

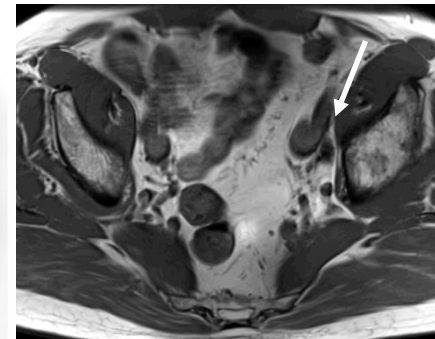
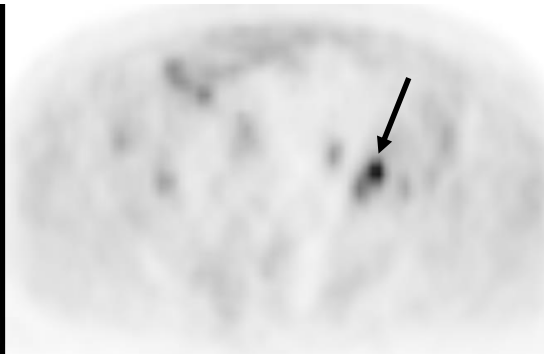
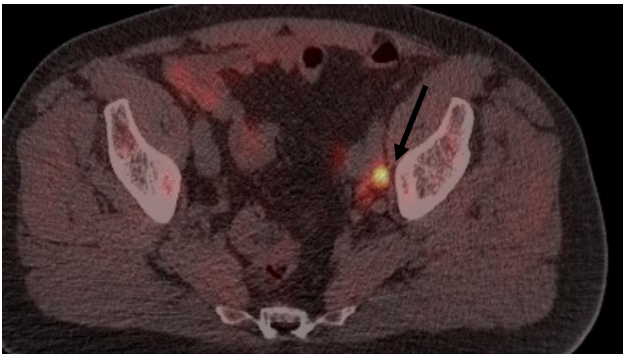
Choline PET/CT in Prostate Cancer Imaging

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Honorary Clinical Senior Lecturer, Division of Cancer, Imperial College
UKRC June 2014*

Aims of talk

1. To understand the role of choline PET in the multimodality pathway of prostate cancer
2. To describe the mechanism of action and technical aspects
3. To understand the main indications of choline PET in prostate cancer
4. To highlight the imaging pearls and pitfalls with case examples.



Prostate cancer

- Most commonly diagnosed cancer in men (PSA screening)
- Second cause of cancer death after lung cancer
- Diagnostic tools DRE, PSA, TRUS and perineal template biopsy
- Controversy regarding – over diagnosis, spectrum of disease, what is clinically significant etc

	Low	Intermediate	High
Stage (DRE)	T1-T2a	T2b	≥T2c
GS	2-6	7	8-10
PSA (ng/ml)	<10	10-20	>20

NCCN/ NICE

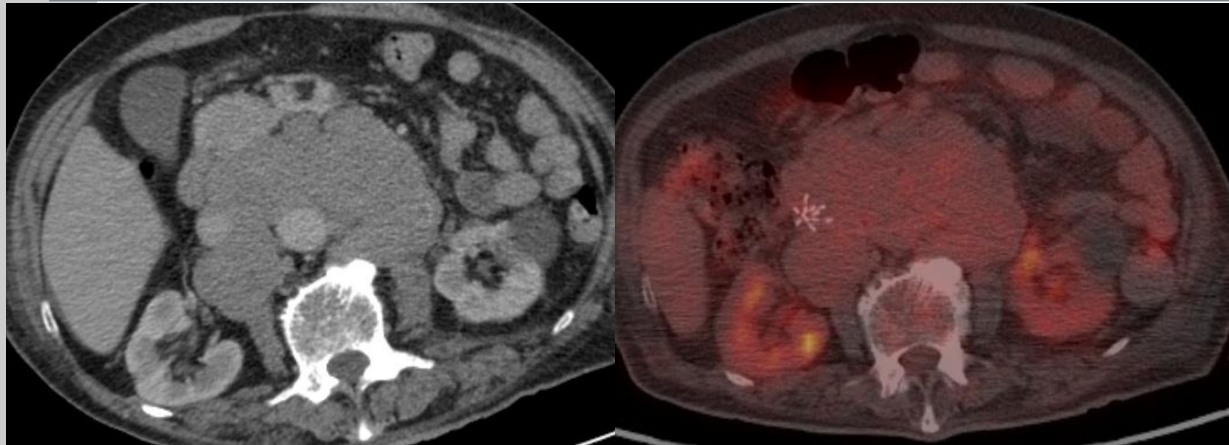
Prostate cancer

- Most frequent metastases to lymph nodes (pelvic / retroperitoneal)
- Bone- 80% of the metastatic sites but only 10% have bone metastases at diagnosis
- Lung and liver (late stages)

Treatment

- LOCALISED: active surveillance, radical prostatectomy, EBRT and brachytherapy
- LOCALLY ADVANCED hormone therapy
- METASTATIC hormone therapy/ chemotherapy/ novel agent

F-18 FDG PET prostate cancer



Pitfall FDG: Limited utility due to relatively low glucose metabolism of most PC

Why Choline?

- Essential component of phospholipids and cell membrane metabolism
- Choline is incorporated into cell membrane phospholipids through phosphoryl choline synthesis *Roivainen A et al 00*
- Choline is phosphorylated by choline kinase & trapped in the cell
- Malignant tumours increased cell membrane metabolism, increased choline use and increased CK expression (enzyme which phosphorylates choline) *Ackerstaff et al, Can Res 2001*



C-11 F-18 choline in prostate cancer

Tracer	Advantages	Limitations
C-11 choline	Low urinary excretion Ideal choline tracer (biologically the same as natural choline)	Half life 20 mins On site cyclotron
F-18 fluoroethylcholine (FEC) F-18 fluoromethylcholine (FMC)	Half life 110 mins	Urinary excretion (FMC < FEC) Limited availability in UK

ORIGINAL ARTICLE

¹⁸F-fluorocholine for prostate cancer imaging: a systematic review of the literature

G Bauman¹, T Belhocine², M Kovacs², A Ward³, M Beheshti⁴ and I Rachinsky²

- Patient prep- fasting 6 hours (reduced bowel uptake)
- Administered activity 330 MBq (approx 10 mSv) *De Grado JNM 01*
- Started with early dynamic pelvic
- Now 45-60 mins pi half body vertex to upper thighs
- Flat bed

Dynamic acquisition followed by static whole-body acquisition		Early acquisition		Delayed acquisition		Early and delayed acquisition	
Authors ^{ref.}	Number of patients	Authors ^{ref.}	Number of patients	Authors ^{ref.}	Number of patients	Authors ^{ref.}	Number of patients
DeGrado <i>et al.</i> ²⁰	4	DeGrado TR <i>et al.</i> ²²	7	Ciernik <i>et al.</i> ⁵⁴	10	Kwee <i>et al.</i> ²⁸	26
DeGrado <i>et al.</i> ²¹	1	Kwee <i>et al.</i> ²⁷	17	Pelosi <i>et al.</i> ⁴³	56	Cimitan <i>et al.</i> ⁴¹	100
Price DT <i>et al.</i> ²⁴	18	Schmid <i>et al.</i> ³²	19	Pinkawa <i>et al.</i> ⁴⁹	12	Igerc <i>et al.</i> ³¹	20
Hacker <i>et al.</i> ³⁵	20	Vees <i>et al.</i> ⁴⁵	11	Uusijarvi <i>et al.</i> ²³	4	Steiner <i>et al.</i> ⁴⁴	47
Heinisch <i>et al.</i> ⁴²	34	Kwee <i>et al.</i> ²⁹	15	Schillaci <i>et al.</i> ⁵⁶	80	Wang <i>et al.</i> ⁵¹	17
Beheshti <i>et al.</i> ³⁷	38	Husarik <i>et al.</i> ³⁶	111	Pinkawa <i>et al.</i> ⁵⁰	66	Weber <i>et al.</i> ⁵²	7
Beheshti <i>et al.</i> ³⁸	70	Kwee <i>et al.</i> ³⁹	30	Panebianco <i>et al.</i> ⁴⁶	84	Beheshti <i>et al.</i> ³⁰	130
Beauregard <i>et al.</i> ³⁴	16	McCarthy <i>et al.</i> ⁴⁸	26			Poulsen <i>et al.</i> ³³	25
		Casamassima <i>et al.</i> ⁴⁷	71				
		Roef <i>et al.</i> ⁵⁵	10				
		Langsteger <i>et al.</i> ⁴⁰	42 ^a				

Abbreviations: CET, computed tomography; ¹⁸F-FCH, [¹⁸F]fluoromethyl-dimethyl-2-hydroxyethyl-ammonium; i.v., intravenous; PET, positron emission tomography. Early acquisition: 0–15 min post-i.v.; delayed acquisition: 30, 40, 45, 60, 90–120 or 65–200 min post-i.v.

Availability and cost

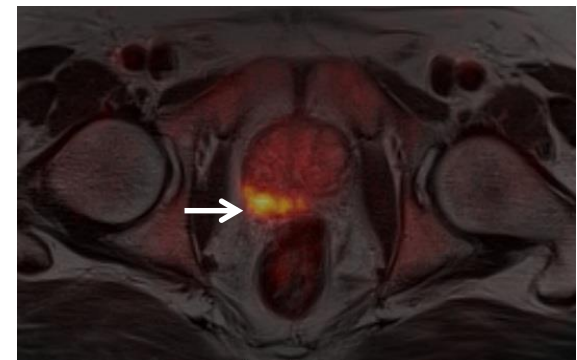
- Erigal F-18 FEC
Tuesdays & Thursdays
- Petnet F-18 FMC
Mondays

Cost £450- £650

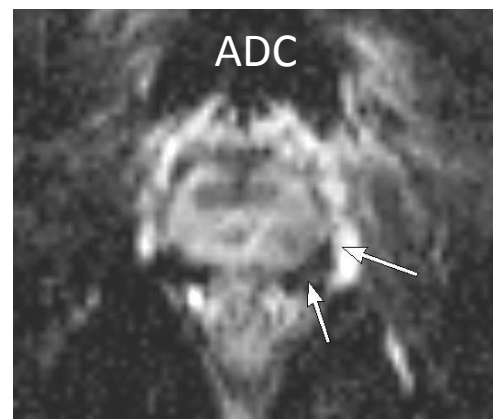
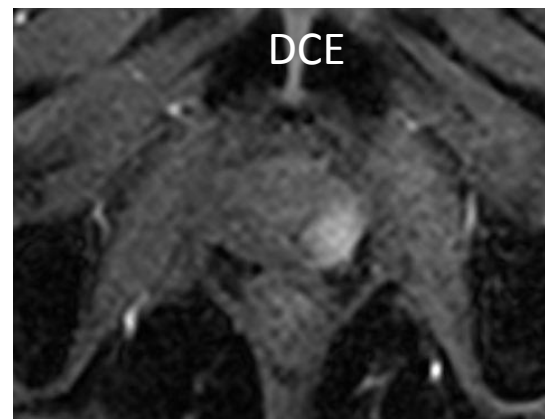
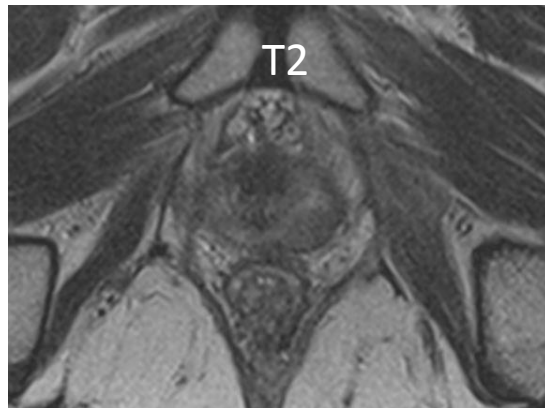


PET/CT in prostate cancer

- Diagnosis
- Localization
- Primary staging
- Biochemical relapse post radical therapy
- Radiation therapy planning
- Response assessment- salvage and systemic therapy



Multiparametric MRI (mp MRI)



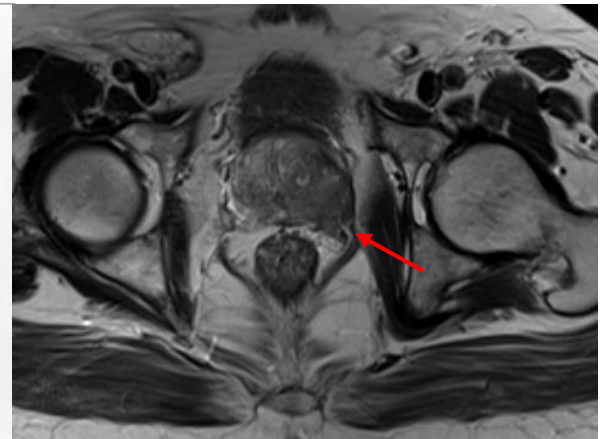
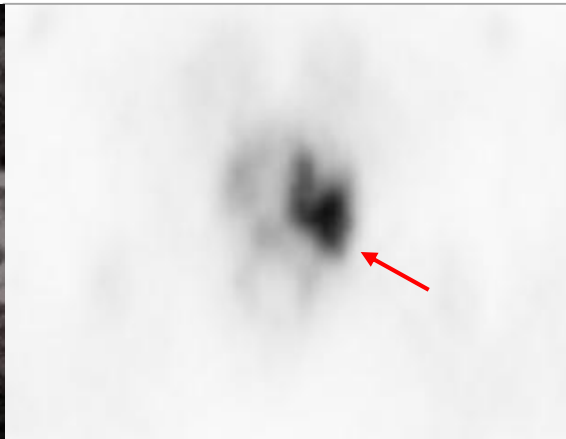
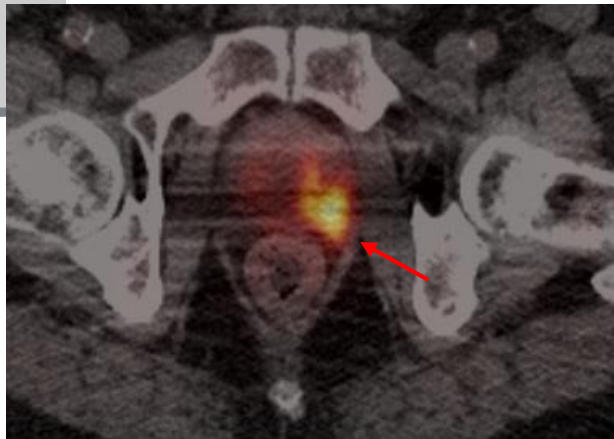
NICE 2014: mpMRI

Men with negative prostate biopsy and elevated PSA

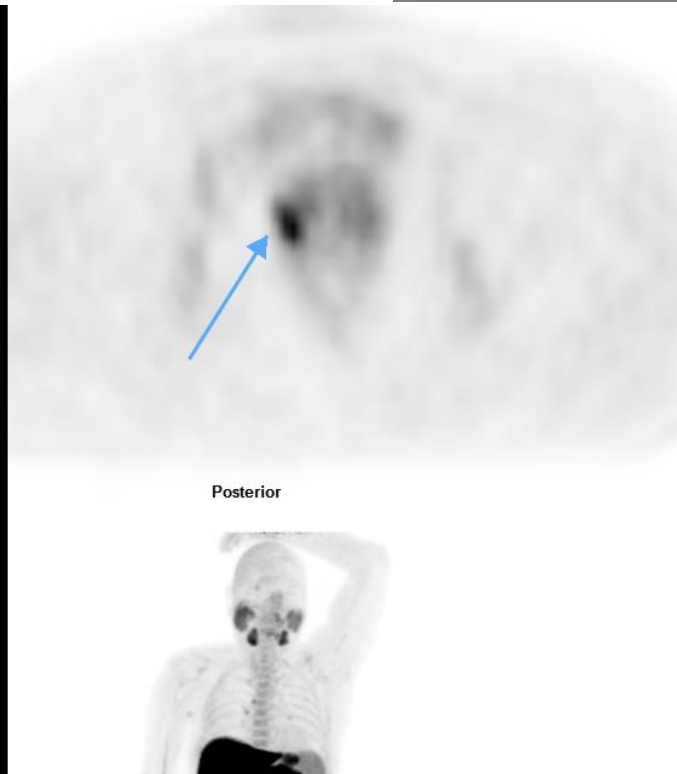
Staging if knowledge of T or N stage could affect management

Staging Prostate cancer

- mpMRI is superior for localisation and T stage
- Choline PET cannot reliably differentiate between BPH and cancer
- Not reliable for ECE and SV invasion
- CECT, Bone scintigraphy



PSA rising , repeated negative biopsies has pacemaker so can't have mpMRI



Pitfall: cannot differentiate between BPH and prostate cancer- NOT for localisation/ T stage

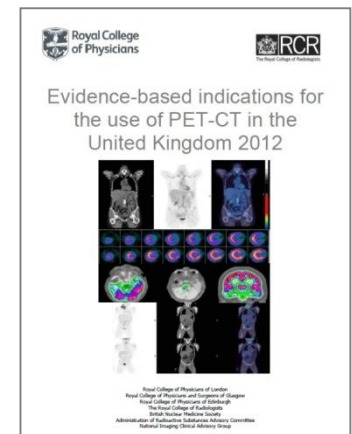
Pearl: may however be useful in cases where MRI contra indicated

PET/CT in prostate cancer

- Diagnosis
- Localization
- Primary staging
- Biochemical relapse post radical therapy
- Radiation therapy planning
- Response assessment- salvage and systemic therapy

Choline PET/CT indications:

1. Rising PSA post radical therapy
2. High risk staging- equivocal finding on CWU



Nodal staging in Prostate cancer

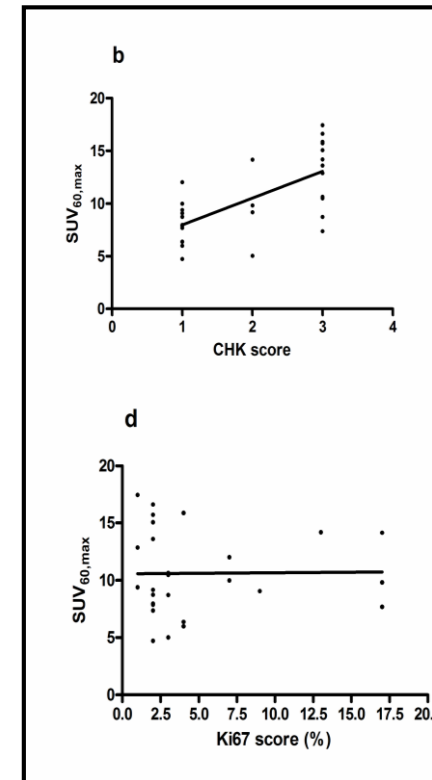
- LN metastases are seen in 25-30% of pts
- LN involvement reduces disease free survival from 85% to 50%
- Pelvic LND – gold standard
 - Invasive
 - 4-5% morbidity
 - Expensive, needs hospitalization
 - May not be able to sample all potential nodal areas
- Standard anatomic imaging has limited diagnostic accuracy
 - Pooled sensitivity – 39%
 - Pooled specificity – 82%

Use of [^{11}C]Choline PET-CT as a Noninvasive Method for Detecting Pelvic Lymph Node Status from Prostate Cancer and Relationship with Choline Kinase Expression

Kaiyumars Contractor¹, Amamath Challapalli¹, Tara Barwick², Mathias Winkler¹, Giles Hellowell¹, Steve Hazell³, Giampaolo Tomasi¹, Adil Al-Nahhas², Paola Mapelli¹, Laura M. Kenny¹, Paul Tadrous⁴, R. Charles Coombes¹, Eric O. Aboagye¹, and Stephen Mangar¹

Cancer Res; 17(24); 7673–83. ©2011 AACR.

- 406 LN in 26 pts lymphadenectomy
- 27/ 406 LN positive- 17/27 <1cm size
- MRI Per nodal Sens 18.5% Spec 98.7%
Per patient Sens 50% Spec 72.2%
- PET/CT Per nodal Sens 51.9 % Spec 98.4%
Per patient Sens 77.8% Spec 82.4%





N Stage

No. of patients	Radiopharmaceutical and imaging scan	Scan
12	11C-Choline	PET
25	11C-Choline	PET
67	11C-Choline	PET
20	18F-Choline	PET/CT
57	11C-Choline	PET/CT
43	18F-Choline	PET/CT
130	18F-Choline	PET/CT
25	18F-Choline	PET/CT
36	11C-Choline	PET/CT
26	11C-Choline	PET and PET/CT

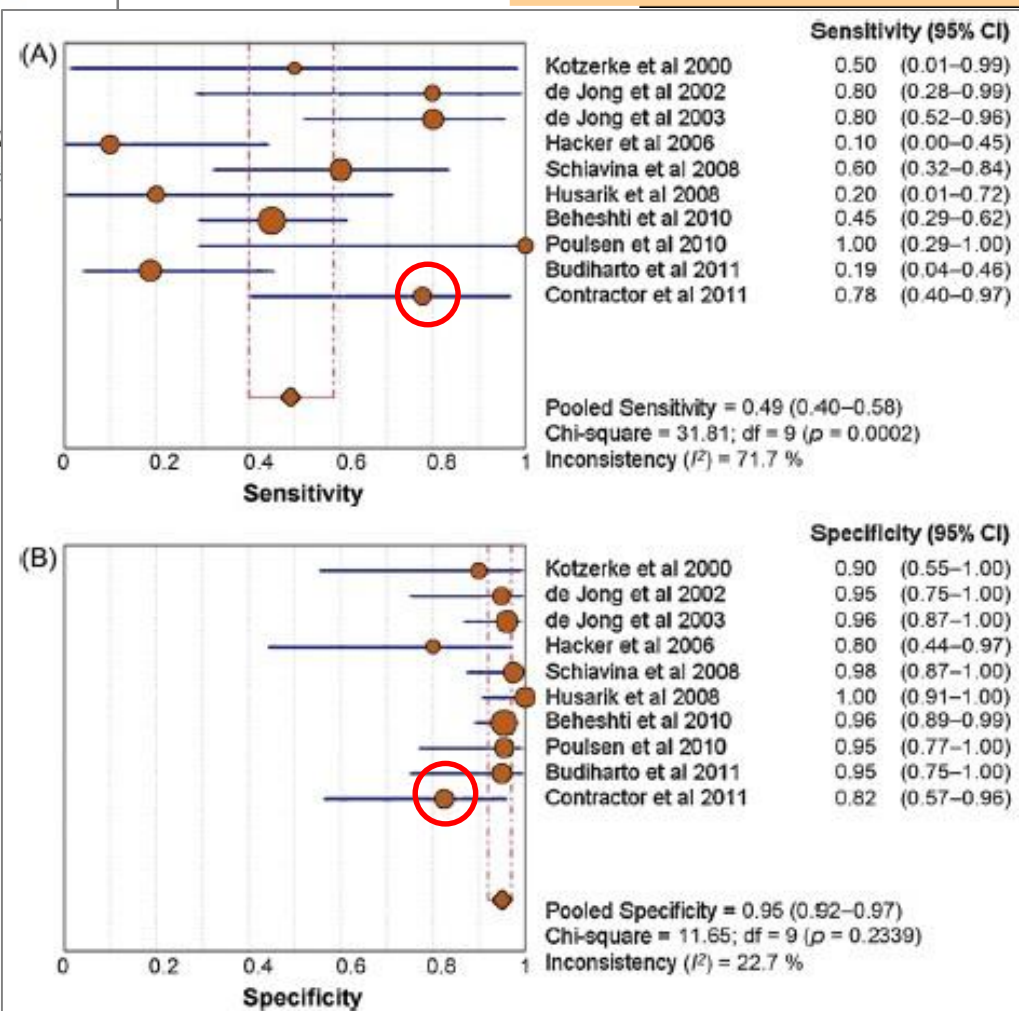
Review – Prostate Cancer

Utility of Choline Positron Emission Tomography/Computed Tomography for Lymph Node Involvement Identification in Intermediate- to High-risk Prostate Cancer: A Systematic Literature Review and Meta-analysis

Laura Evangelista^{a,*}, Andrea Guttilla^b, Fabio Zattoni^b, Pier Carlo Muzzio^c, Filiberto Z...

^a Radiotherapy and Nuclear Medicine Unit, Istituto Oncologico Veneto IOV – IRCCS, Padua, Italy; ^b Department of Oncological and Surgical Sciences, University of Padua, Italy; ^c Radiology Oncology Unit, Istituto Oncologico Veneto IOV – IRCCS, Padua, Italy

Heterogenous sensitivity
Patient selection
Inhomogenous- risk
Surgical technique



M stage- bone metastases

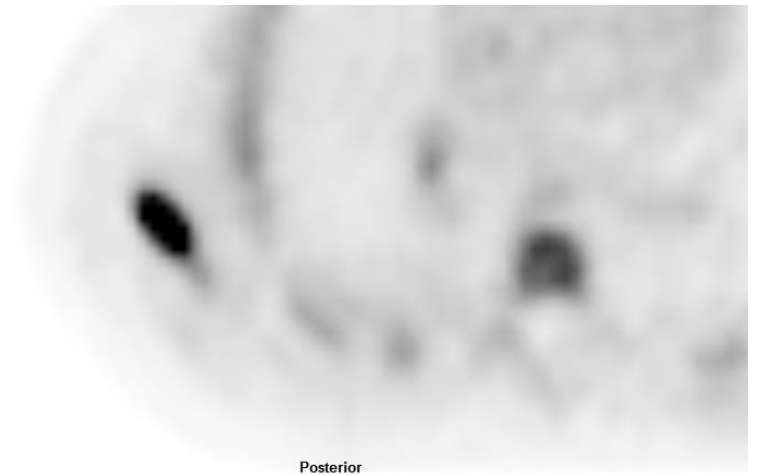
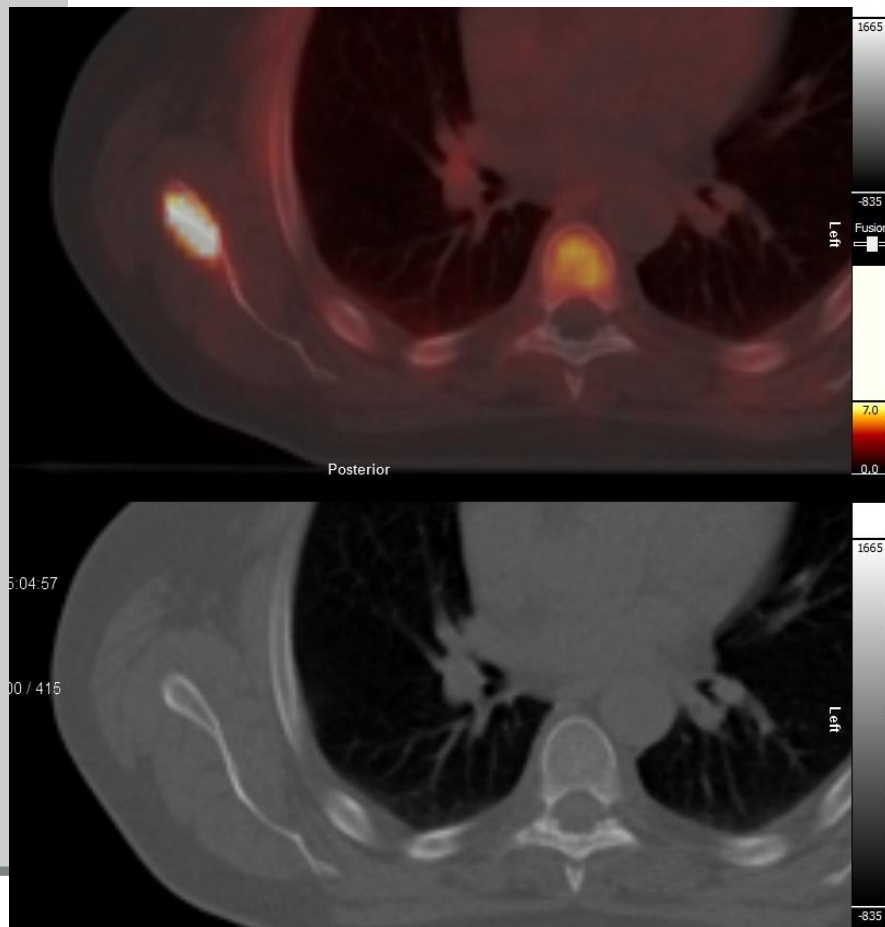
Modality	Advantages	Disadvantages
99mTc MDP Planar bone scan	Widely available Cheap Sensitive	Non specific marker of osteoblastic activity Reflects osteoblastic in response in cortex –will miss early marrow disease
Planar plus SPECT		
MRI	Early marrow High spatial and contrast resolution Neural compromise No Radiation	Not good for ribs Availability / cost
WB- MRI	Visceral and bony disease No Radiation	?specificity Body coils Availability/ cost
Choline PET/CT	Visceral and bony disease	PET- spatial resolution
Choline PET/ MR		

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

Guohua Shen • Houfu Deng • Shuang Hu • Zhiyun Jia

Choline PET/CT highest specificity
MRI higher sensitivity

Good study comparing FCH and WB MRI lacking

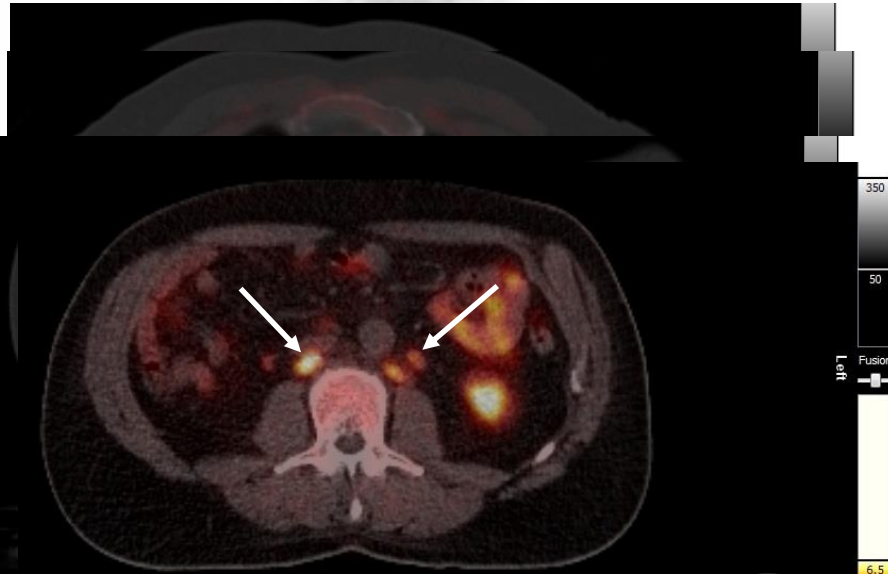


Pearl: Bone metastases often not sclerotic

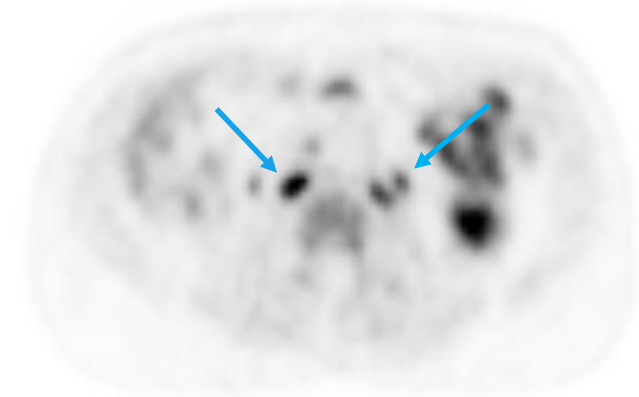
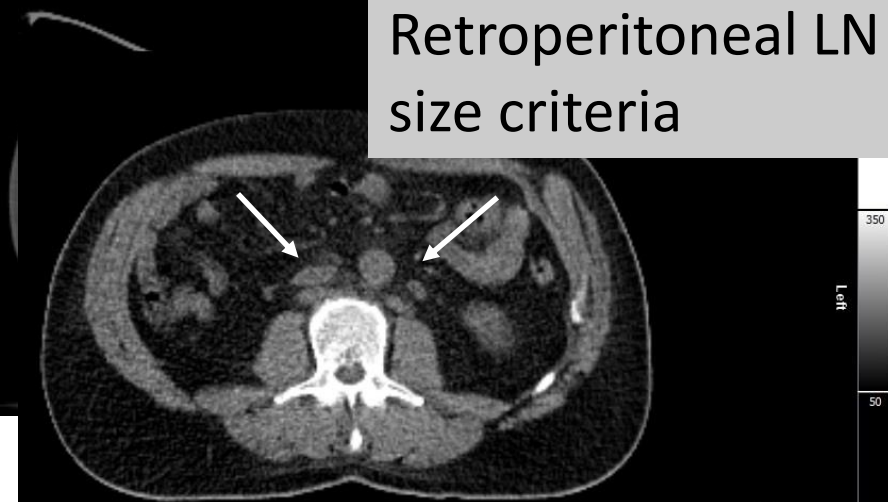
Tc99mc MDP

Staging PSA 55 Gleason 4 +5

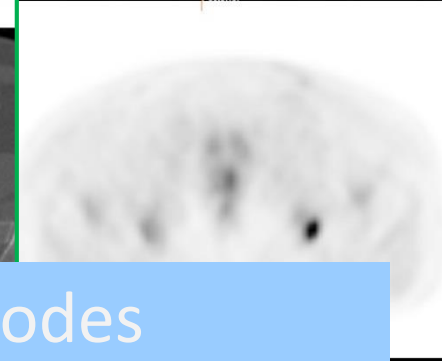
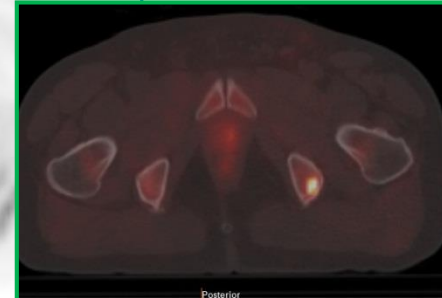
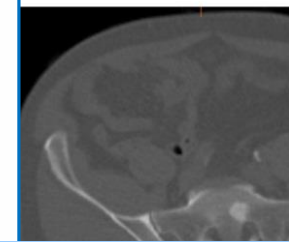
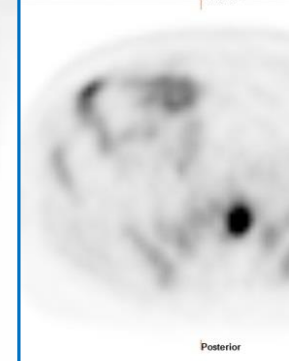
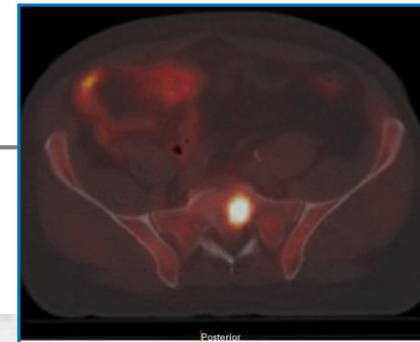
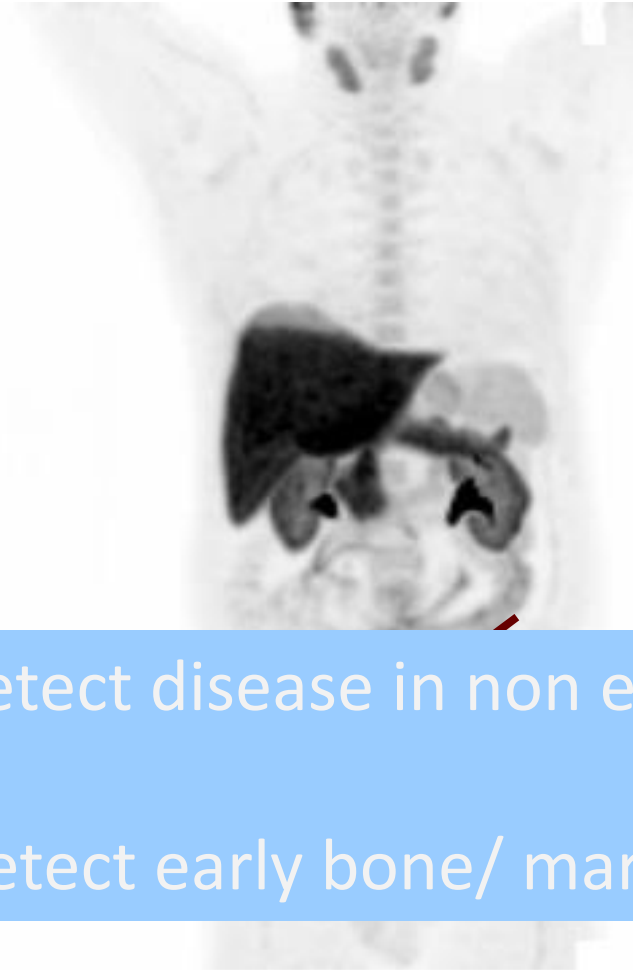
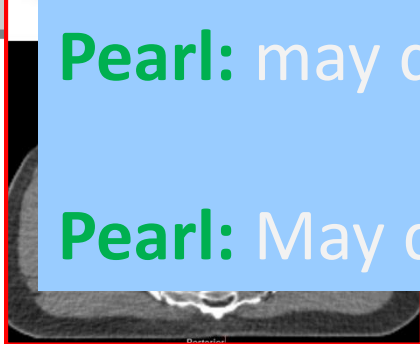
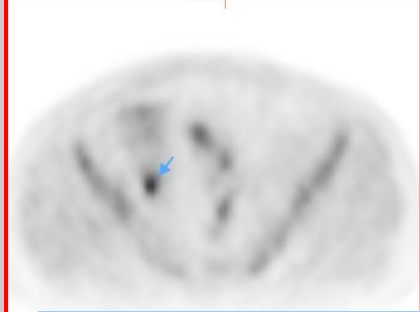
F-18 FCH



Retroperitoneal LN mets: below size criteria



High risk staging : Gleason 4 + 5, sclerotic lesion L5 on staging MRI



Pearl: may detect disease in non enlarged nodes

Pearl: May detect early bone/ marrow involvement

Rising PSA post radical treatment

- 15-40% men biochemical relapse within 10 years of post radical Rx (RT or prostatectomy)
- Recurrence-
 - 15-25% local
 - 20-25% metastatic only
 - 45-55% both local and metastatic
- **IMPORTANT TO ESTABLISH IF SUITABLE FOR LOCAL SALVAGE (Surgery or RT) OR SYSTEMIC RX**
- After Radical Prostatectomy PSA >0.2 ng/ml
- After Radiation therapy PSA > 2 + nadir ng/ml

Rising PSA post radical treatment

- C11choline overall detection rate 40-71% *Picchio et al, Krause et al, Reske et al*
- FCH overall detection rates 43- 55% *Pelosi et al, Marzola et al, Cimitan et al*
- High Specificity & PPV , less high sensitivity and NPV
- Sensitivity increases with trigger PSA value
 - PSAdt (doubling time)
 - PSAvel (velocity)
- Even if detecting disease in only 30% with PSA levels 1.5ng/ml
 1. Cure after RP with salvage RT is more successful when lower PSA-levels (<1 ng/ml)
 2. local therapy not appropriate if systemic disease present

Role of ^{18}F -Choline PET/CT in Biochemically Relapsed Prostate Cancer After Radical Prostatectomy

Correlation With Trigger PSA, PSA Velocity, PSA Doubling Time, and Metastatic Distribution

Clinical Nuclear Medicine • Volume 38, Number 1, January 2013

Maria Cristina Marzola, MD,* Sotirios Chondrogiannis, MD,* Alice Ferretti, MD,† Gaia Grassetto, MD,* Lucia Rampin, MD,* Arianna Massaro, CNMT,* Paolo Castellucci, MD,‡ Maria Picchio, MD,§ Adil Al-Nahhas, MD, Patrick M. Colletti, MD,¶ Adriano Marcolongo, MD,# and Domenico Rubello, MD*

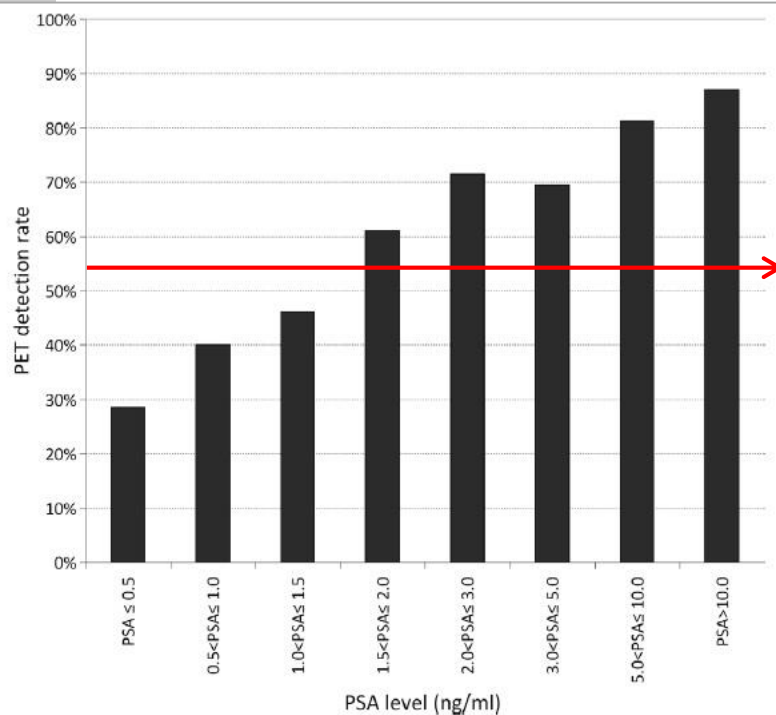
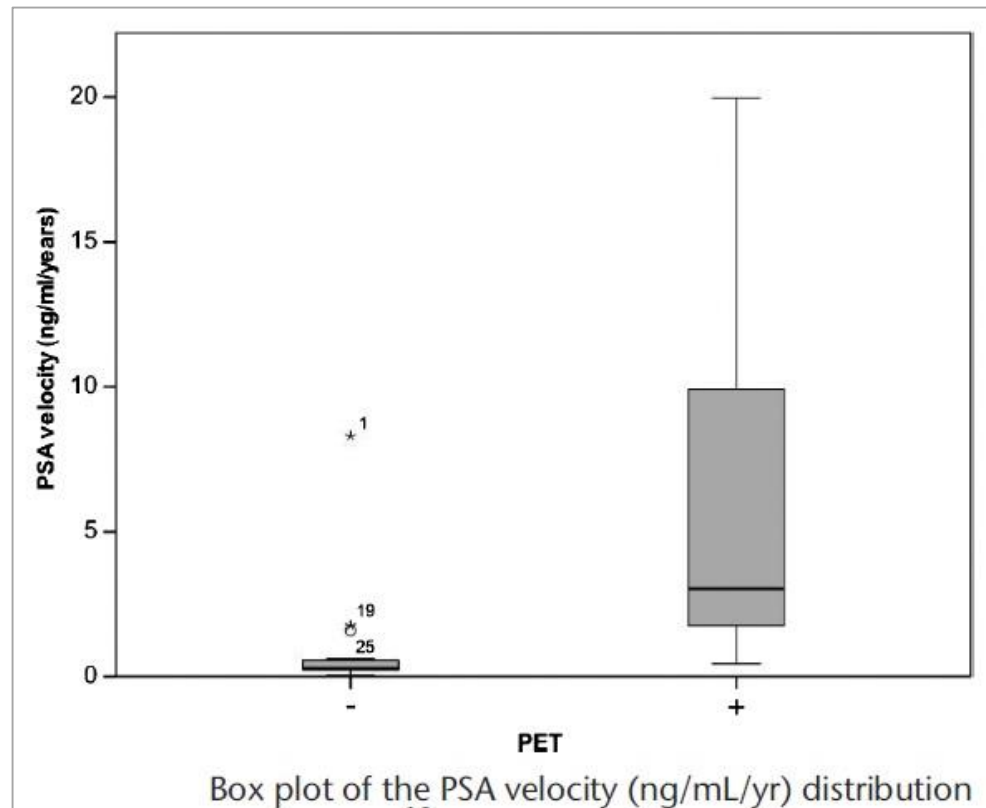
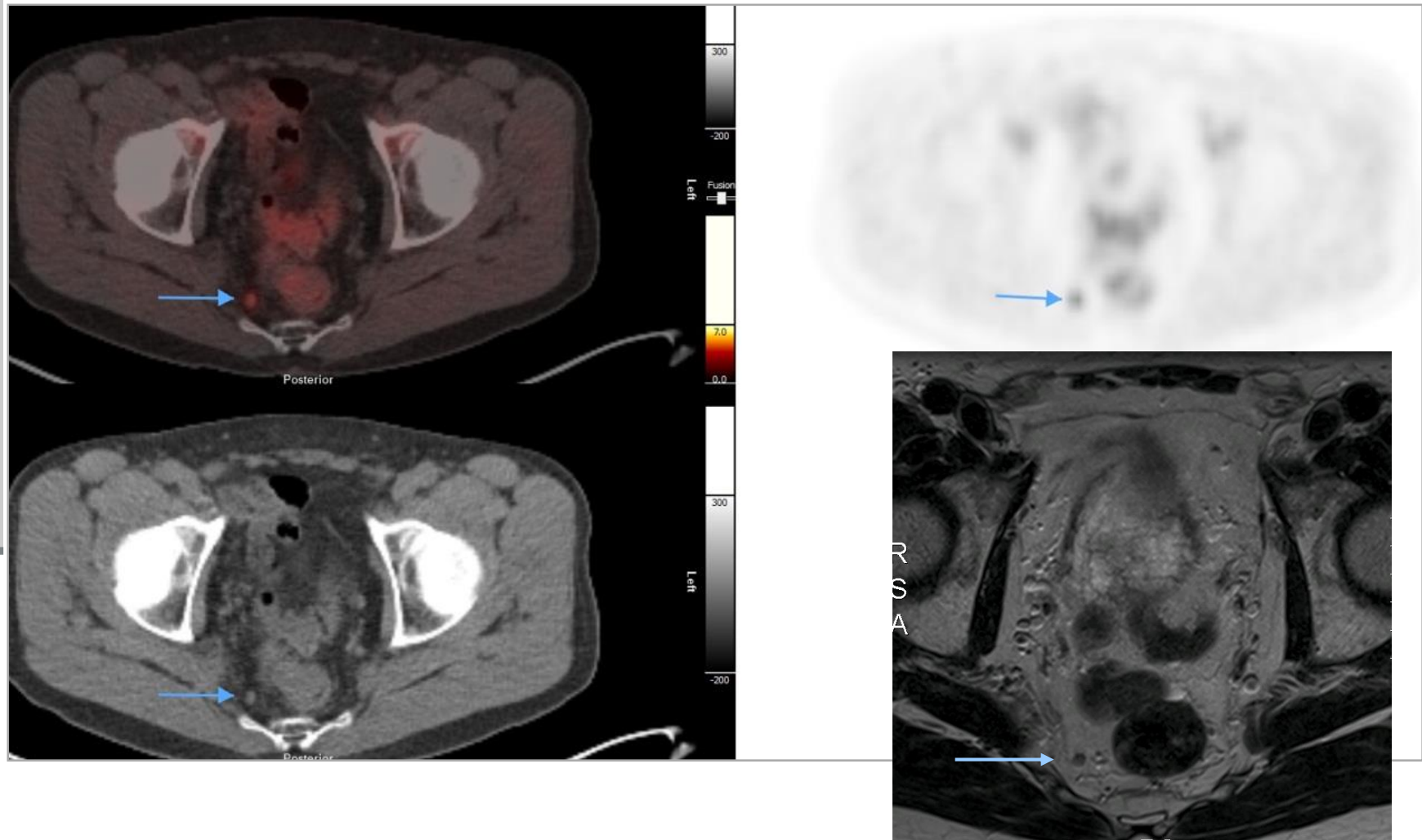
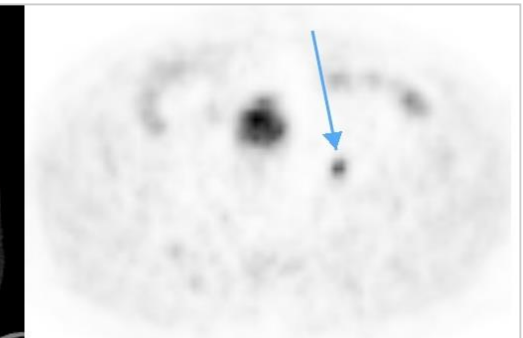
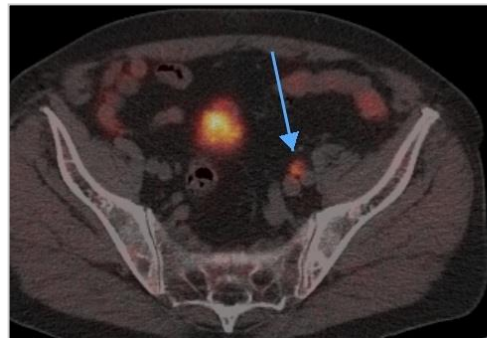
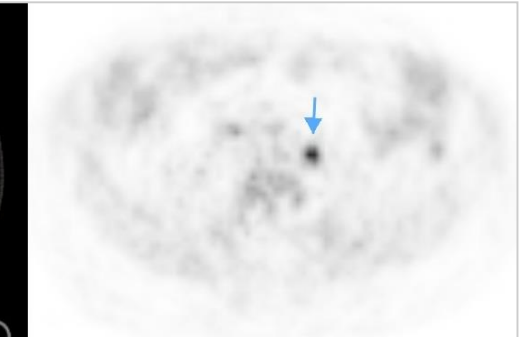
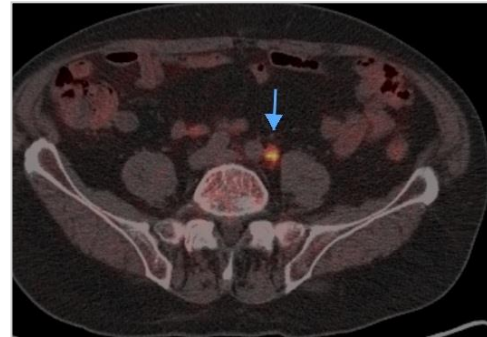
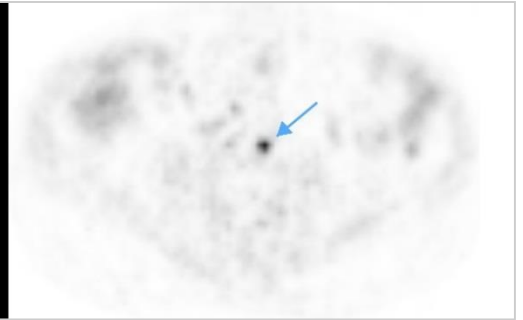
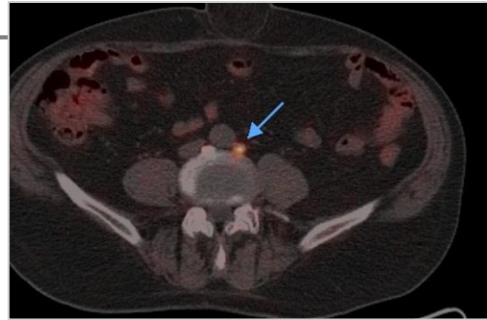


FIGURE 1. ^{18}F -Choline PET/CT detection rate versus trigger PSA level obtained in the whole sample of 233 patients.



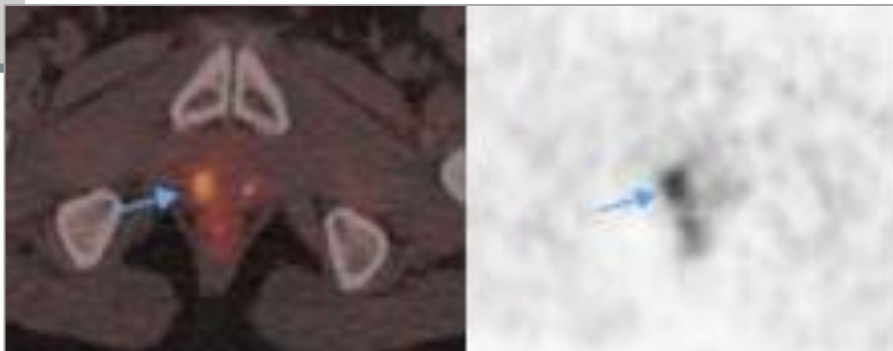
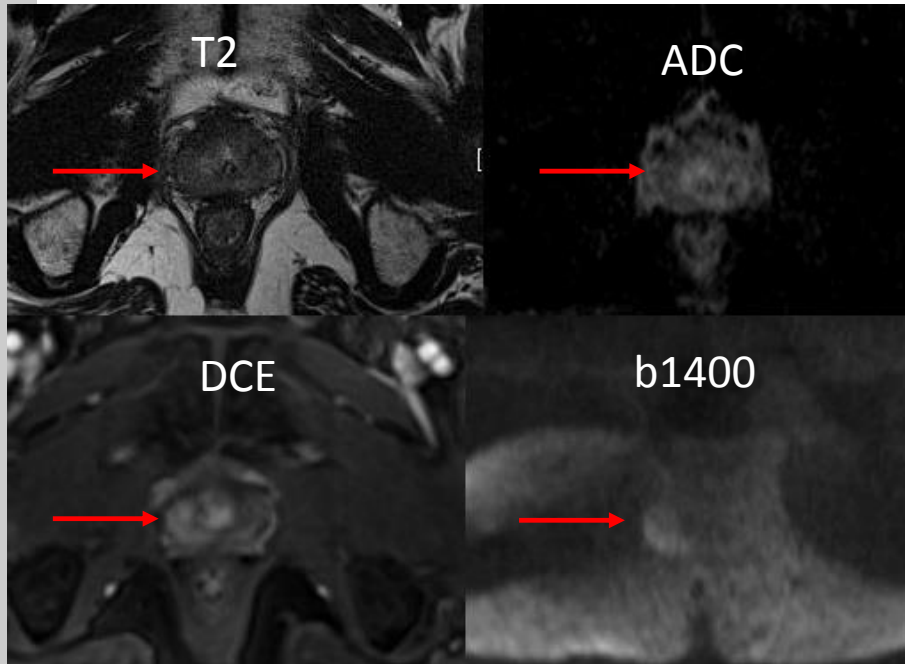
Rising PSA post radical prostatectomy. PSA 1.62

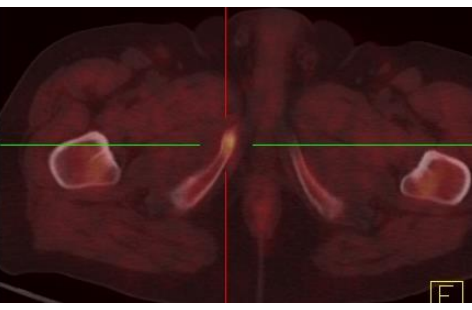
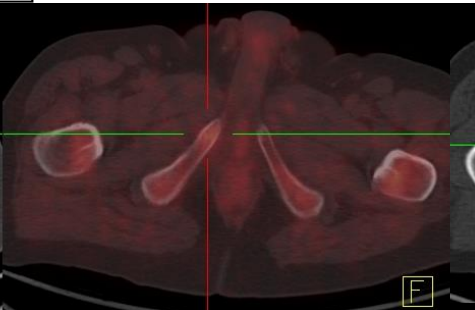
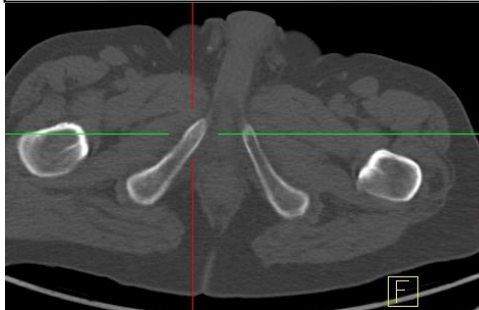
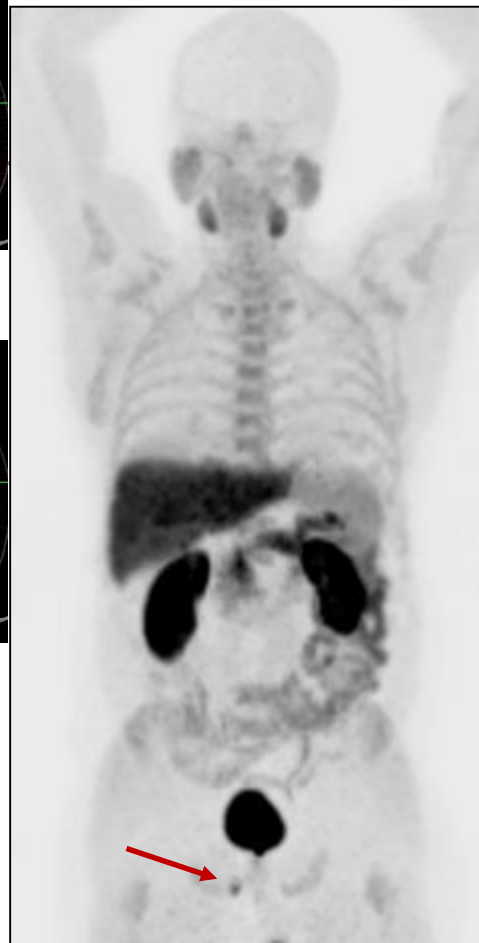
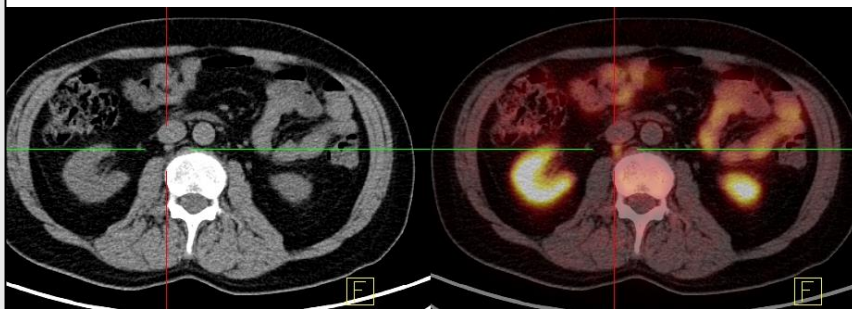
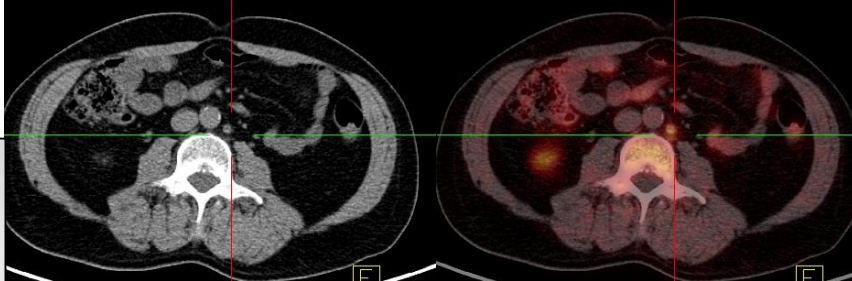




77 yr old post radical RT biochemical relapse PSA 6

Rising PSA post radical radiotherapy





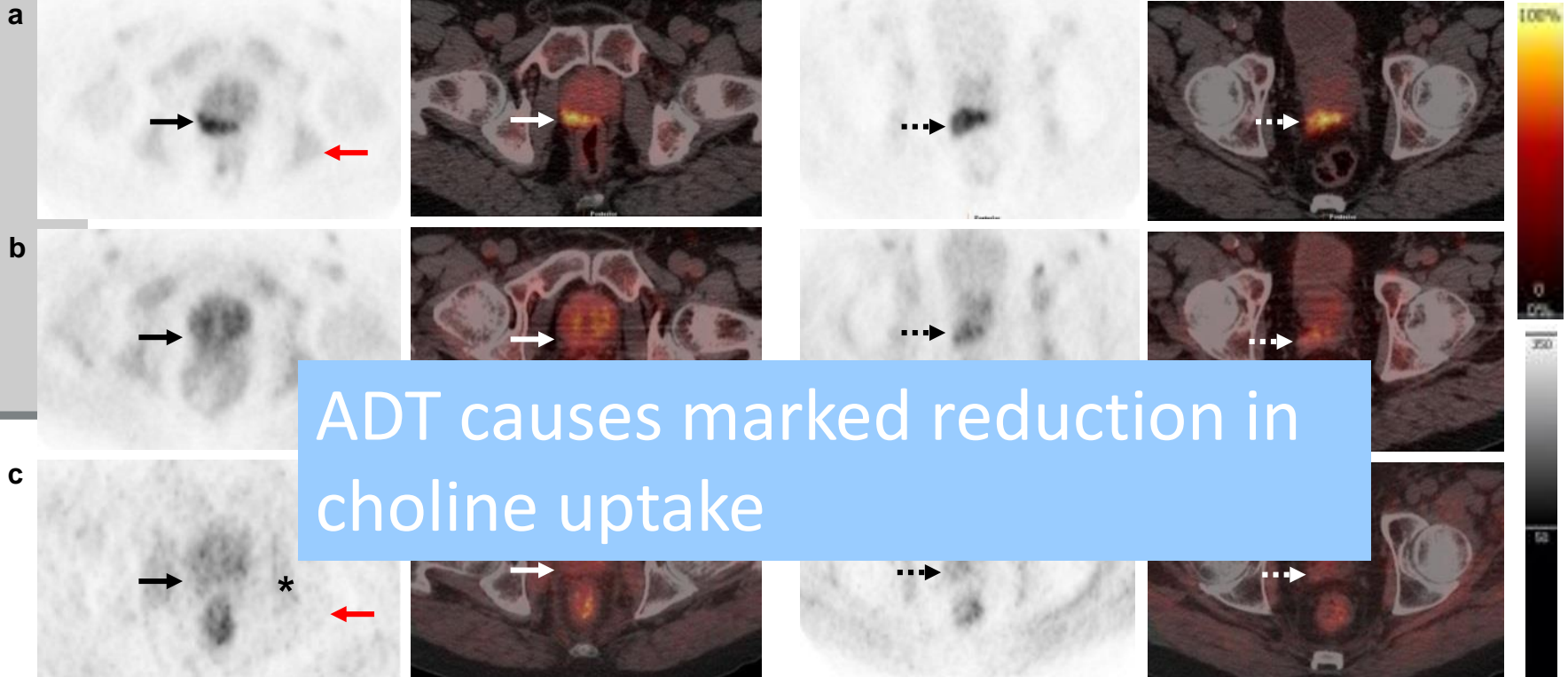
Original article

Exploring the potential of [^{11}C]choline-PET/CT as a novel imaging biomarker for predicting early treatment response in prostate cancer

Amarnath Challapalli^a, Tara Barwick^b, Giampaolo Tomasi^a, Michael O' Doherty^c, Kaiyumars Contractor^a, Simon Stewart^a, Adil Al-Nahhas^b, Kevin Behan^a, Charles Coombes^a, Eric O. Aboagye^a and Stephen Mangar^a

Lesion at level of Prostate

Lesion at level of Seminal vesicles

Axial ^{11}C -choline PETAxial ^{11}C -choline PET/CTAxial ^{11}C -choline PETAxial ^{11}C -choline PET/CT

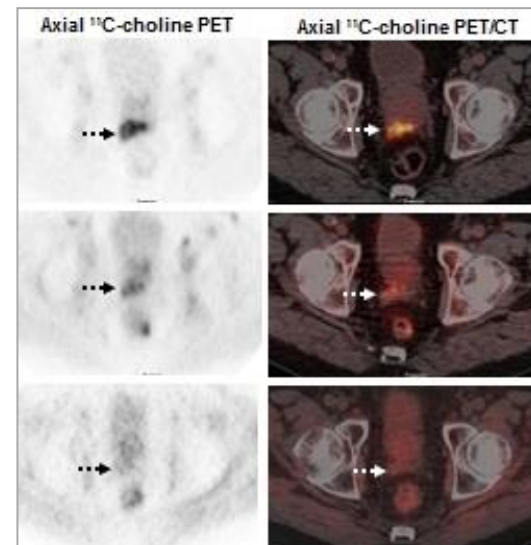
Do we have to withdraw antiandrogenic therapy in prostate cancer patients before PET/CT with [^{11}C]choline?

Giampiero Giovacchini

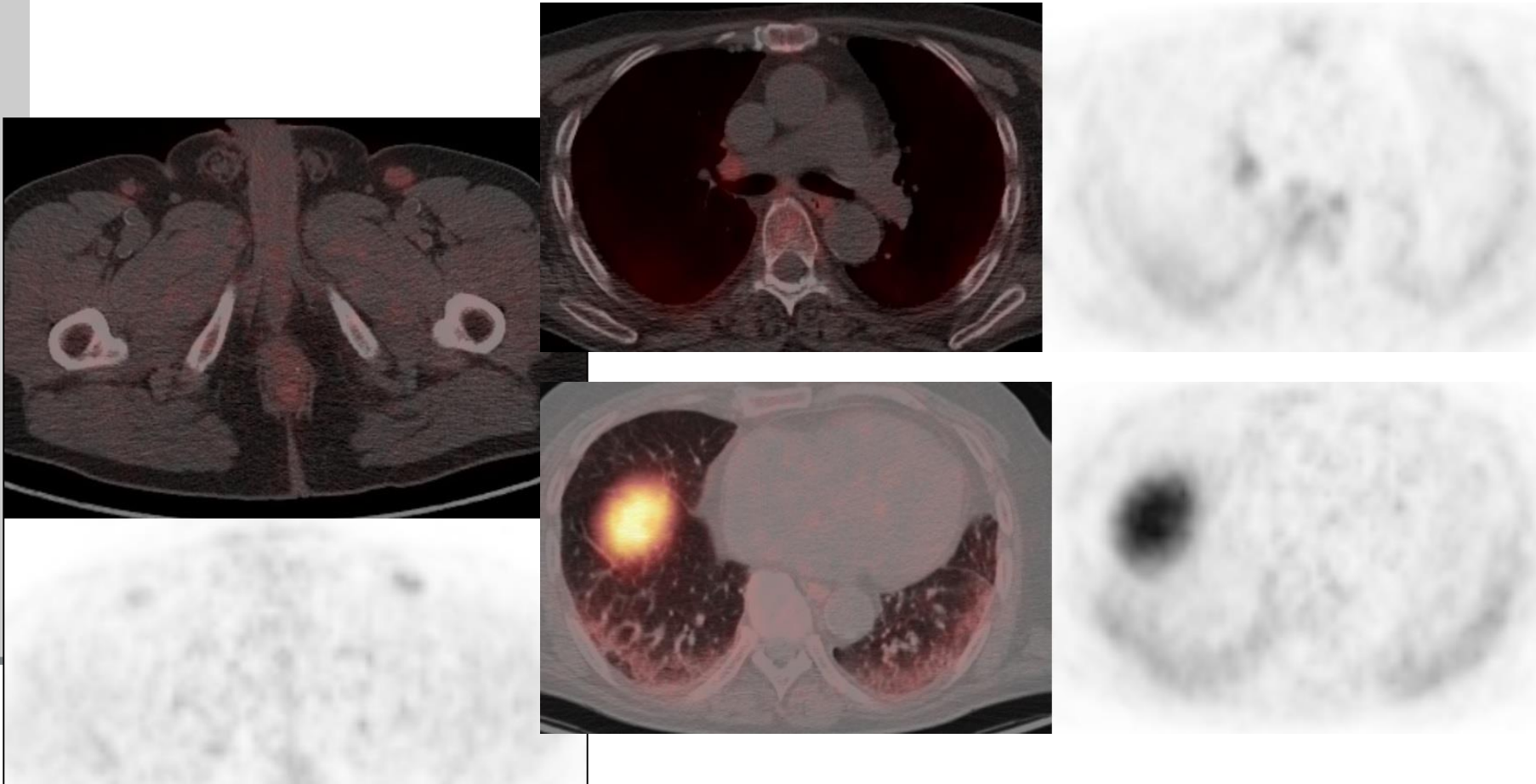
Influence of ADT

- ADT - neoadjuvant, primary and adjuvant treatment
- In vitro & in vivo studies report ADT to reduce choline uptake in hormone sensitive PCa *De Grado, Giovacchini*
- ***Implications for initial staging***
- Biochemical failure on ADT (hormone resistant Pca) are more likely to have a positive choline than hormone sensitive *Giovacchini, Castellucci, Husarik*

'In absence of strong evidence for an inhibitory effect of ADT in hormone resistant PCa prolonged withdrawal of ADT in patients experiencing progression of disease may be ethically questionable'

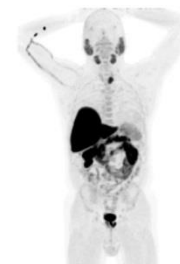
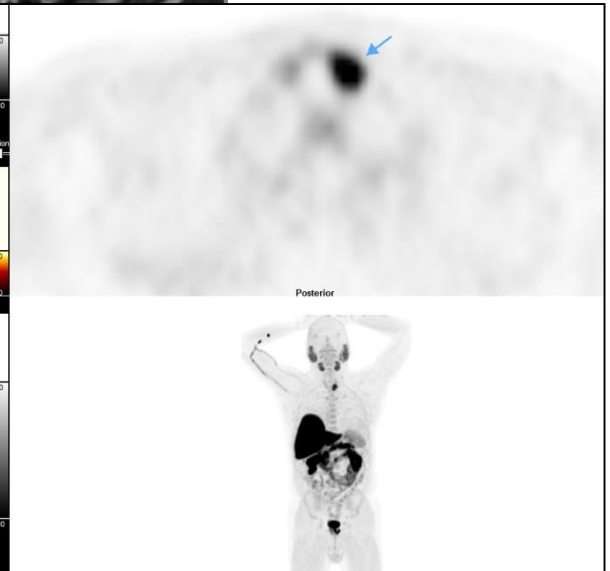
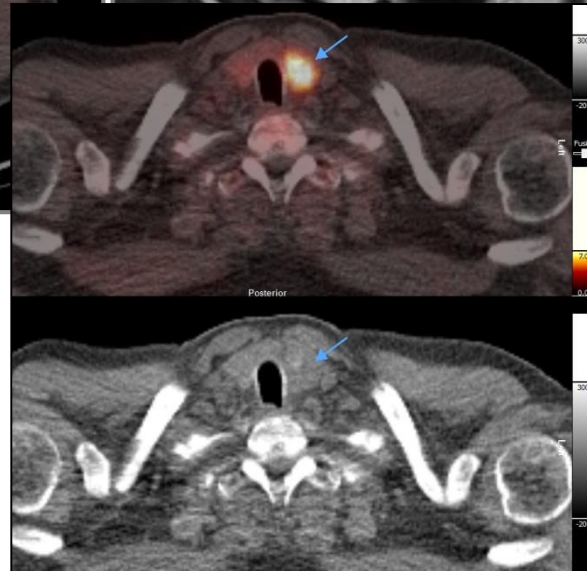
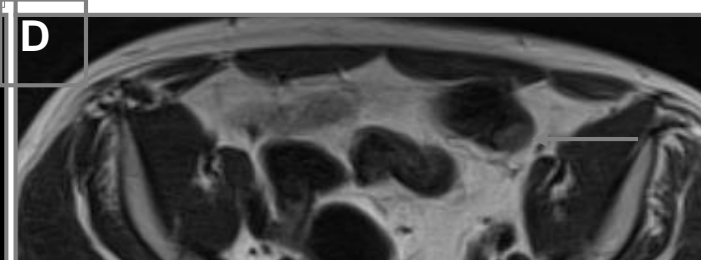
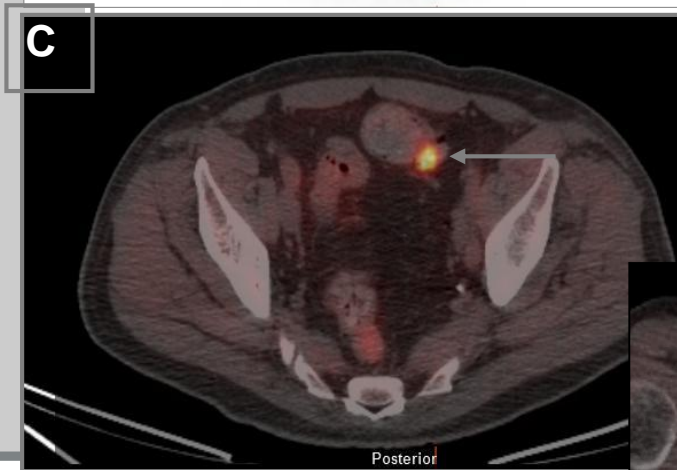
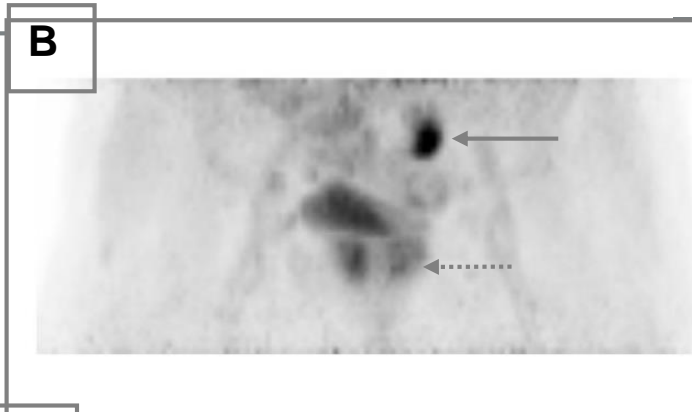
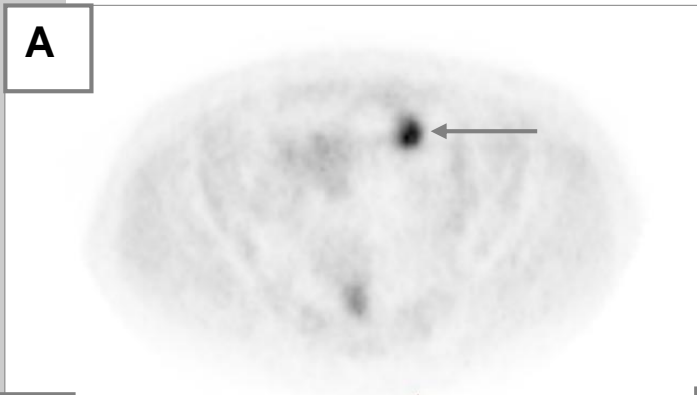


Inguinal and mediastinal LN

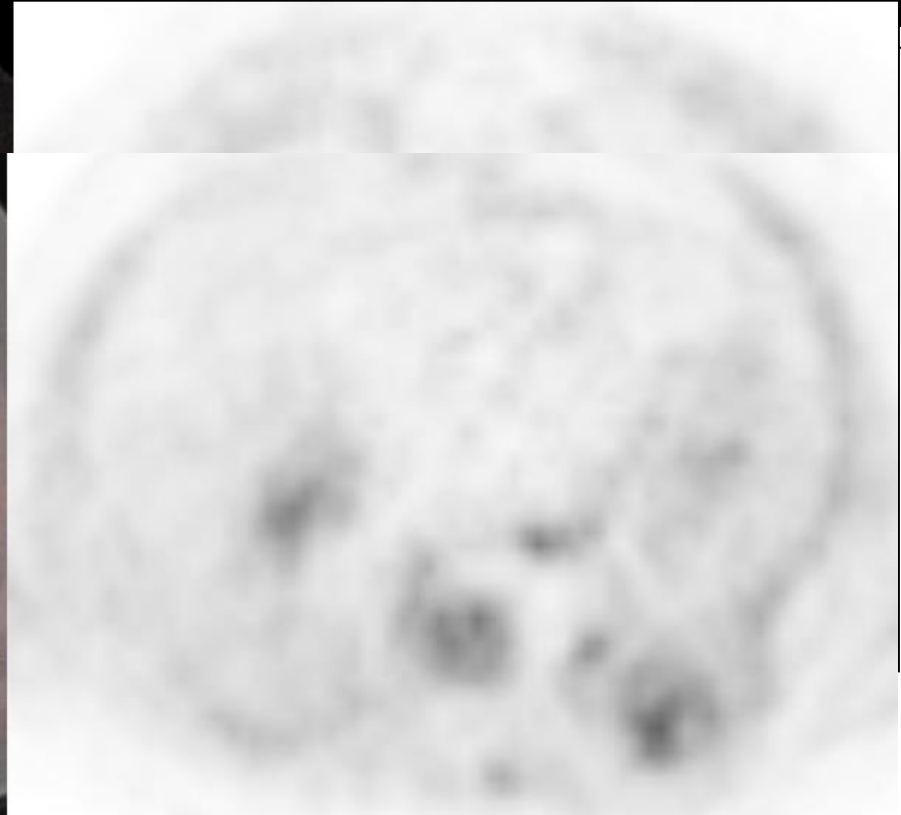
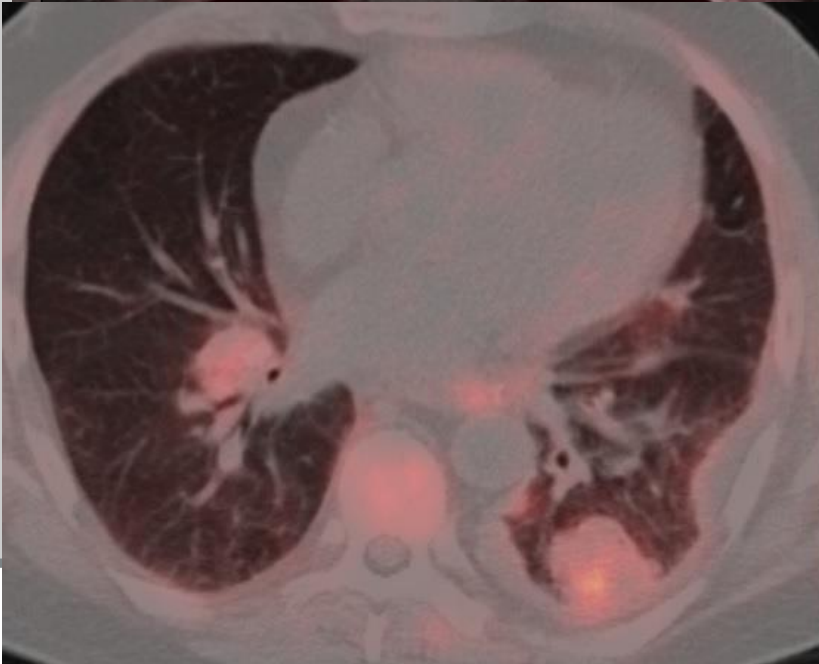
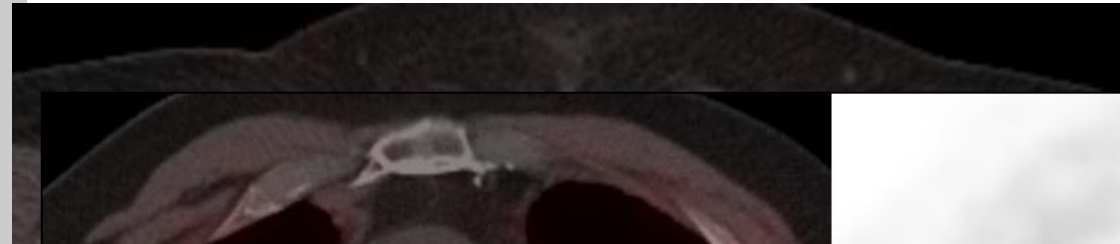


Pitfall: Active infection/ inflammation can be choline avid

Incidental findings



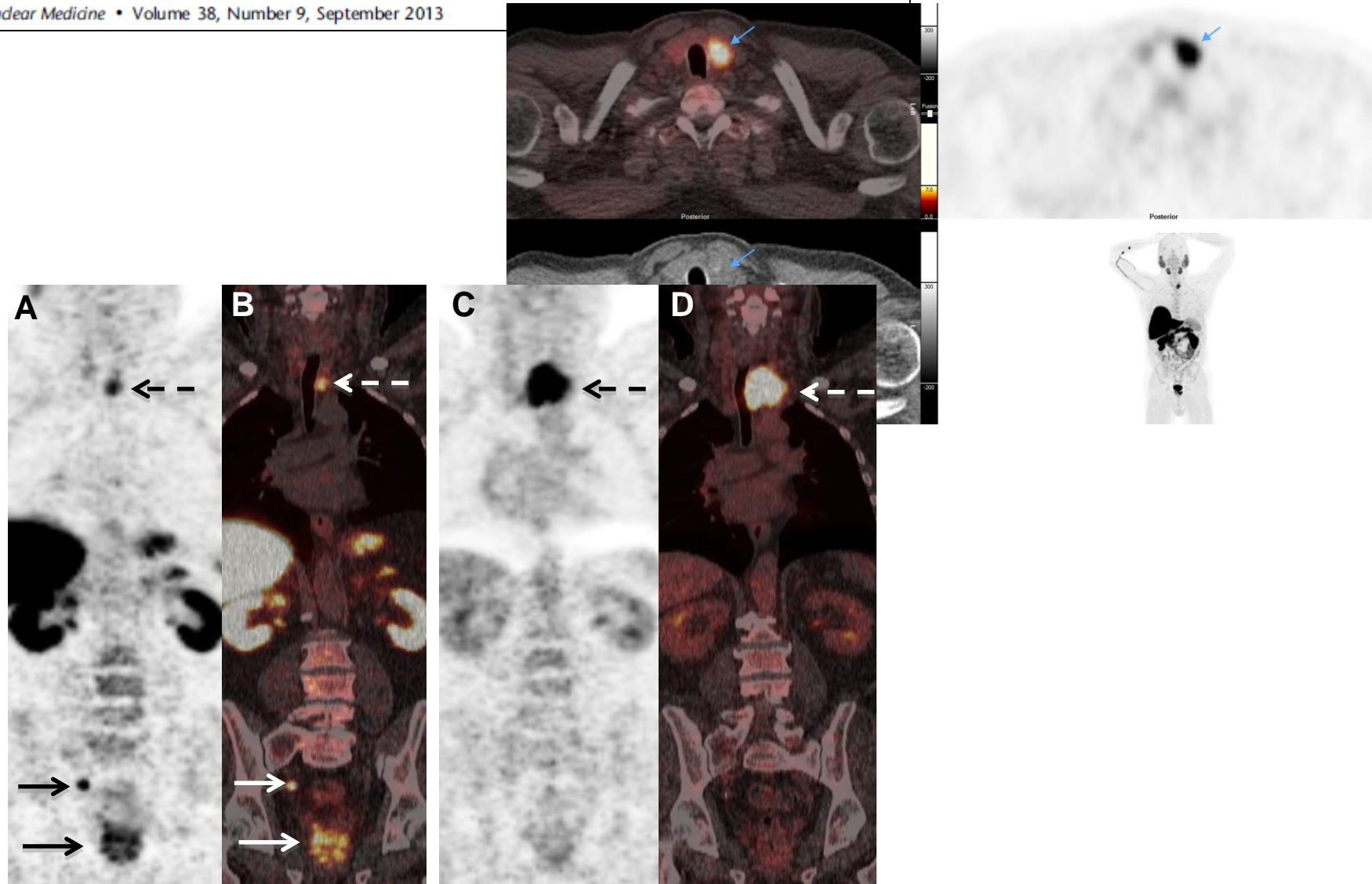
Incidental findings



Thyroid Lymphoma Incidentally Detected by ^{18}F -Fluorocholine (FCH) PET/CT

Amy Eccles, MB BChir, FRCR, Amarnath Challapalli, MBBS, MD, MRCP, FRCR,
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Conclusion

Indications for choline PET/CT in prostate cancer:

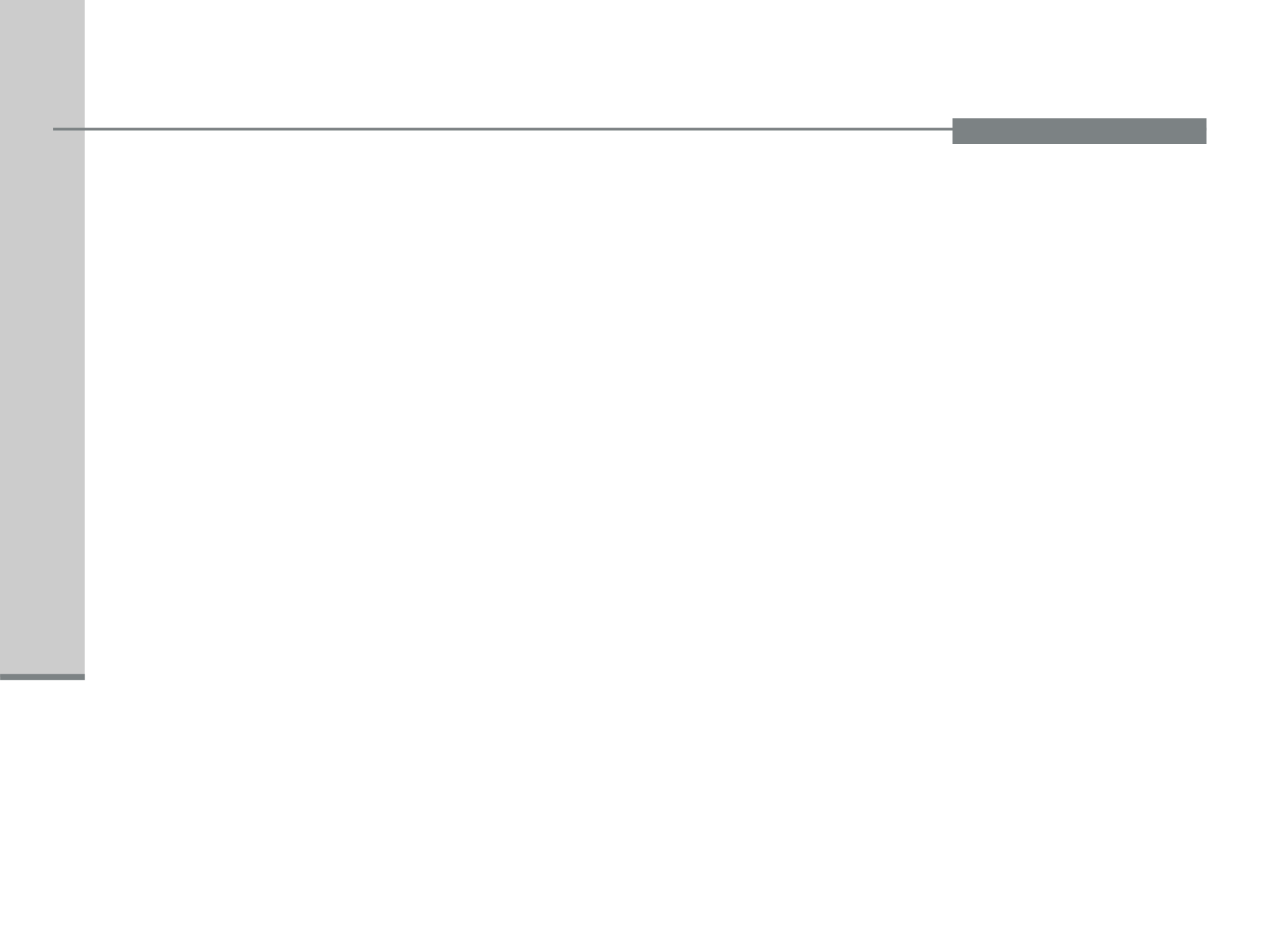
- Rising PSA post radical therapy (PSA kinetics)
- High risk staging- equivocal finding on CWU



Thanks to Amar Challapalli, Steve Mangar, Eric Aboagye, Sameer Khan, Stefano Fanti

Thank you for your attention





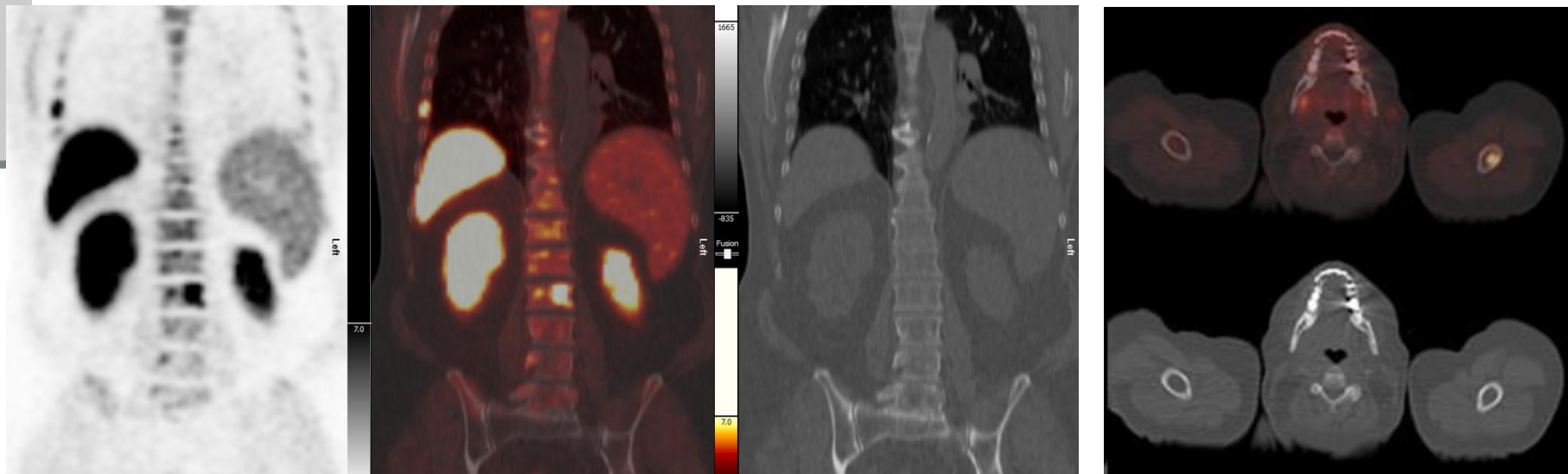
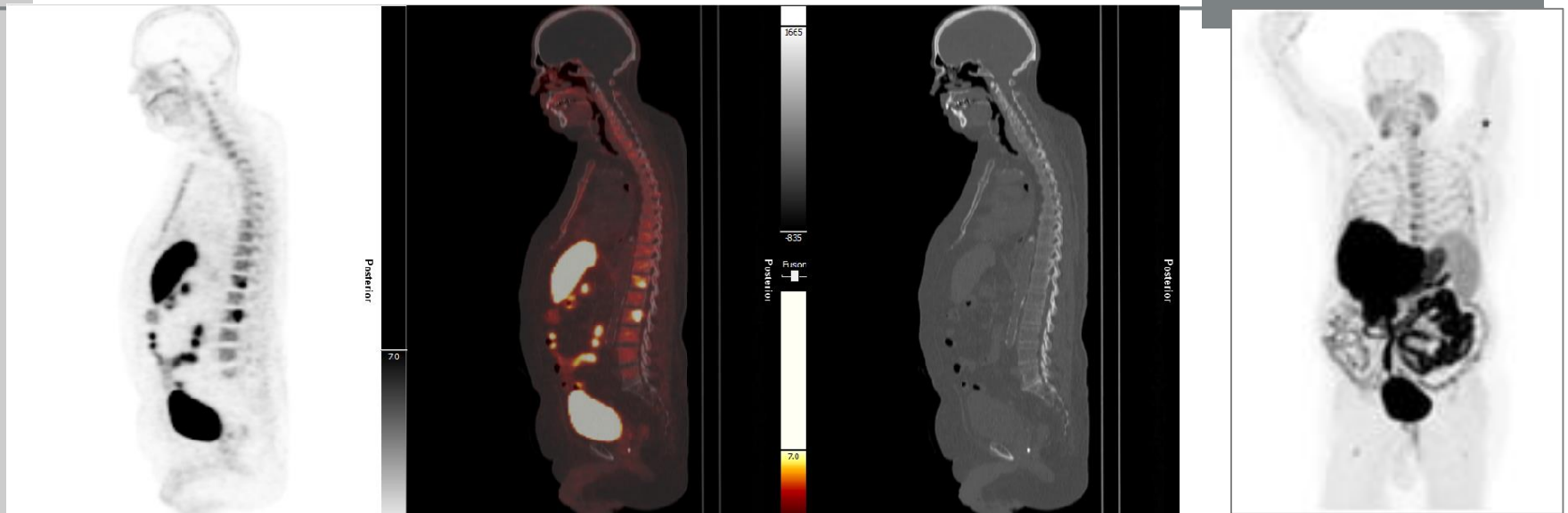
M stage- bone metastases

- **BS vs Choline PET:** Relapse & Neg BS- Choline PET identified bone mets in 15% *Fuccio 12*
- **BS vs NaF F-18 PET:** F-18 NaF PET/CT more sensitive and specific than BS *Even-Sapir 06*
- **WB DW MRI vs F-18 NaF PET:** WB MRI higher specificity but lower sensitivity *Mosavi 12*

early

Choline more sensitive than bone scintigraphy
Choline PET and WB MRI complimentary-
?PET/MRI

Rising PSA post radical prostatectomy.



65 yr old. PSA 11. Staging
suspicious pelvic nodes on MRI

