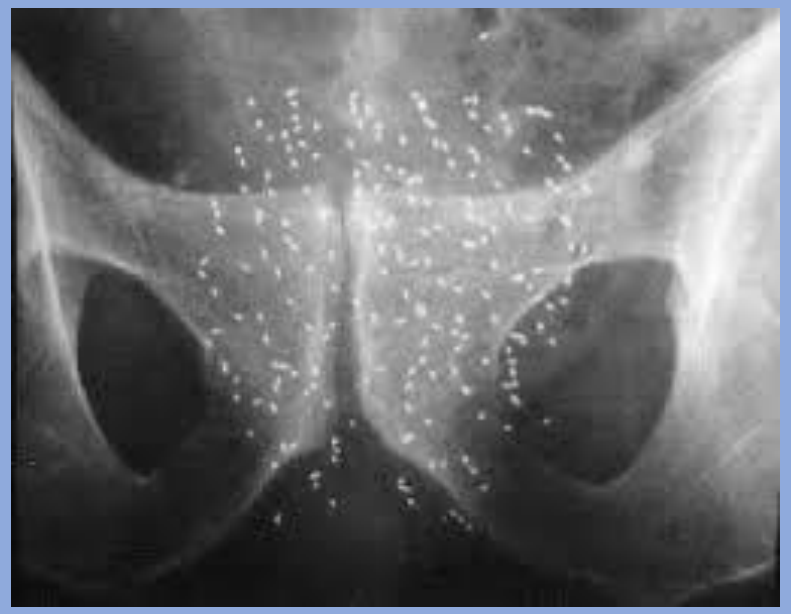
Salvage post brachytherapy:
What to image, how to do it and when



Meeran Naji

Consultant radiologist and nuclear medicine

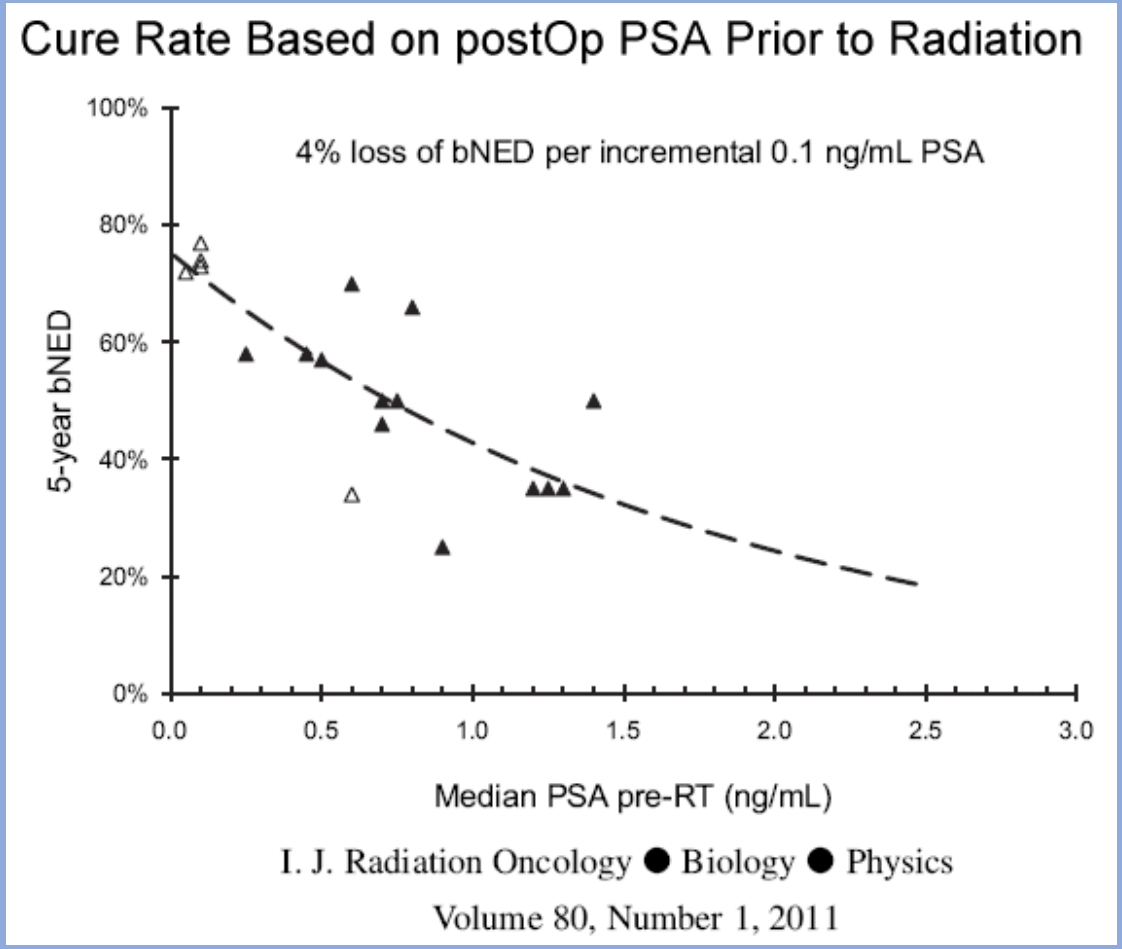
Maidstone and Tunbridge Wells NHS Trust

PROSTATE BRACHYTHERAPY
UK & Ireland Conference 2018

Introduction

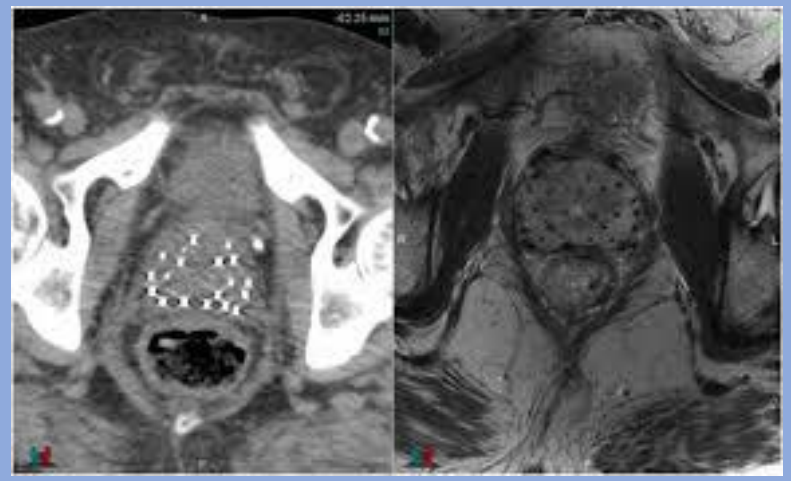
<u>Detection of prostate cancer recurrence and treatment planning</u>

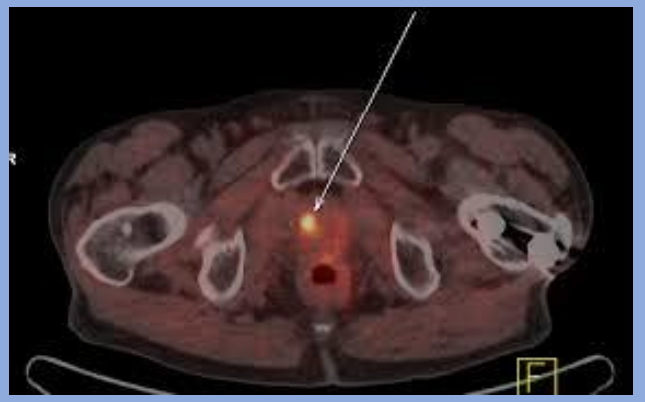
- Early detection of site of recurrence
- Differentiation between local and metastatic disease
- Treatment planning



Imaging tool box

- CT
- Bone scintigraphy
- MRI
- PETCT





Traditional imaging techniques -
CT and bone scintigraphy

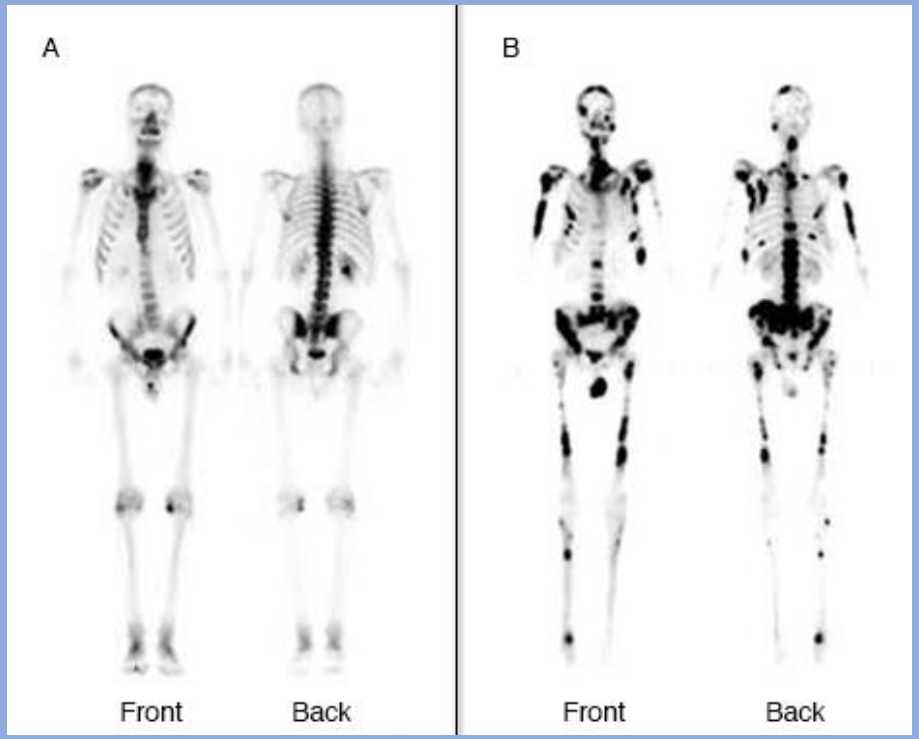
- CT – lymph node metastases
- Bone scintigraphy – skeletal metastases

Limited value of bone scintigraphy and computed tomography in assessing biochemical failure after radical prostatectomy☆

Christopher J Kane, Christopher L Amling, Peter A.S Johnstone, Nali Pak, Raymond S Lance, J.Brantley Thrasher, John P Foley, Robert H Riffenburgh, Judd W Moul

Kane CJ, et al. Urology. 2003;61(3):607-11

- In a series of 132 men with biochemical failure
- Positive bone scan - 9.4%
- Positive CT scan - 14%



Traditional imaging techniques -
CT and bone scintigraphy

Low diagnostic yield in PSA <10 ng/ml

Limited value of bone scintigraphy and computed tomography in assessing biochemical failure after radical prostatectomy☆

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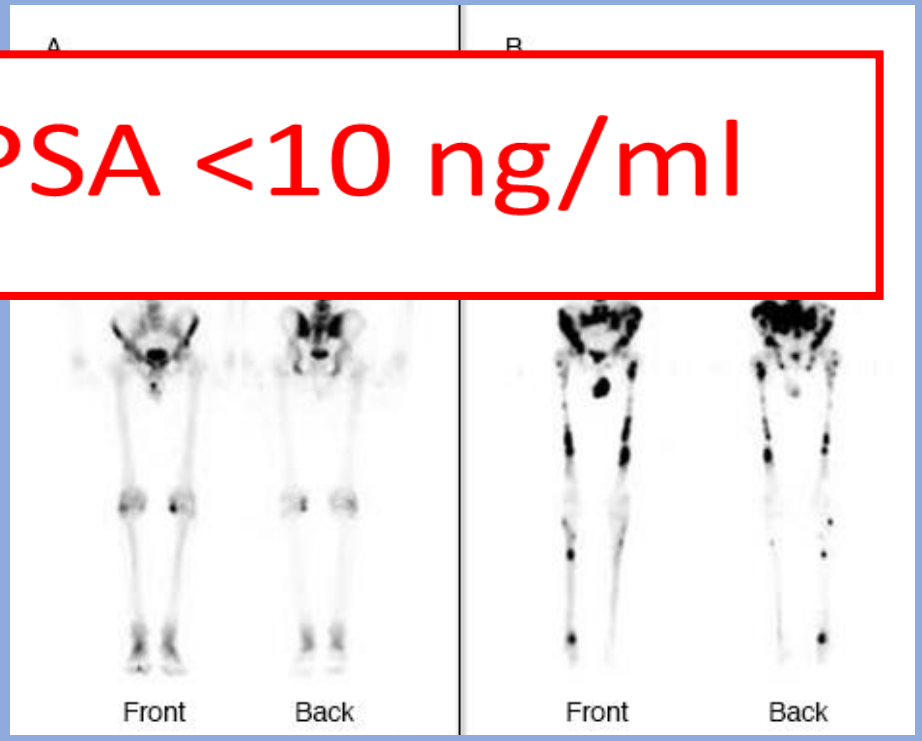


- In a series of 132 men with biochemical failure
- Positive bone scan - 9.4%
- Positive CT scan - 14%

Local recurrence vs. distant metastases

Biochemical recurrence

Local

Regional

Distant

Local recurrence vs. distant metastases

- Evaluation of the risk of micro-metastases
- Clinical/laboratory and histopathological criteria
- Tumour characteristics
- PSA kinetics

Table 2 Factors pointing towards metastatic development in the event of biochemical failure.

	Factors favouring metastatic development
Factors related to the initial tumour (before first treatment)	Gleason score ≥ 8 T3-T4 stage PSA ≥ 20 ng/mL
Time interval between initial treatment and biochemical failure	Free interval between treatment and biochemical failure less than 2 to 3 years
Factors related to the PSA concentration at the time of biochemical failure	Concentration ≥ 10 ng/mL Velocity ≥ 2 ng/mL per year Doubling time less than 8 to 12 months

O. Rouvière . Diagnostic and Interventional Imaging. 2012; 93, 279—290

Local recurrence vs. distant metastases

Biochemical recurrence

Local

Regional

Distant

Local recurrence vs. distant metastases

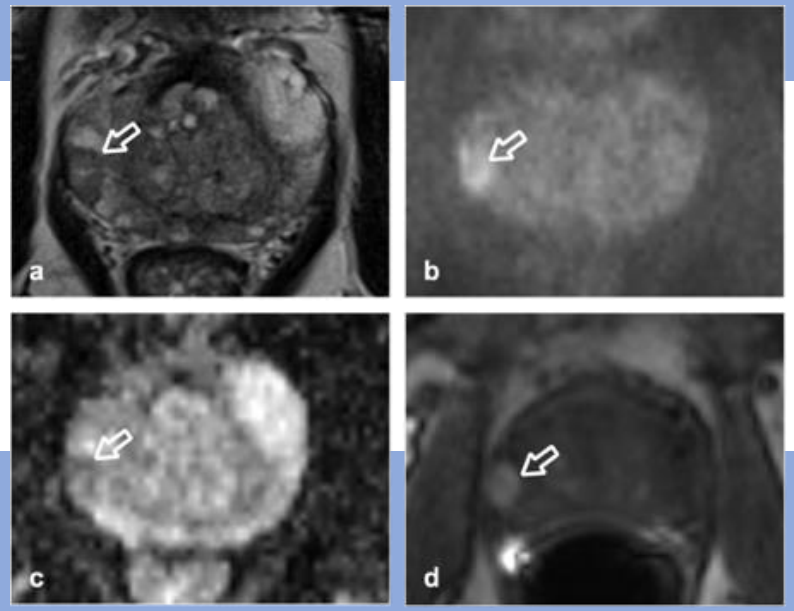
Biochemical recurrence

Local → mp-MRI

Regional

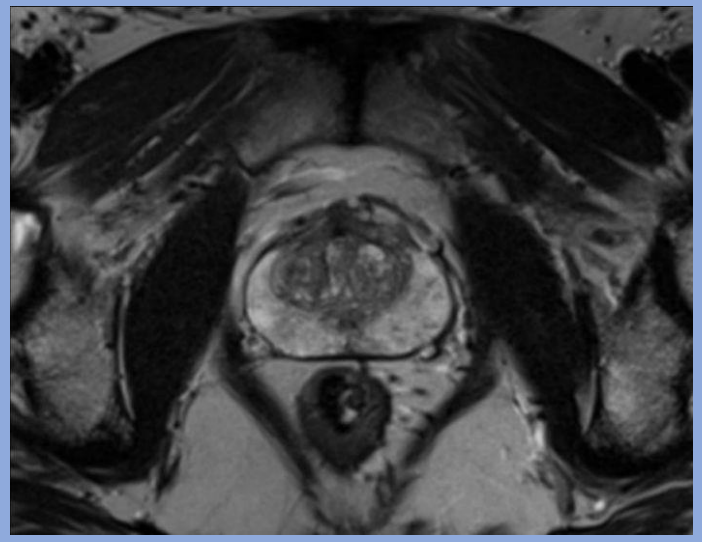
Distant

Advanced imaging techniques –
multiparametric MRI (mp-MRI)



<u>mp-MRI</u>

1. Morphological (T2)
2. Diffusion imaging (DWI)
3. Dynamic contrast-enhanced MRI (DCE)
4. MR spectroscopy (MRSI)



<u>MRI strengths</u>

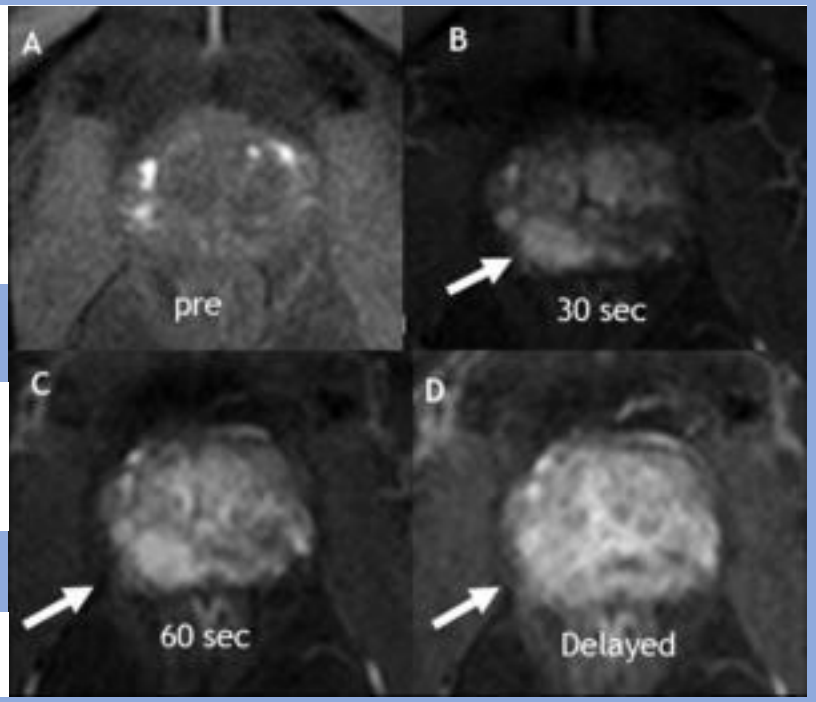
MRI – inherently superior contrast and special resolution

Functional MRI techniques – detection of small recurrences (<1cm)

Advanced imaging techniques –
multiparametric MRI (mp-MRI)

DCE – critical sequence to detect local recurrence

Characteristics - rapid enhancement
- early washout



DWI - low signal on ADC maps
- hyperintensity on high b-value DWI

T2 – hypointense nodule

Current recommendation – useful in guiding biopsy procedures to potential sites of recurrence

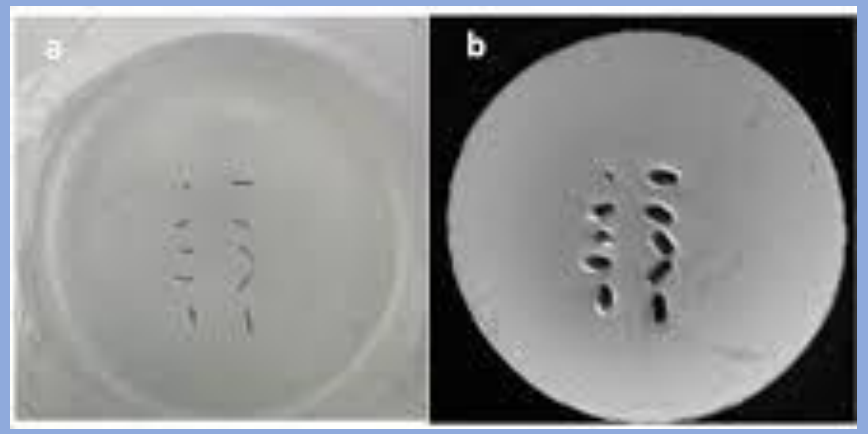
Advanced imaging techniques – multiparametric MRI (mp-MRI)

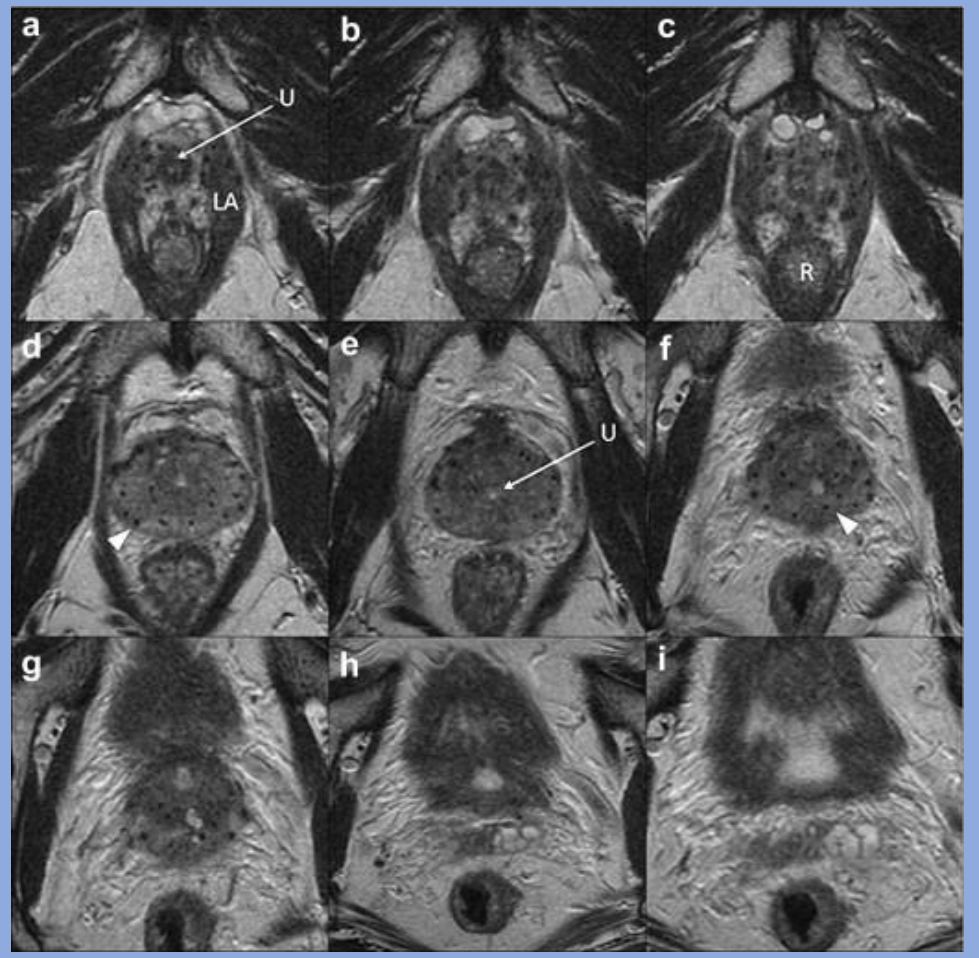
MRI limitations

mp MRI - lack of whole-body coverage

Brachytherapy – diffuse hypointense T2 + loss of normal anatomy

Brachytherapy seeds/implants – susceptibility artefacts + images distortion





mp-MRI
Detecting local recurrence post brachytherapy

- 16 patients with biochemical failure
- Sensitivity:
- T2 - 27%
- DCE - 50%
- DWI - 68%
- Mp-MRI – sensitivity (77%), specificity (92%)

Genitourinary Imaging • Original Research

Locally Recurrent Prostate Cancer After High-Dose-Rate Brachytherapy: The Value of Diffusion-Weighted Imaging, Dynamic Contrast-Enhanced MRI, and T2-Weighted Imaging in Localizing Tumors

Tsutomu Tamada[1]
Teruki Sone[1]
Yoshimasa Jo[2]
Junichi Hiratsuka[3]
Atsushi Higaki[1]
Hiroki Higashi[1]
Katsuyoshi Ito[1]

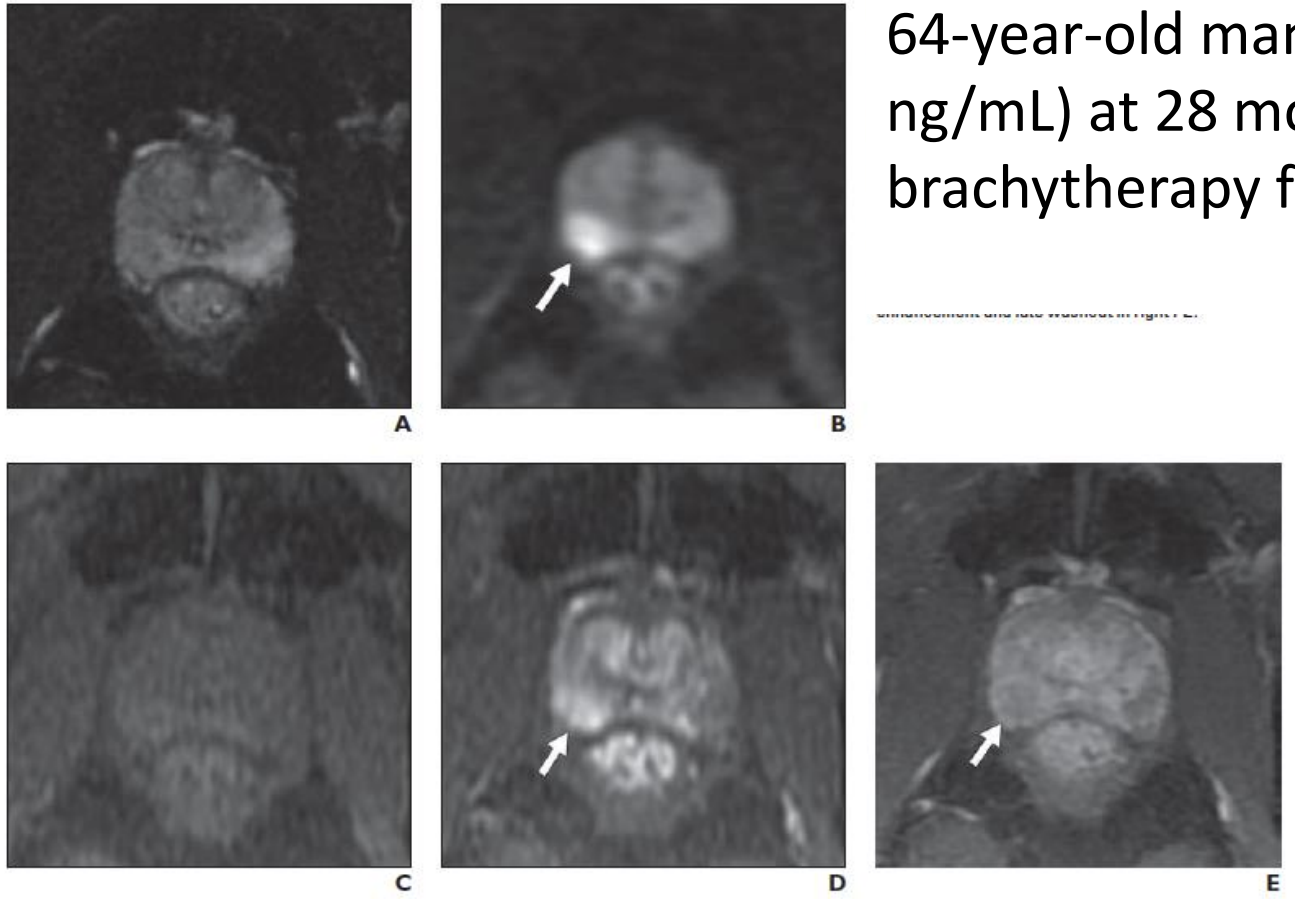
OBJECTIVE. The purpose of this article is to retrospectively evaluate the utility of prostate MRI for detecting locally recurrent prostate cancer after high-dose-rate (HDR) brachytherapy.

MATERIALS AND METHODS. Sixteen men with biochemical failure after HDR brachytherapy for prostate cancer underwent prostate MRI, including T2-weighted imaging, dynamic contrast-enhanced MRI (DCE-MRI), and diffusion-weighted imaging (DWI), using a 1.5-T MRI unit before 12-core-specimen biopsy. Two radiologists in consensus assessed the presence of tumor on each sequence within eight regions of the prostate (six from the peripheral zone [PZ] and two from the transition zone [TZ]) on the basis of biopsy.

RESULTS. Biopsy revealed locally recurrent prostate cancer in 22 (17 in PZ and five in TZ) of 128 regions (17.2%). The sensitivity, specificity, and accuracy of each MRI method in the detection of recurrent tumor were 27%, 99%, and 87%, respectively, for T2-weighted imaging; 50%, 98%, and 90%, respectively, for DCE-MRI; and 68%, 95%, and 91%, respectively, for DWI. The sensitivity of DWI in detecting recurrent tumor was significantly higher than that of T2-weighted imaging ($p = 0.004$). Multiparametric MRI achieved the highest sensitivity (77%) but with slightly decreased specificity (92%).

CONCLUSION. These results indicate that a multiparametric MRI protocol that includes DWI provides a sensitive method to detect local recurrence after HDR brachytherapy.

mp-MRI
Detecting local recurrence post brachytherapy



64-year-old man with increased PSA level (5.27 ng/mL) at 28 months after high-dose-rate brachytherapy for prostate cancer

Local recurrence vs. distant metastases

Biochemical recurrence

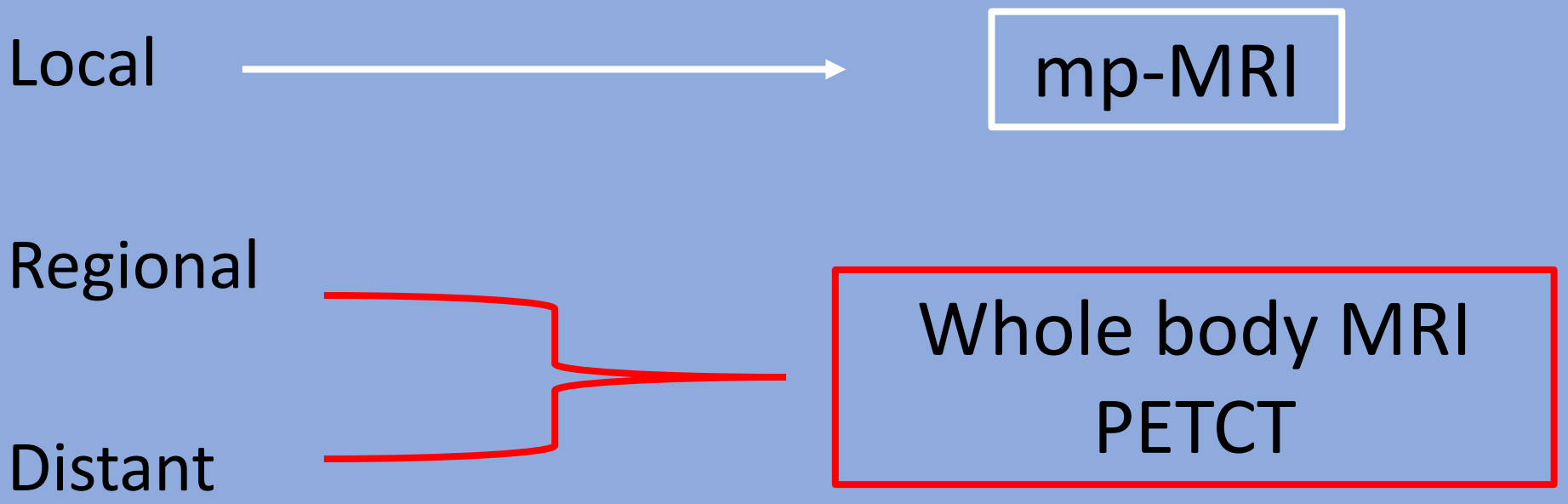
Local → mp-MRI

Regional

Distant

Local recurrence vs. distant metastases

Biochemical recurrence



Whole body MRI

Skeletal Radiol. 2014 Nov;43(11):1503-13. doi: 10.1007/s00256-014-1903-9. Epub 2014 May 20.

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

Shen G[1], Deng H, Hu S, Jia Z.

Sensitivities	Specificities
Choline – 91%	Choline – 99%
MRI – 97%	MRI – 95%
BS – 79%	BS – 82%

Whole body MRI

76 yo. LDR brachytherapy 2012. Rising PSA (8.9 ng/ml). Performance status 1. Right hip replacement 2007. Query suitable for salvage therapy.

Functional imaging techniques with PETCT

- F18-FDG
- F18-Choline
- C11-Choline
- Ga68-PSMA
- F18-PSMA
- Cu64-PSMA
- C11-Acetate
- F18-Fuoride
- F18-fluciclovine
- Ga68-Bombesin
- F18-Bombesin

Functional imaging techniques with F18-FDG PETCT

- FDG is widely used to study tumour metabolism
- Poor sensitivity
- The FDG uptake seems to correlate with degree of differentiation
- It may be most useful in detecting aggressive disease

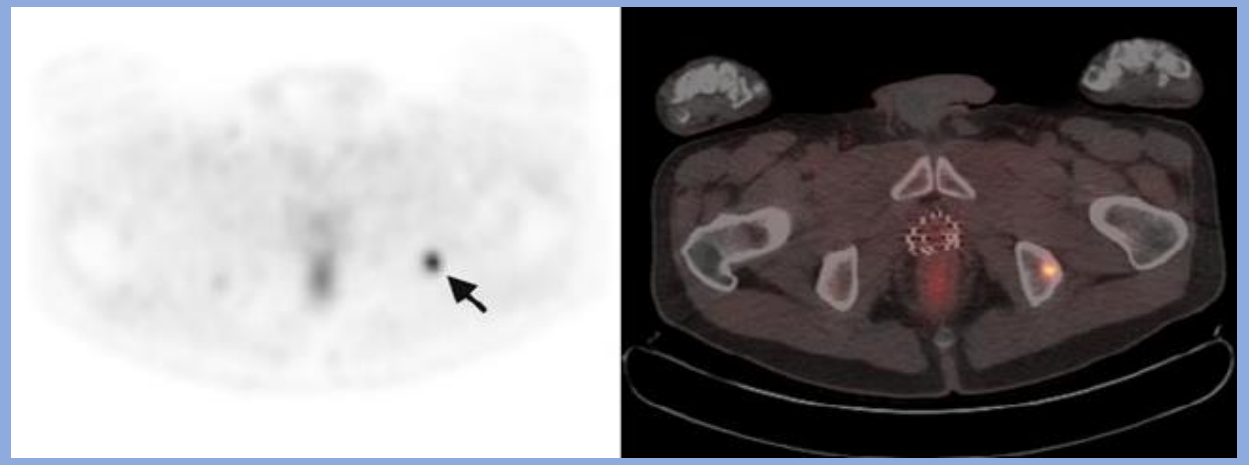
Functional imaging techniques with F18-Choline PETCT

- Choline - synthesis of phospholipids in cell membranes
- Products - C11-Choline and F18-Choline
- F18-Choline - more widely available
- Limitations - false positives in several benign conditions
- Advantage - whole body examination
  - provide metabolic and anatomical information

Functional imaging techniques with F18-Choline

Local Recurrence
PSA - 2.1

Distant metastasis
PSA – 4.5



Functional imaging techniques with F18-Choline

- The detection rate and sensitivity of F18-Choline is connected with the PSA value
- The higher the PSA level, the higher is the positive detection rate
- The detection rate also correlates with the PSA kinetics

Giovacchini et al (2012). Clin Nucl Med 37: 325-331

Functional imaging techniques with F18-Choline

- The detection rate and sensitivity of F18-Choline is connected with the PSA serum level
- The higher the PSA level, the higher is the positive detection rate
- Correlation between the detection rate and PSA kinetics

Giovacchini et al (2012). Clin Nucl Med 37: 325-331

PSA cut-off value ?

Functional imaging techniques with F18-Choline

Meta-analysis article
19 studies
1555 patients
Mix cases of C11 and F18 Choline

Sensitivity of 85.6%
Specificity of 92.6%

Clinical Nuclear Medicine. 38(5):305–314, MAY 2013
DOI: 10.1097/RLU.0b013e3182867f3c, PMID: 23486334
Issn Print: 0363-9762
Publication Date: 2013/05/01

Share Print

Choline PET or PET/CT and Biochemical Relapse of Prostate Cancer: *A Systematic Review and Meta-Analysis*

Laura Evangelista; Fabio Zattoni; Andrea Guttilla; Giorgio Saladini; Filiberto Zattoni; Patrick M. Colletti; Domenico Rubello

Functional imaging techniques with F18-Choline

Treatment	Number of patients
Radical prostatectomy	28
Radiation therapy	13
Brachytherapy	9

Ann Nucl Med (2012) 26:501–507
DOI 10.1007/s12149-012-0601-8

ORIGINAL ARTICLE

Detection of recurrent prostate cancer with 18F-fluorocholine PET/CT in relation to PSA level at the time of imaging

Sandi A. Kwee · Marc N. Coel · John Lim

Received: 10 February 2012 / Accepted: 4 April 2012 / Published online: 2 May 2012

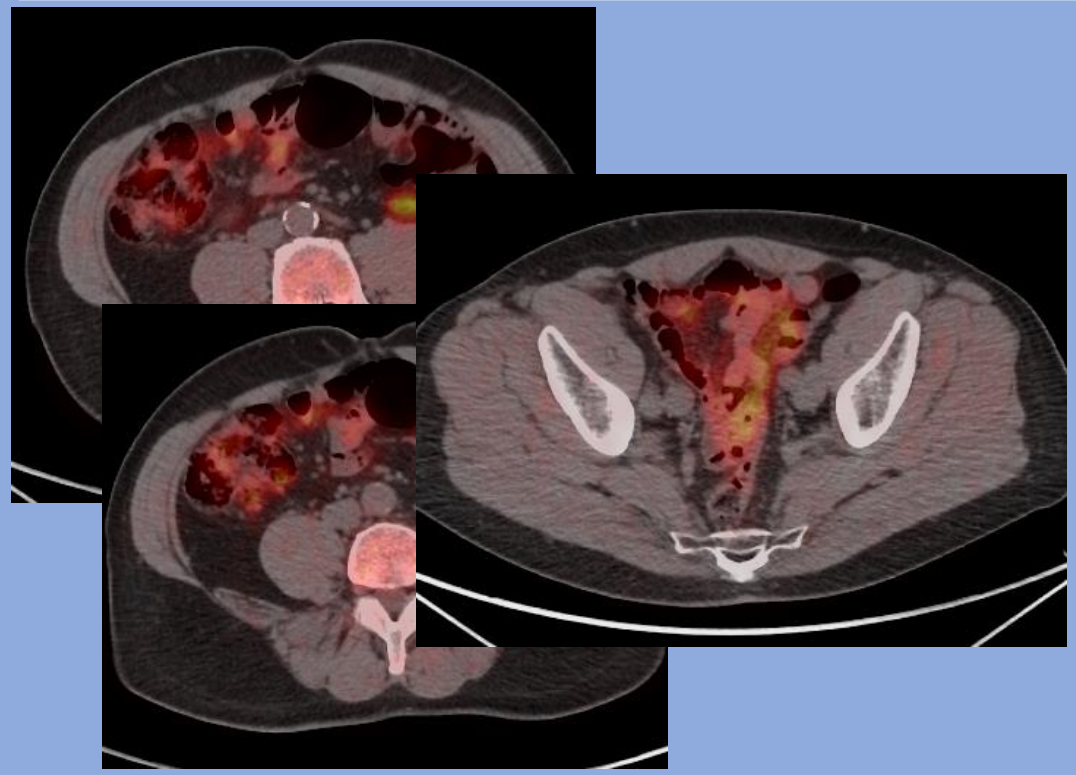
Kwee et at
Evaluated F18 choline for the detection of recurrent prostate cancer in relation to PSA level
50 patients with rising PSA levels were reviewed
The detection rates were determined at various PSA threshold

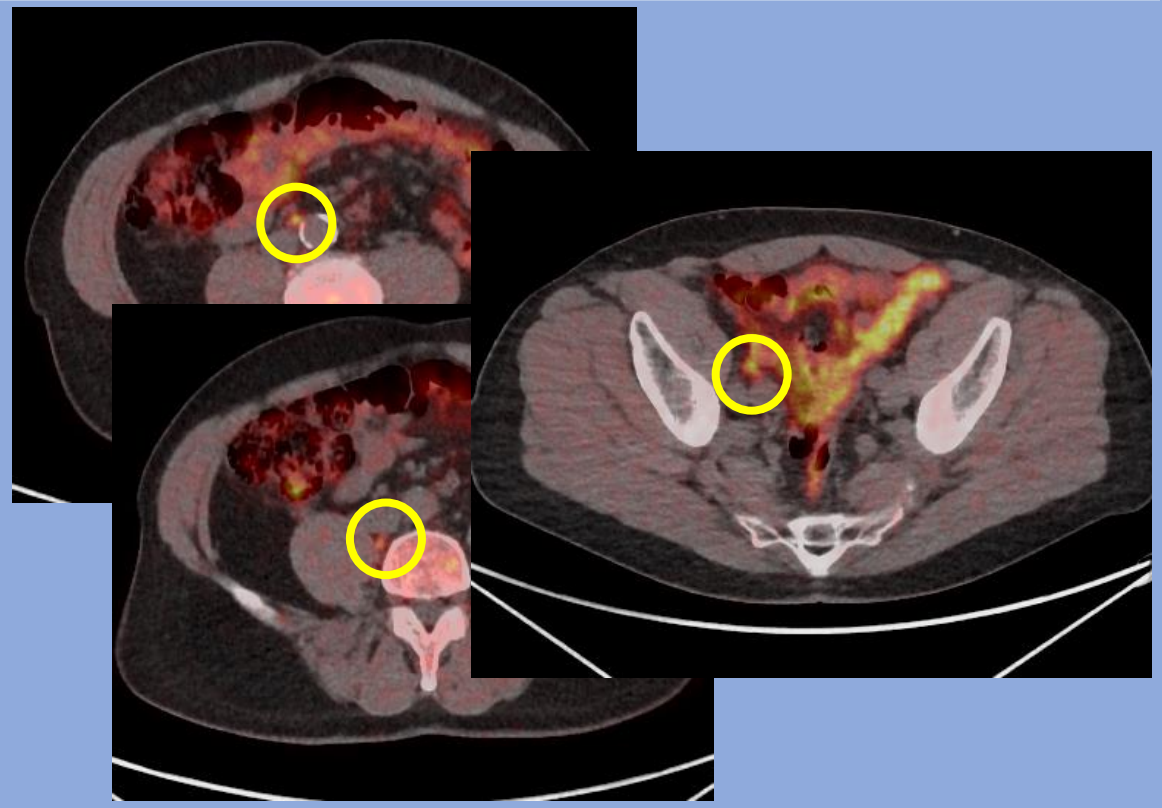
Functional imaging techniques with F18-Choline

Positive scans (%)	PSA level
94%	> 4
85%	2-4
29%	0.5-2
8%	<0.5

Kwee et at
Evaluated F18 choline for the detection of recurrent prostate cancer in relation to PSA level
50 patients with rising PSA levels were reviewed
The detection rates were determined at various PSA threshold

Functional imaging techniques with F18-Choline





Case 1
Prostate cancer
Radical radiotherapy
Rising PSA

PSA - 1

PSA - 4

10 months

Functional imaging techniques with F18-Choline – pitfalls and false positives

Clin Nucl Med. 2014 Feb;39(2):122-30. doi: 10.1097/RLU.0000000000000303.

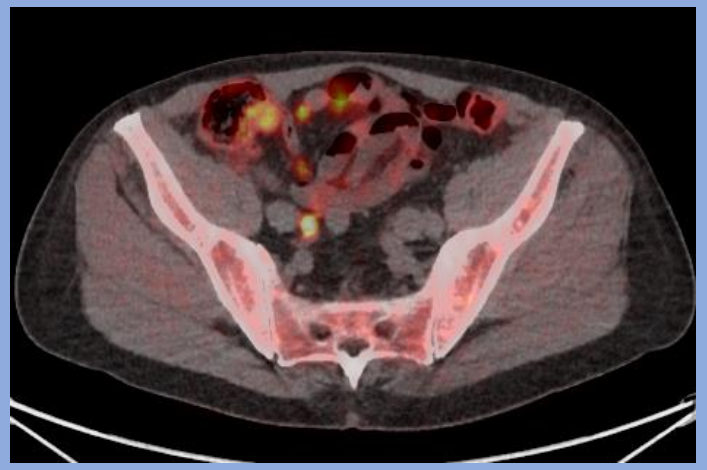
(18)F-choline PET/CT pitfalls in image interpretation: an update on 300 examined patients with prostate cancer.

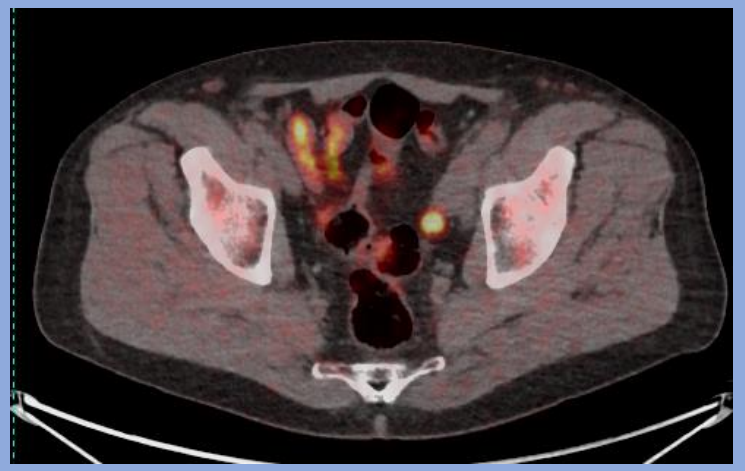
Calabria F[1], Chiaravalloti A, Schillaci O.

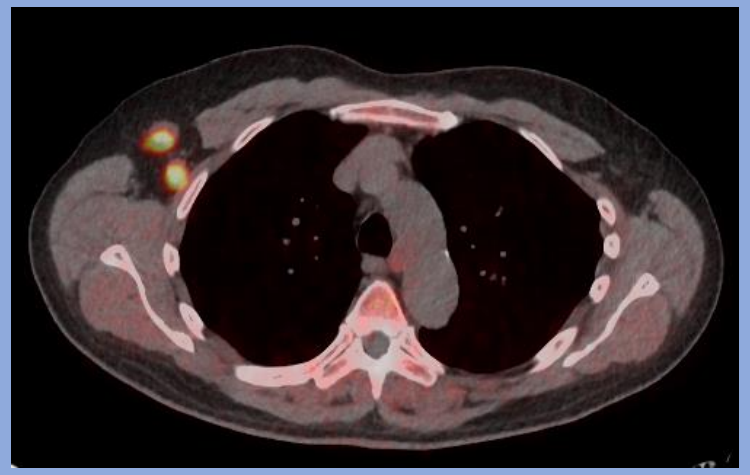
Author information

1. Inflammatory processes
2. Sarcoidosis
3. Thymoma
4. Adrenal adenoma
5. Meningioma
6. Malignancies – colonic cancer, myeloma and lymphoma

Functional imaging techniques with F18-Choline – pitfalls and false positives

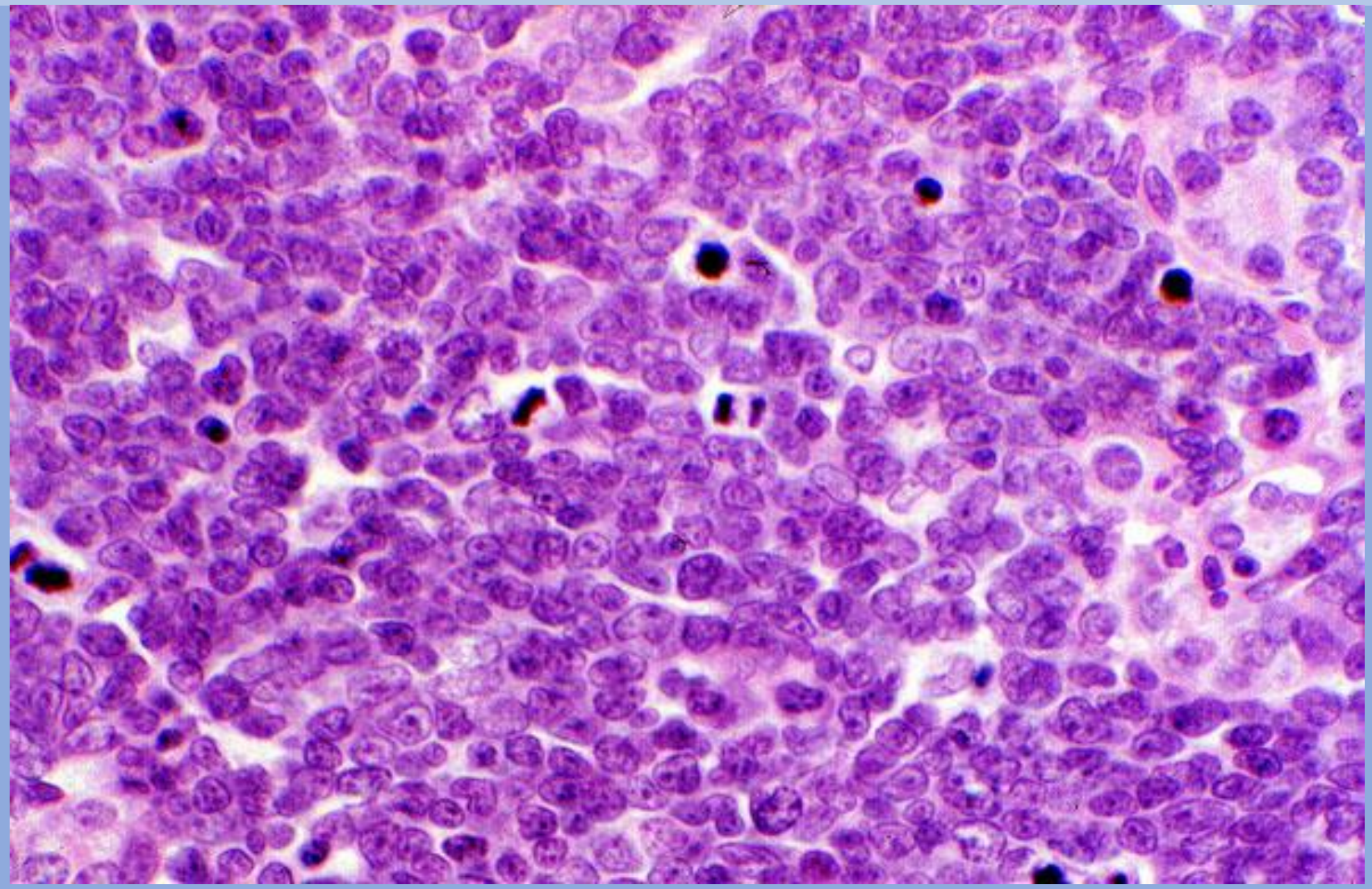






- Prostate Ca, Gl 3+4
- T3a N0 M0
- Radical RT in 2008
- Rising PSA, latest PSA 1.8

Functional imaging techniques with F18-Choline – pitfalls and false positives



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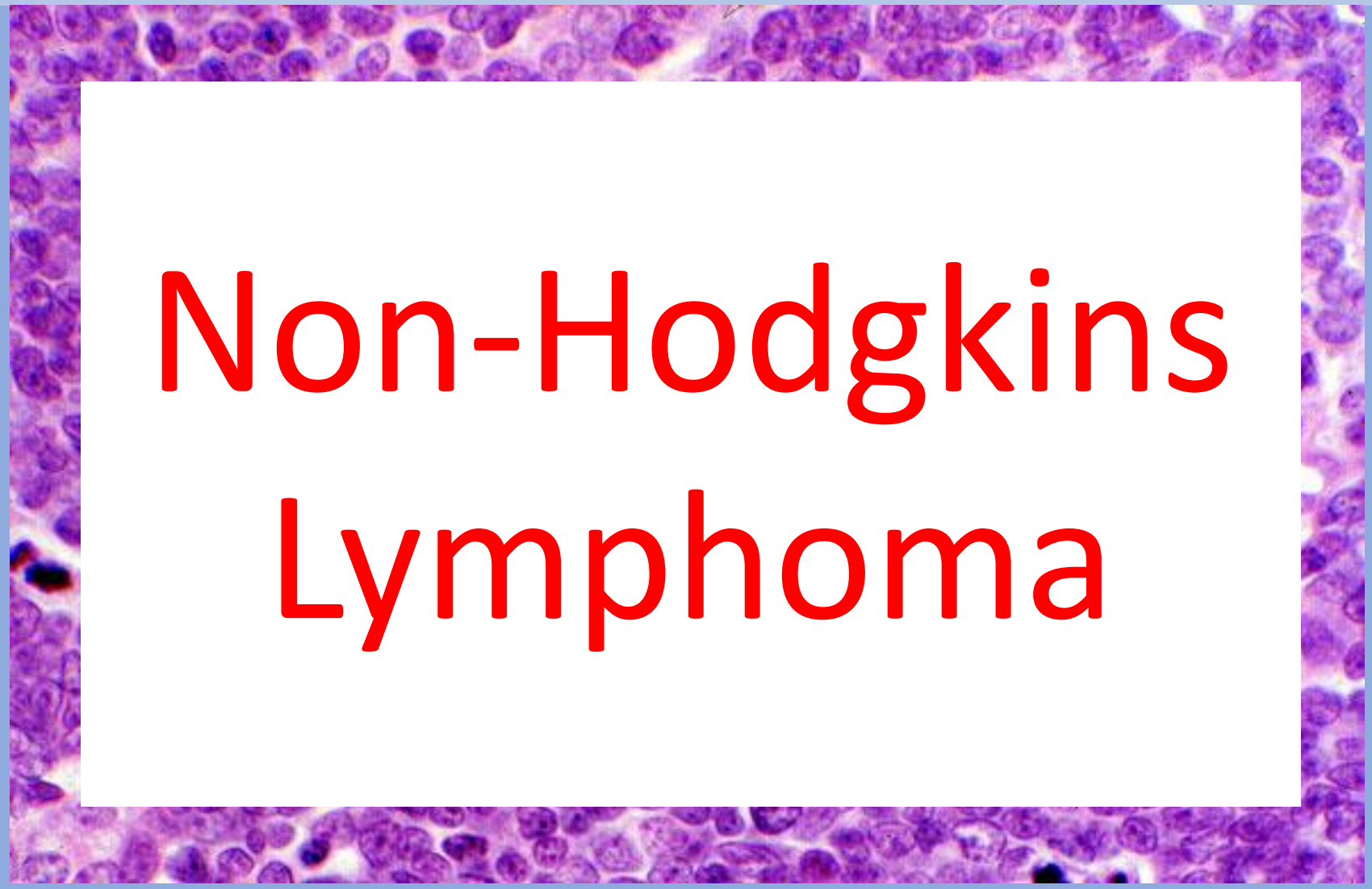
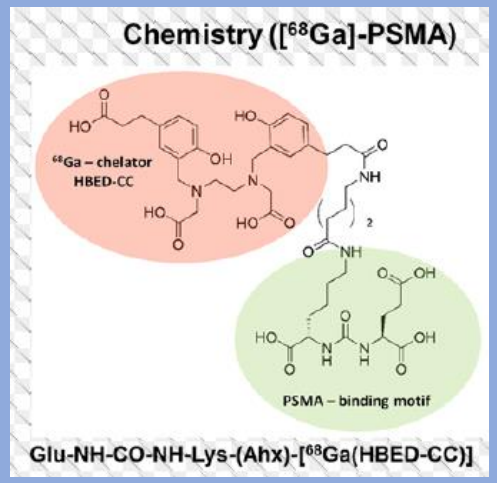
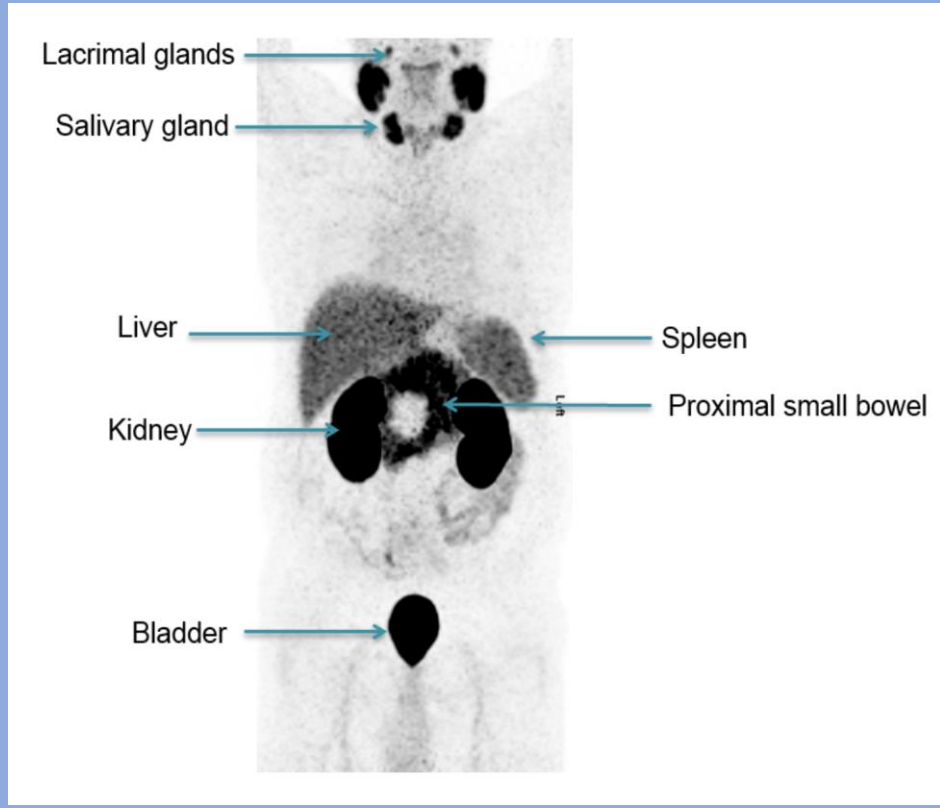


Functional imaging techniques with Ga68 PSMA PETCT



- PSMA – prostate specific membrane antigen
- Membrane bound glycoprotein
- Overexpressed in prostate cancer
- Coupled with Gallium 68 -Ga68 PSMA
- PSMA - expressed in small intestine, renal tubules, salivary glands



Functional imaging techniques with Ga68 PSMA

Table 1. *Characteristics of the studies investigating the utility of 68Ga-PSMA PET/CT in recurrent prostate cancer*

Author	Study type (year)	Study group number	Inclusion criteria	Median GS (range)	Median PSA ng/ml, (range)	68Ga-PSMA detection rate	Factors correlated with PET positivity	Factors not correlated with PET positivity
Asfhar-Oromieh [40]	retrospective (2015)	319	BCR (n=292), primary staging (n=27)	7 (5-10)	4.59 (0.01-41395)	82.8%	PSA level ADT	GS PSAdt
Ceci [4]	retrospective (2015)	70	BCR	7 (5-9)	1.7 (0.2-32.2)	74.2%	PSA level PSAdt	PSAvel ADT age GS time from PT TNM
Demirkol [41]	retrospective (2015)	14	BCR or disease progression	n/a	2.5 (0.2-191.5)	100%	PSA level	n/a
Eiber [6]	retrospective (2015)	248	BCR	7 (6-10)	2.0 (0.2-59.4)	89.5%	PSA level PSAvel GS	PSAdt ADT

ADT – androgen deprivation therapy; BCR – biochemical recurrence; GS – Gleason score; PSAdt – PSA doubling time; PSAvel – PSA velocity; PT – primary therapy; TNM – tumour-node-metastasis

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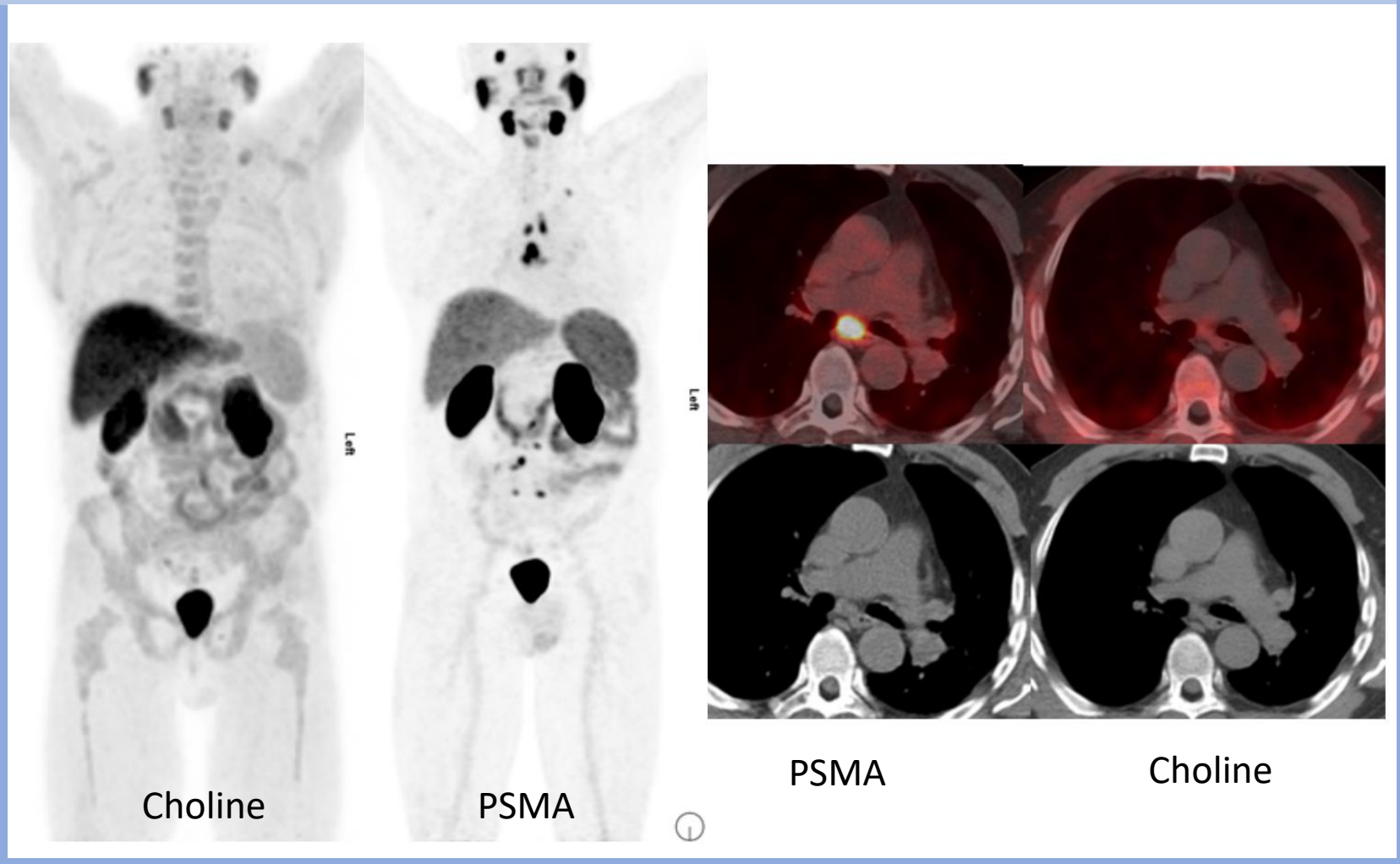
ADT – androgen deprivation therapy; BCR – biochemical recurrence; GS – Gleason score; PSAdt – PSA doubling time; PSAvel – PSA velocity; PT – primary therapy; TNM – tumour-node-metastasis

Functional imaging techniques with Ga68 PSMA

Author	Compared radiotracers	Study type (year)	Study group number	Inclusion criteria	PSA level, mean (±SD)	Time window between PET/ CT scans	Detection rate
Morigi [11]	68Ga-PSMA *vs.* 18F-choline	prospective (2015)	38	BCR	1.72 (±2.54)	30 days	PSA level <0.5: 50% *vs.* 12.5% PSA level 0.5-2.0: 71% *vs.* 36% PSA level >2.0: 88% *vs.* 63% **overall:** 66% *vs.* 32%
Afshar-Oromieh [43]	68Ga-PSMA *vs.* 18F-choline	retrospective (2014)	37	BCR	11.1 (±24.1)	30 days	PSA level ≤2.82: 68.8% *vs.* 43.5% PSA level >2.82: 100% *vs.* 90.5% **overall:** 86.5% *vs.* 70.3%

Functional imaging techniques with Ga68 PSMA

Ga68 PSMA
vs.
F18 Choline



Key points

- In the context of BCR, the choice of imaging modality depends on several factors (absolute PSA value, PSA kinetics and clinical suspicion)
- mp MRI is considered the modality of choice in the evaluation of the prostate/local recurrence
- Whole-body MRI and PET/CT offer better accuracy in identifying sites of nodal recurrence and distant metastases
- Choline PET/CT performs well in patients with PSA ≥2 ng/mL or fast doubling time (< 6months)
- PSMA is superior to choline and it might overcome some of its limitations

Thank you