline vs Fluoride or bone scan?
- Choline PET/CT is of additional benefit in patients with biochemical recurrence
- Choline will probably be replaced with PSMA
- PET/MRI will probably show best overall accuracy

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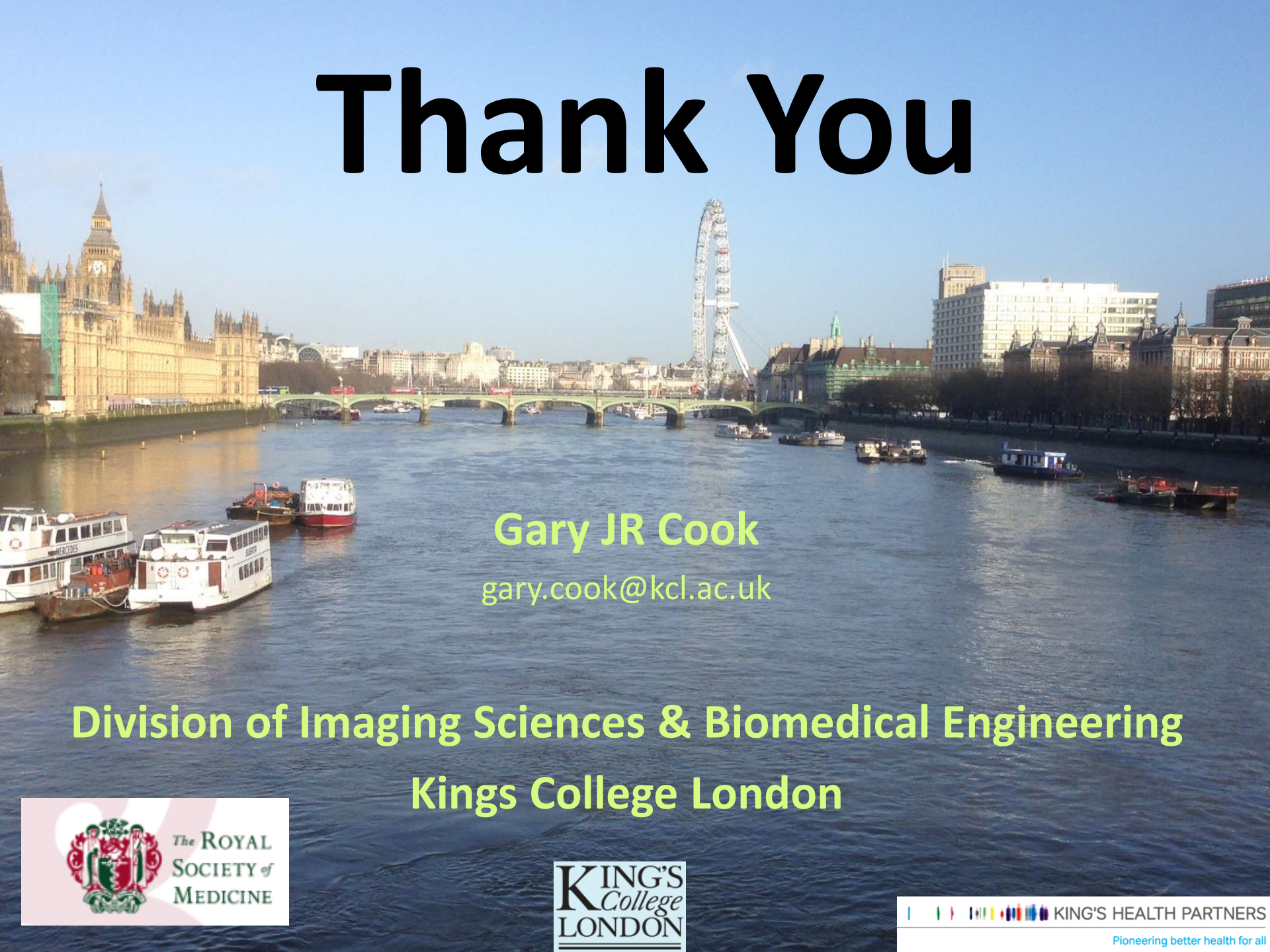
# Thank You




**Gary JR Cook**

gary.cook@kcl.ac.uk

**Division of Imaging Sciences & Biomedical Engineering**

**Kings College London**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