

# Pitfalls of PSMA PET/CT in APC imaging

Ian Davis

Professor of Medicine, Monash University and Eastern Health

Head, Eastern Health Clinical School

Chair, ANZUP Cancer Trials Group

NHMRC Practitioner Fellow

 @Prof\_IanD

- Chair, ANZUP:
  - proPSMA (ACTRN12617000005358):  
 $^{68}\text{Ga}$ -PSMA PET/CT accuracy and impact (early PC for surgery or RT)
  - TheraP (NCT03392428):  
 $^{177}\text{Lu}$ -PSMA vs cabazitaxel, mCRPC
  - ENZA-p (Louise Emmett: funded, in development):  
 $^{177}\text{Lu}$ -PSMA / enzalutamide, mCRPC
  - #UpFrontPSMA (Michael Hofman: funded, in development):  
 $^{177}\text{Lu}$ -PSMA / docetaxel, mHSPC

Thanks to Louise Emmett and Michael Hofman for sharing slides

## $^{68}\text{Ga}$ -PSMA PET/CT is great, but...

- False positives
  - False negatives
  - True positives but who cares
  - Inappropriate changes in management
  - Other pitfalls
- 
- Note: the “CT” component is important.

# False positives

- PSMA expression in non-prostatic tissues:
  - Kidney, gut, breast, brain, adrenal, ovary, salivary gland, coeliac ganglion, small intestine, NSCLC, neuroendocrine tumors, Paget's bone disease, reactive nodes
  - Asymmetry can be misinterpreted
- Upregulation of PSMA in prostate cancer with AR inhibition



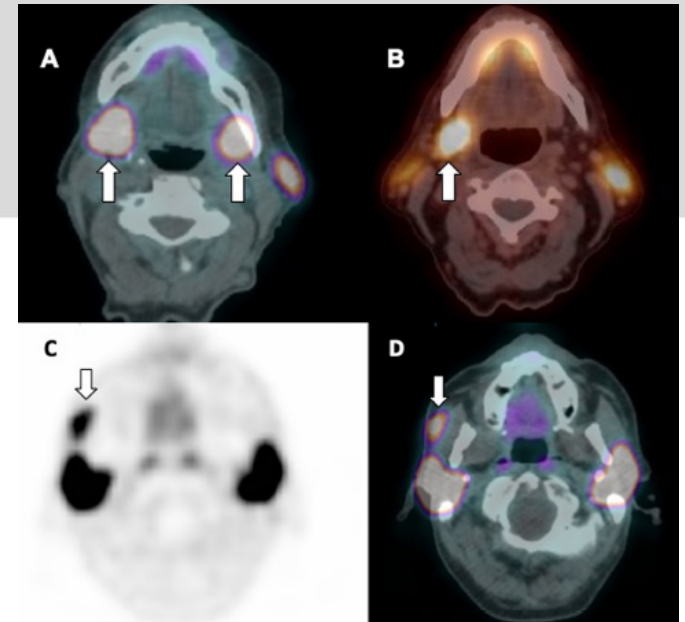
# False positives

R submandibular node

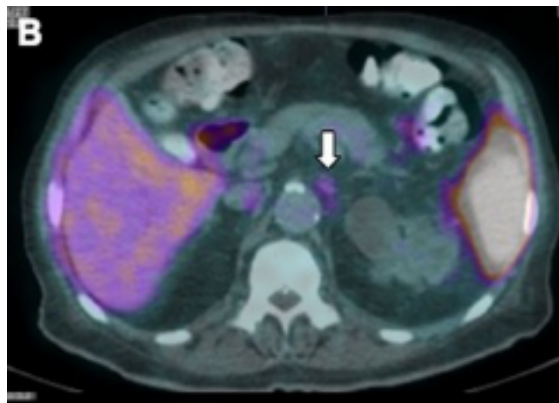
- Pitfalls:

- Misdiagnosis as metastatic prostate cancer
- Missing another critical diagnosis
- Inappropriate selection of treatment

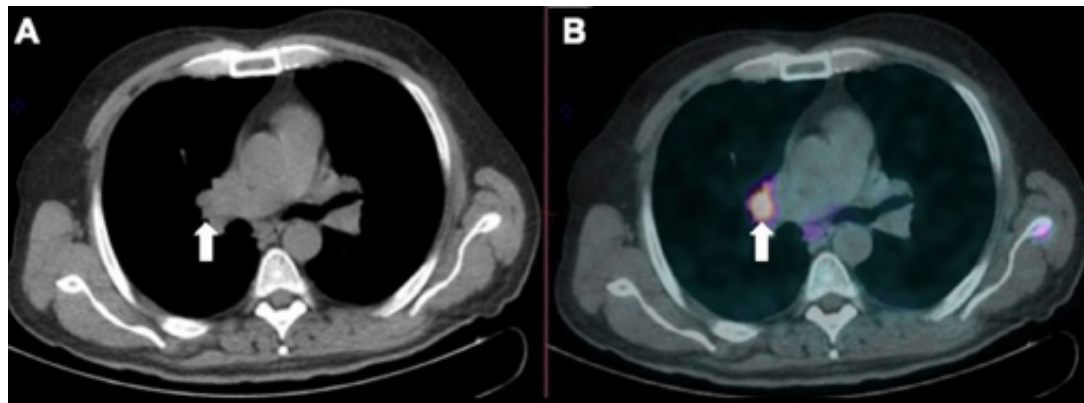
Accessory R parotid



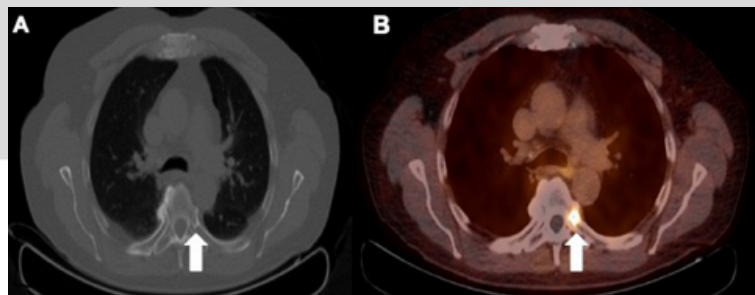
Left coeliac ganglion



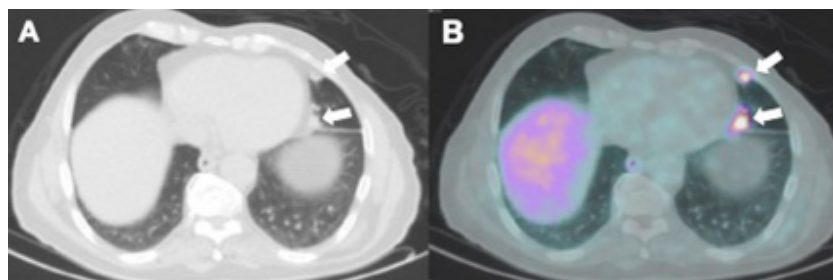
Right pulmonary hilum



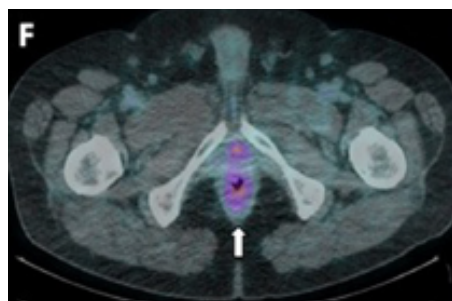
Costochondral junction



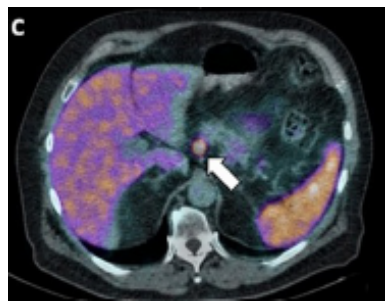
Recurrent NSCLC



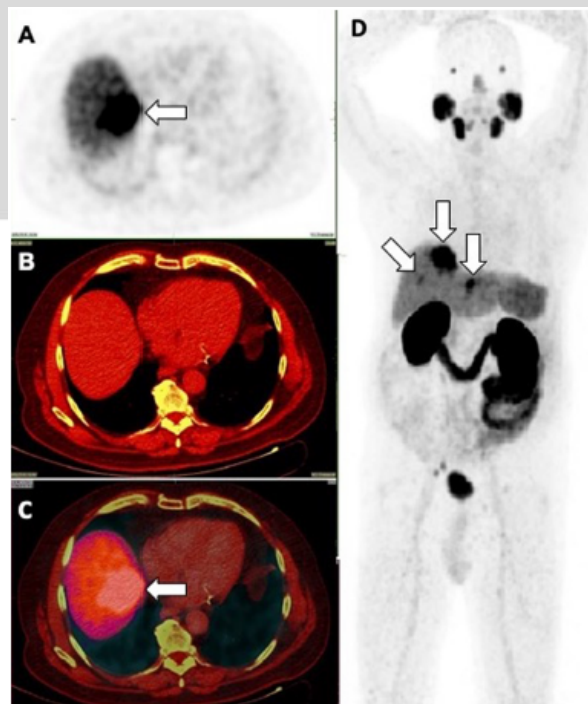
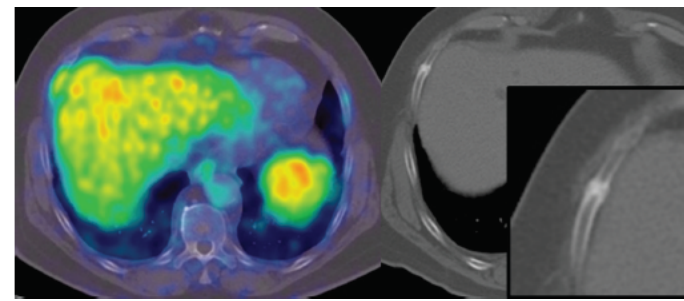
Rectal adenoca



Neuroendocrine



Rib fracture

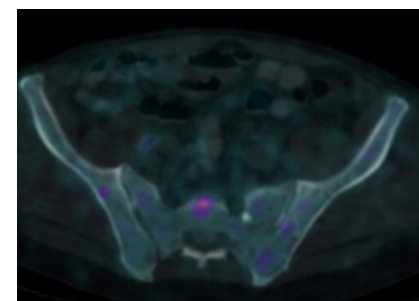


Shetty D et al. Tomography 4: 182-193, 2018  
Hofman MS et al. RadioGraphics 38: 200-217, 2018

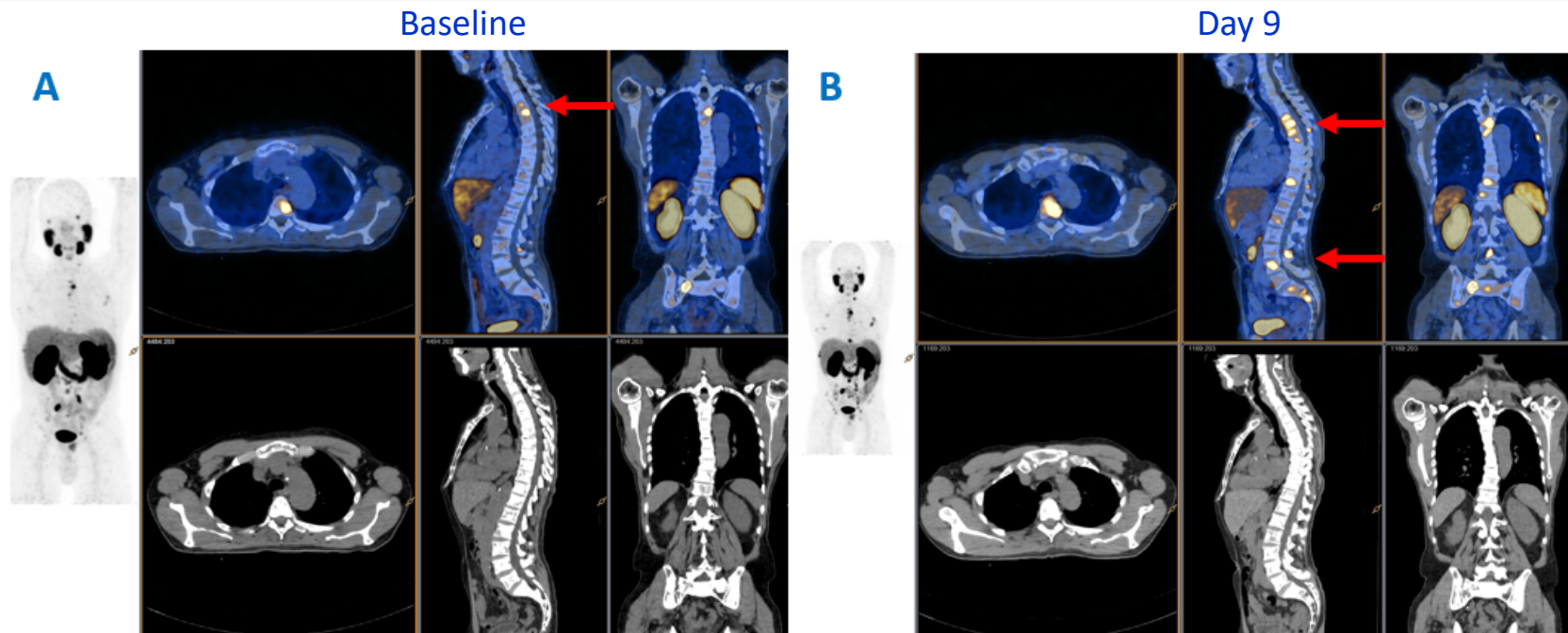


Hepatocellular carcinoma

Polycythemia rubra vera



# False positives: longitudinal imaging



- Increase in SUVmax from 20 (baseline) to 30 (day 9) on ADT, with PSA response
- Increase in number of lesions (arrows)

# False negatives

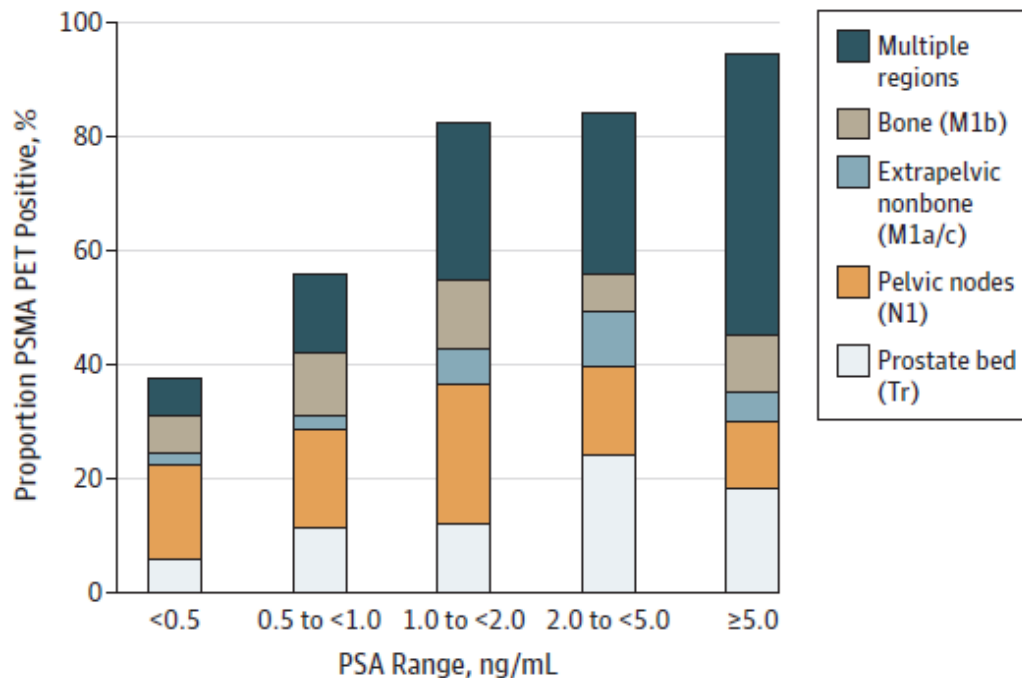
- Sensitivity:
  - Not much of an issue in overt metastatic disease setting
  - Low sensitivity for nodes <4mm BUT most node mets are <5mm
    - Cannot detect <2mm
    - 60% sensitivity 2.0 - 4.9mm (Louise Emmett)
  - 5-10% of prostate cancers do not express PSMA
    - Beware PSMA-neg FDG-pos
    - Can decrease with therapy
- Pitfalls:
  - Radical treatment of incurable patients
  - Unnecessary multimodality treatment for “localized” PC (actually metastatic)

# False negatives

JAMA Oncology | Original Investigation

## Assessment of $^{68}\text{Ga}$ -PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer

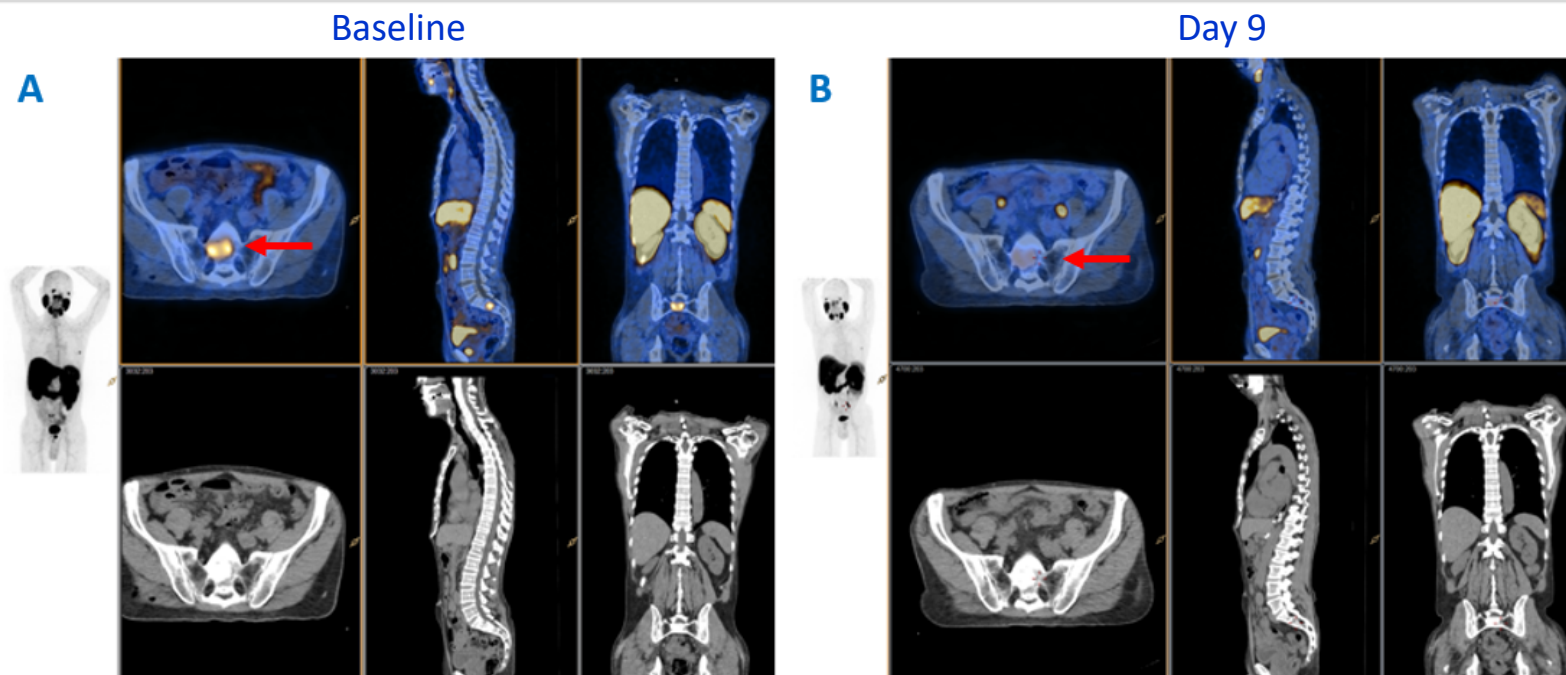
A Prospective Single-Arm Clinical Trial



- UCLA / UCSF
- N=223 with composite endpoint
  - Median followup 9 months
  - 93 with histopathology validation
  - 75% positive
  - No association with PSADT
- PPV 0.92 (composite reference)
- PET-directed focal therapy:
  - PSA>50% drop in 80%
- Brisbane series (N=208):
  - Specificity 94%, sensitivity 38%
  - PPV 68%, NPV 81%
- Sydney series (N=30):
  - Specificity 95%, sensitivity 64%
  - PPV 88%, NPV 82%



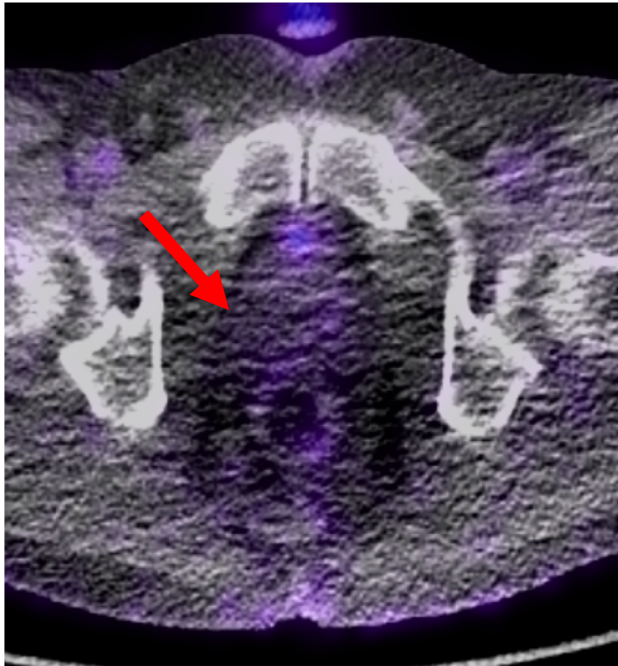
# False negatives: response to therapy



- SUVmax reduced from 8 (baseline) to 3 (day 9) with LHRH agonist plus bicalutamide



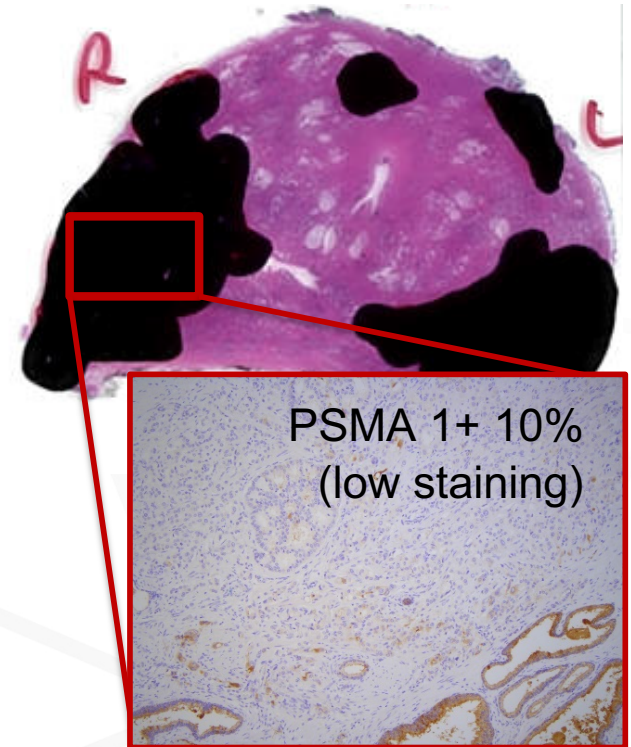
# Not all prostate carcinomas are PSMA-avid



**PSMA PET -ve**



**MRI PIRADS 5**



IHC courtesy of Dr Catherine Mitchell, PeterMac

- Gleason 5+5=10 prostate carcinoma
- No uptake on  $^{68}\text{Ga}$ -THP-PSMA or  $^{68}\text{Ga}$ -HBED-PSMA PET/CT

**immunohistochemistry**

# True positives but who cares?

- Known extensive metastases
  - Any value above conventional imaging?
- Known likely metastases but planning local therapy
  - Eg: ADT + RT to primary with high-risk features
- Converse:
  - Useful when trying to find a reason NOT to give radical therapy

# Inappropriate changes in management

- High risk primary:
  - PSMA-detected metastases leading to decision not to treat primary
  - Extrapolation of high/low volume (risk) definitions to PSMA PET findings
- Unnecessary additional investigations, or delays in treatment
  - Eg: rib biopsies
- Influencing decisions on trial participation
- (Controversy alert!):
  - Off-study treatment of PSMA-detected synchronous oligometastases

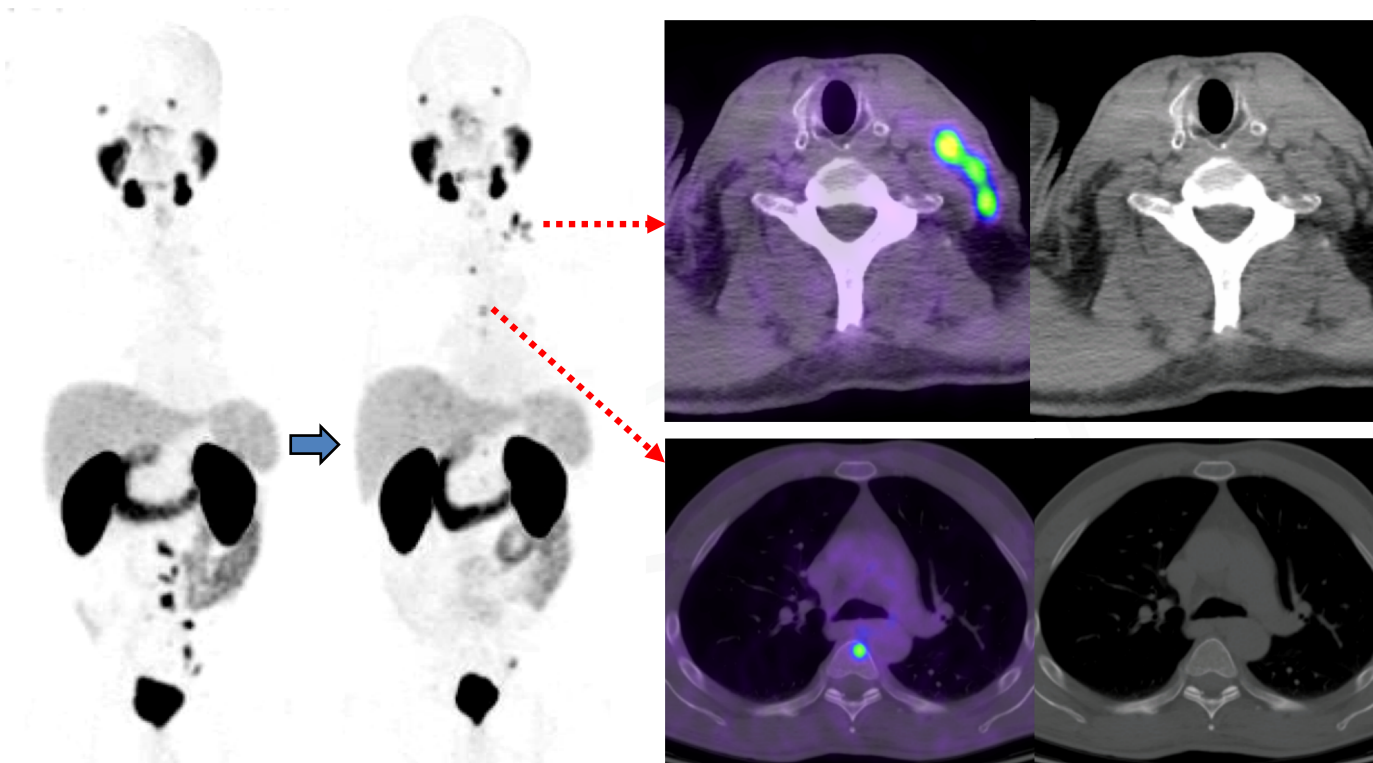
# Management

## The Impact of $^{68}\text{Ga}$ -PSMA PET/CT on Management Intent in Prostate Cancer: Results of an Australian Prospective Multicenter Study

- Australian study
  - 431 men, 4 centres
- Overall 51% change in plan
- Biochemical recurrence:
  - 62% change in plan
  - 51% more disease, 10% less
- Diagnosis of oligometastases 10% → 38%
  - “can be treated ... with SBRT”
  - (van Leeuwen: 35% had SBRT to oligometastases)

Extent of disease	BF		<i>P</i>
	Before $^{68}\text{Ga}$ -PSMA	After $^{68}\text{Ga}$ -PSMA	
No evidence of active disease	22 (7%)	21 (7%)	NS
Biochemical recurrence, site unknown	240 (77%)	59 (19%)	<0.001
Disease confined to prostate bed	12 (4%)	51 (16%)	<0.001
Oligometastatic (1–3 lesions) disease	32 (10%)	119 (38%)	<0.001
Polymetastatic disease ( $\geq 4$ lesions)	2 (1%)	60 (19%)	<0.001
Not stated/incomplete	4 (1%)	2 (1%)	
Total	312 (100%)	312 (100%)	

## 4 months after extended nodal dissection...



biochemical response  
... shortly after followed by  
progression



**Peter Mac**  
Peter MacCann Cancer Centre  
Victoria Australia

Slide courtesy of Michael Hofman

## Other pitfalls

- Situations exist where PSMA PET is clearly of value, but...
- ... sometimes no added value to management plan
  - Clinical situations where PET result will not alter plan
- ... PSMA PET sometimes comes with incomplete information
  - Decisions made without treatment context
  - Lack of histology / genomic data
  - No parallel FDG PET
  - CT component not of diagnostic quality
- Patient distraction
  - A new “PSMA neurosis”?