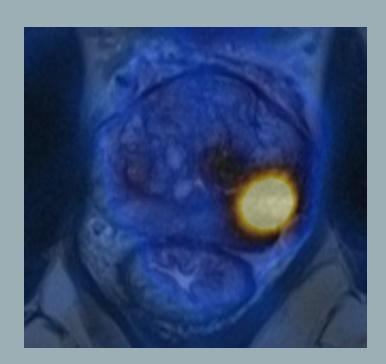
PROSTATE CANCER IMAGING: WHAT & WHEN









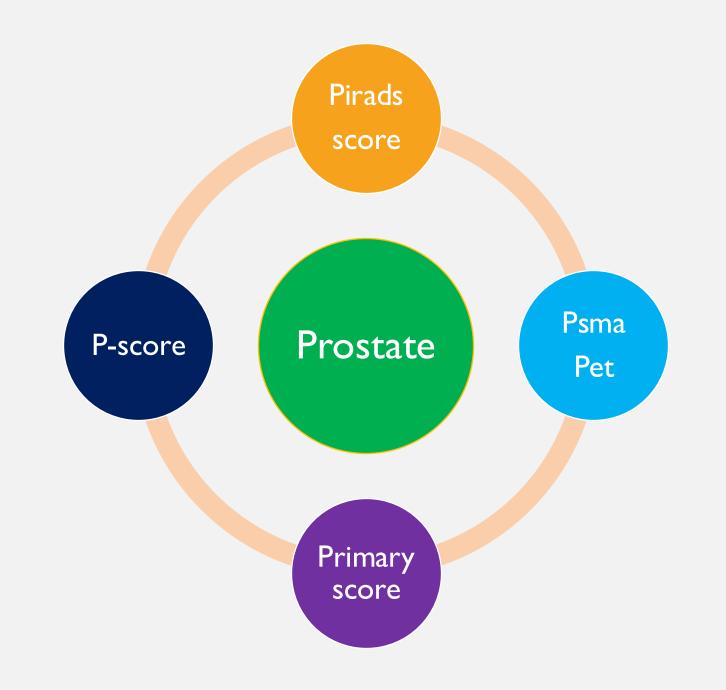


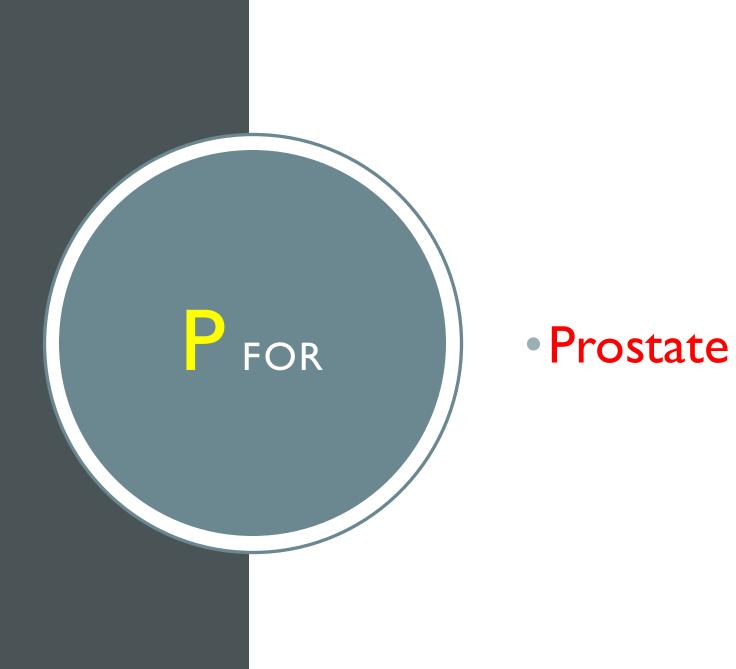




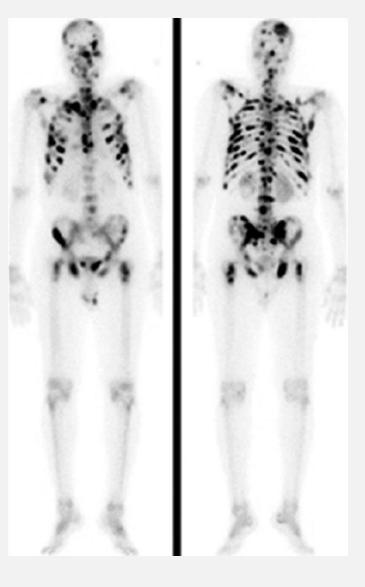




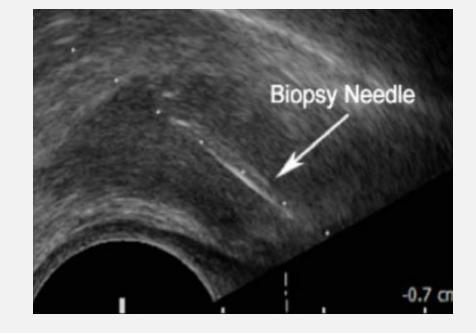


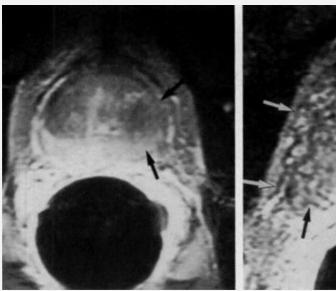


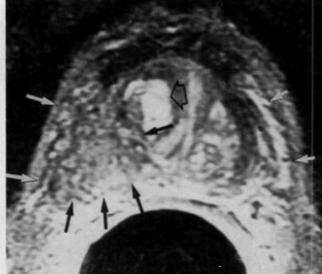












Staging

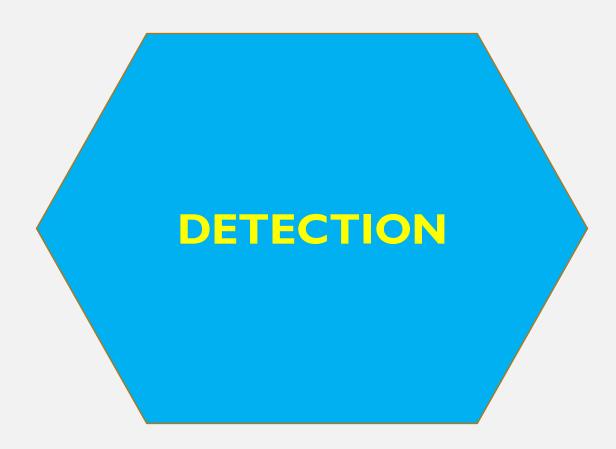
- PET
- MRI
- Bone scan

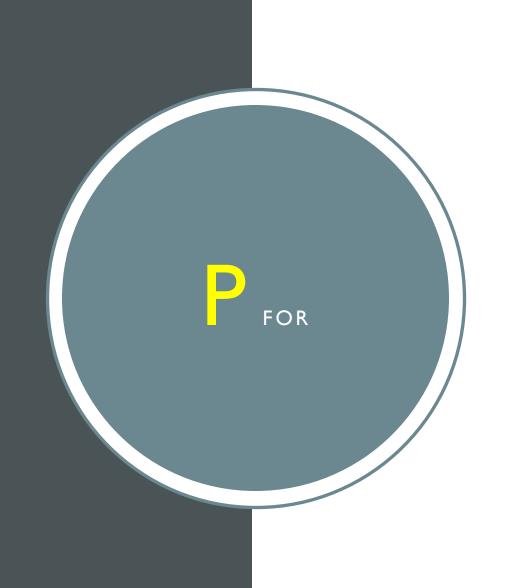
Detection

- MRI
- PET

Biochemical recurrence

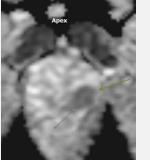
- PET
- MRI

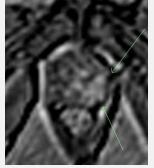




- Promis and Precision
- PI-RADS

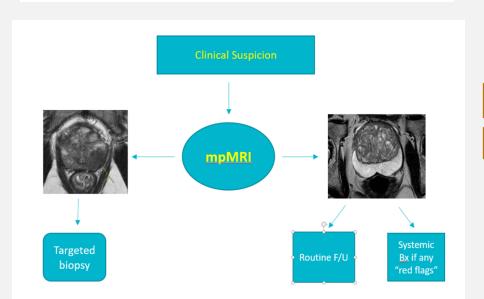
Арех

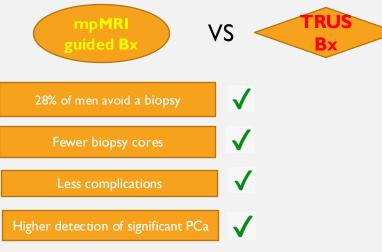




Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed*, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group!





MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

V. Kasivisvanathan, A.S. Rannikko, M. Borghi, V. Panebianco, L.A. Mynderse, M.H. Vaarala, A. Briganti, L. Budäus, G. Hellawell, R.G. Hindley, M.J. Roobol, S. Eggener, M. Ghei, A. Villers, F. Bladou, G.M. Villeirs, J. Virdi, S. Boxler, G. Robert, P.B. Singh, W. Venderink, B.A. Hadaschik, A. Ruffion, J.C. Hu, D. Margolis, S. Crouzet, L. Klotz, S.S. Taneja, P. Pinto, I. Gill, C. Allen, F. Giganti, A. Freeman, S. Morris, S. Punwani, N.R. Williams, C. Brew-Graves, J. Deeks, Y. Takwoingi, M. Emberton, and C.M. Moore, for the PRECISION Study Group Collaborators*

Precision: Moderate agreement (78%) between sites and central read.

Promis:

Any Gleason score 7 (>=3+4)	mpMRI, % (95% CI)
Sensitivity	88 (84-91)
Specificity	45 (39-51)
PPV	65 (60-69)
NPV	76 (69-82) – I in 4 may have Gleason pattern 4 cancer

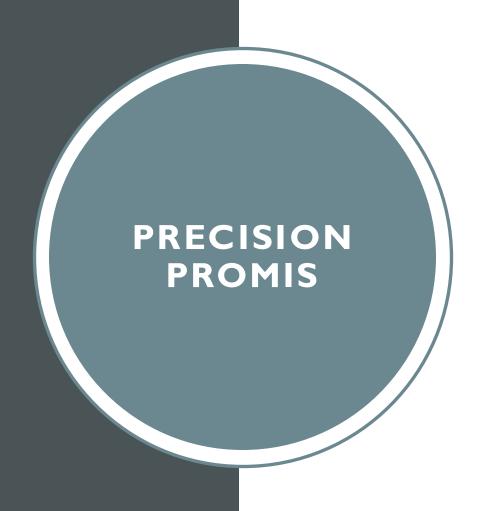
Systemic review: mpMRI sensitivity 58-96% specificity 23-87% NPV 63-98%

For *clinically significant Pca*, MP-MRI was more sensitive (93%, 95% CI 88–96%) than TRUS-biopsy (48%, 42–55%; p<0.0001)

Lancet. 2017 Feb 25;389(10071):815-822.

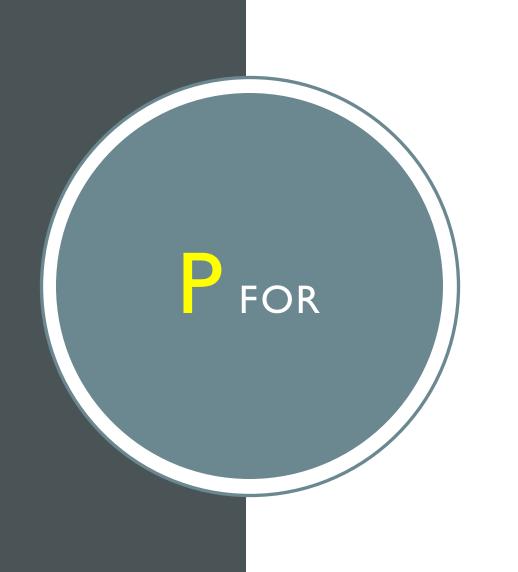
N Engl J Med. 2018 May 10;378(19):1767-1777

Less detection of insignificant PCa



• BUT,

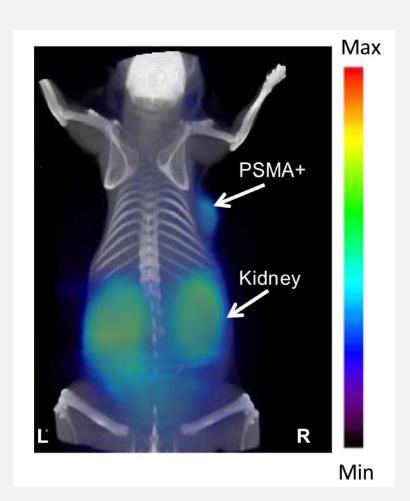
- PROMIS: 25% with –ve MRI → ISUP 2 on template biopsy. Is it safe not to biopsy clinically high risk PIRADs 2 MRI?
- **PRECISION:** PIRADs 2 not biopsied but many biopsies using MRI triaging remain negative. Can we minimize these –ve biopsies?
- **PRECISION:** Moderate agreement (78%) between sites and central read.
- Systemic review: mpMRI sensitivity 58-96% specificity 23-87% NPV 63-98%
- PPV of MRI remains low at 34-68% → unnecessary biopsies and overdetection of iPca.
- Is there a way we can further safely reduce biopsy so we only biopsy those men who have significant malignancy?



• PSMA PET

68Ga-Labeled Inhibitors of Prostate-Specific Membrane antigen (PSMA) for Imaging Prostate Cancer

Sangeeta Ray Banerjee, Mrudula Pullambhatla, Youngjoo Byun, Sridhar Nimmagadda, Gilbert Green, James J. Fox, Andrew Horti, Ronnie C. Mease, and Martin G. Pomper Russell H. Morgan Department of Radiology and Radiological Sciences, Johns Hopkins Medical Institutions, Baltimore, MD 21231



J Med Chem. Author manuscript; available in PMC 2012 May 02.

Compounds [68Ga]3 and [68Ga]6 demonstrate PSMA-specific tumor imaging *in vivo*. Because of higher target-to-nontarget ratios with comparable absolute uptake values to [68Ga]3, [68Ga]6 will be pursued in additional animal models and for toxicity testing *en route* to clinical translation. In this manner we hope to add this cyclotron-independent radiopharmaceutical to the array of emerging agents for imaging prostate cancer.

PSMA

Prostate Specific Membrane Antigen (PSMA):

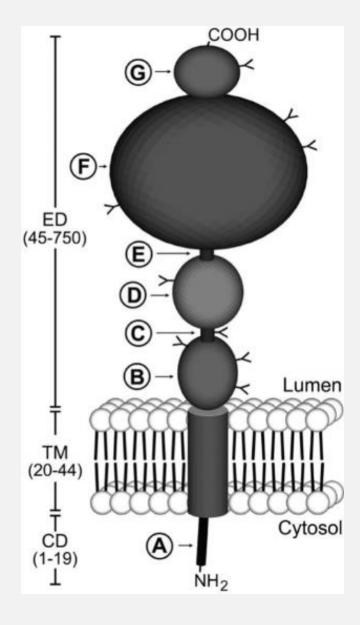
Cell surface folate hydrolase, N-acetyl-a-linked acidic dipeptidase I or glutamate carboxypeptidase II, type II transmembrane glycosylated protein.

Expressed 100-1000 x higher in prostate cancer than in benign prostate.

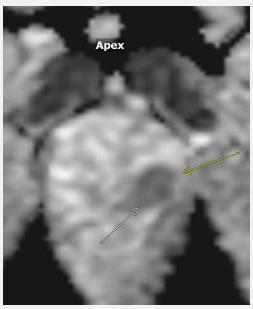
PSMA expression increased in metastatic and castration- resistant Pca

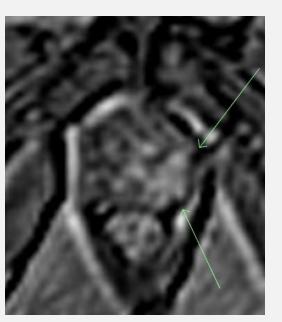
PSMA-binding ligands are bound to the extracellular domain of PSMA

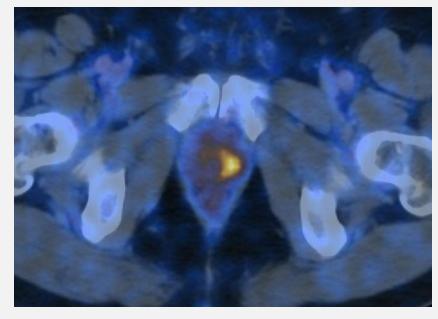
Increased PSMA expression in neovasculature of solid tumours but not in normal tissue vasculature











Diagnostic accuracy of ⁶⁸ Ga-prostate-specific membrane antigen (PSMA) positron-emission tomography (PET) and multiparametric (mp)MRI to detect intermediate-grade intra-prostatic prostate cancer using whole-mount pathology: impact of the addition of ⁶⁸ Ga-PSMA PET to mpMRI.

 $\frac{\text{Scheltema MJ}^{1,2,3}, \text{ Chang JI}^{1,2}, \text{ Stricker PD}^{1,2}, \text{ van Leeuwen PJ}^{1,2,4}, \text{ Nguyen QA}^{1}, \text{ Ho B}^{5}, \text{ Delprado W}^{6}, \text{ Lee J}^{5}, \text{ Thompson JE}^{1,2}, \text{ Cusick T}^{1}, \text{ Spriensma AS}^{3}, \\ \frac{\text{Siriwardana AR}^{1,2}, \text{ Yuen C}^{7}, \text{ Kooner R}^{7}, \text{ Hruby G}^{8}, \text{ O'Neill G}^{7}, \text{ Emmett L}^{1,5}.}$

Intermediate Pca (GG 2/3) with pre-op mpMRI and PSMA-PET/CT prior to RP

Per-patient basis	PSMA	mpMRI
Sensitivity	100%	97%

	Diagnostic Accuracy	Sensitivity	Specificity	NPV	PPV
mpMRI	0.79	68%	91%	87%	76%
PSMA	0.91	88%	93%	95%	85%

- PSMA-PET is accurate in detecting GG 2/3 intra-prostatic malignancies, compared with and complementary to mpMRI.
- PSMA identified ISUP >= 2 more frequently than ISUP =< 1 (sensitivity 88% vs 18% respectively)

ORIGINAL RESEARCH • GENITOURINARY IMAGING

Radiology

Diagnostic Accuracy of ⁶⁸Ga-PSMA-11 PET/MRI Compared with Multiparametric MRI in the Detection of Prostate Cancer

Robert M. Hicks, MD • Jeffry P. Simko, MD • Antonio C. Westphalen, MD, PhD • Hao G. Nguyen, MD, PhD • Kirsten L. Greene, MD, MS • Li Zhang, PhD • Peter R. Carroll, MD, MPH • Thomas A. Hope, MD

The sensitivity of gallium 68-labelled prostate-specific membrane antigen-II PET/MRI in the detection of prostate cancer is better than that of multiparametric MRI.

Prostate Cancer

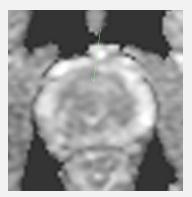
Simultaneous ⁶⁸ Ga-PSMA HBED-CC PET/MRI Improves the Localization of Primary Prostate Cancer

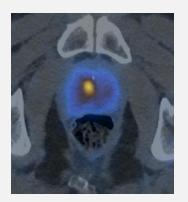
Matthias Eiber ^a ^a ^t [⊠], Gregor Weirich ^{b, †}, Konstantin Holzapfel ^c, Michael Souvatzoglou ^{a, d}, Bernhard Haller ^e, Isabel Rauscher ^a, Ambros J. Beer ^{a, d}, Hans-Jürgen Wester ^f, Juergen Gschwend ^g, Markus Schwaiger ^{a, ‡}, Tobias Maurer ^{g, ‡}



PRIMARY trials













Platinum Priority - Prostate Cancer - Editor's Choice

Editorial by Marinus J. Hagens and Pim J. van Leeuwen on pp. 690-692 of this issue

The Additive Diagnostic Value of Prostate-specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study

Louise Emmett ^{a,b,*}, James Buteau ^c, Nathan Papa ^d, Daniel Moon ^e, James Thompson ^{f,l}, Matthew J. Roberts ^g, Kris Rasiah ^h, David A. Pattison ^g, John Yaxley ^l, Paul Thomas ^g, Anthony C. Hutton ^f, Shikha Agrawal ^b, Amer Amin ^b, Alexandar Blazevski ^b, Venu Chalasani ^h, Bao Ho ^a, Andrew Nguyen ^a, Victor Liu ^a, Jonathan Lee ^a, Gemma Sheehan-Dare ^a, Raji Kooner ^j, Geoff Coughlin ^l, Lyn Chan ^a, Thomas Cusick ^b, Benjamin Namdarian ^j, Jada Kapoor ^e, Omar Alghazo ^e, Henry H. Woo ^k, Nathan Lawrentschuk ^e, Declan Murphy ^e, Michael S. Hofman ^c, Phillip Stricker ^l

PRIMARY

Imaging trial

Additive value of **DSM Prostate Specific** Membrane Antigen

in the diagnosis of **Prostate Cancer**















1 In 6 men is diagnosed with Prostate Cancer during their lifetime.

CURRENT DIAGNOSTIC PATHWAY

1 in 5 men will needlessly undergo blopsles for false positive PSA & DRE.

MRI alds diagnosis

many unnecessary blopsles.

but still results in



Elevated PSA



BIOPSY

Can PSMA PET combined with MRI better diagnose clinically Prostate Cancer (csPCa)?



296 men with suspected **Prostate Cancer**

- · Abnormal DRE
- Elevated PSA < 20ng/mL
- . No prior diagnostic blopsy

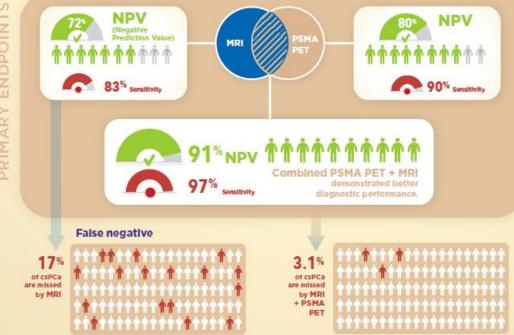


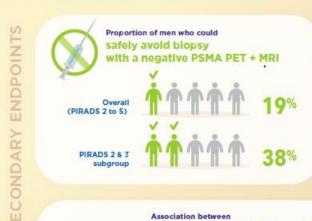


BIOPSY as planned, based on clinical risk & MRI result



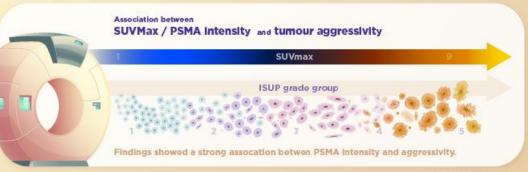
ENDPOINTS PRIMARY





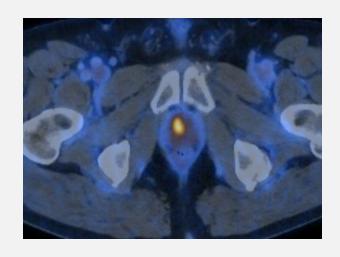
PROSPECTIVE MULTI-CENTRE STUDY

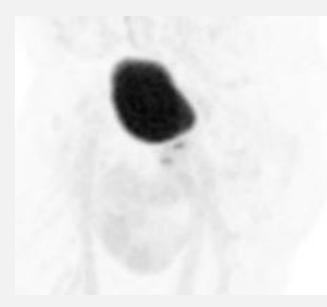


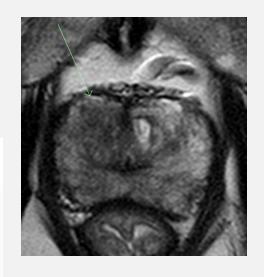


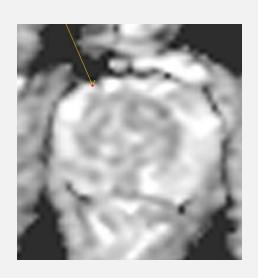
Eur Urol: Volume 80, Issue 6, December 2021, Pages 682-689

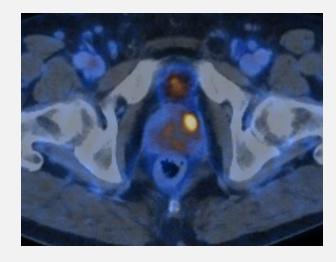
© 2021 Copyright Prof. Louise Emmett

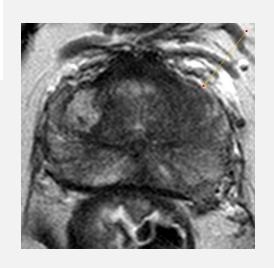


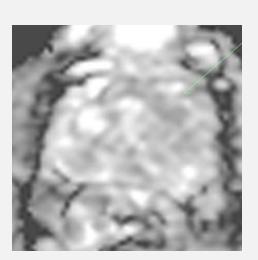




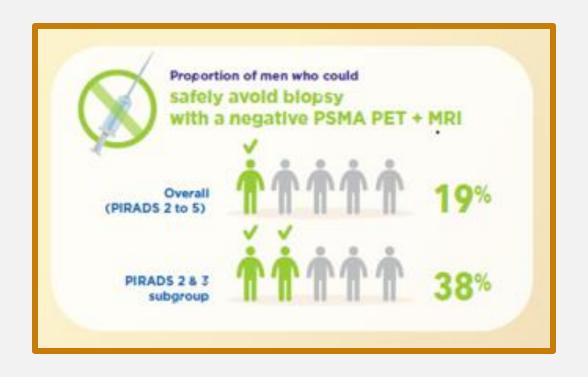








Images provided courtesy of St Vincent's Public Hospital, Sydney

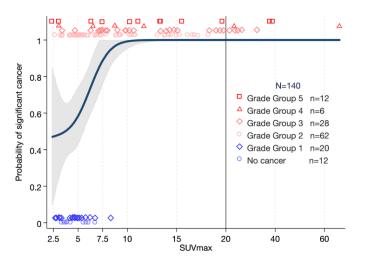


PI-RADS 2 - 28% csPCa PI-RADS 3 - 47% csPCa PSMA positive in 90% PI-RADS 2/3 with csPCa.

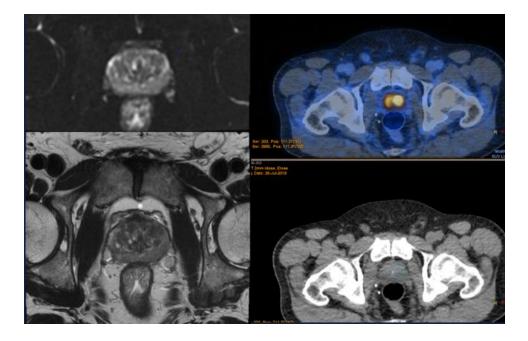
38% PI-RADS 2/3 MRIs are negative on PSMA. 91% -ve for csPCa. 9% +ve: 4/5 ISUP 2 and 1/5 ISUP 3 small volume

DE-INTENSIFY BIOPSY IN PIRADS 4/5?









PRIMARY MESSAGE

01

Improved NPV and sensitivity for combined PSMA + MRI may allow further safe reduction in biopsy in an already MRI triaged population.

02

Highest impact in men with PI-RADS 2/3 with improved detection of csPCa and potential to reduce biopsy by 38% (19% overall)

03

Impact in PI-RADS 4/5 less.Will still need to biopsy men with PI-RADs 4/5 with -ve PSMA PET.

Can we de-intensify biopsy in men with PIRADS 4/5 and strongly +ve PSMA PET?

STORY SO FAR ...

Mp MRI has an established role for the Dx of csPCa with superior diagnostic accuracy to TRUS Bx



PRIMARY: significant improvement in sensitivity (97% vs 83%) and NPV (91% vs 72%) of MRI + PSMA PET vs MRI alone.

 38% of pts with PI-RADS 2/3 were true Negative on PSMA PET → potentially benefit from avoiding transperitoneal prostate biopsy.



PRIMARY 2: PSMA PET to MRI PI-RADS 2/3 may help to improve detection of csPCa, enable some men to avoid TPPBx without missing csPCa, and will facilitate Bx targeting of PSMA-avid sites.

Clinical Trial in Progress

Abstract # TPS397 Louise.Emmett@svha.org.au

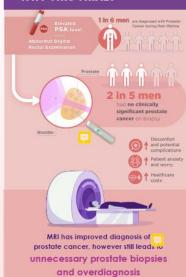
PRIMARY2: A phase III, multi-centre,

randomised controlled trial investigating the additive diagnostic value of

[68Ga]Ga-PSMA-11 PET/CT in men with negative/equivocal MRI in the diagnosis of clinically significant prostate cancer

James P Buteau^{1,2}, Daniel Moon^{3,4}, Michael T Fahey^{2,5}, Matthew J Roberts⁴, James Thompson⁷, Declan G Murphy^{0,3}, Nathan Papa⁸, Catherine Mitcheli^{2,9}, Veeru Kasivisvanathan^{3,10} Philip Stricker¹¹, Jonathan O'Brien²³, William Counter¹², Gaurav Sharma¹, Shikha Agrawal¹², Bao Ho¹², Theresa Yeung⁶, Richard De Abreu Lorenco¹³, Haryana M Dhillon¹⁴, Michael S Hofman*1.7, Louise Emmett*12

WHY THIS TRIAL?



HYPOTHESIS

The addition of PSMA PET is non-inferior to standard of care with MRI to detect clinically significant prostate cancer, while providing the advantages of

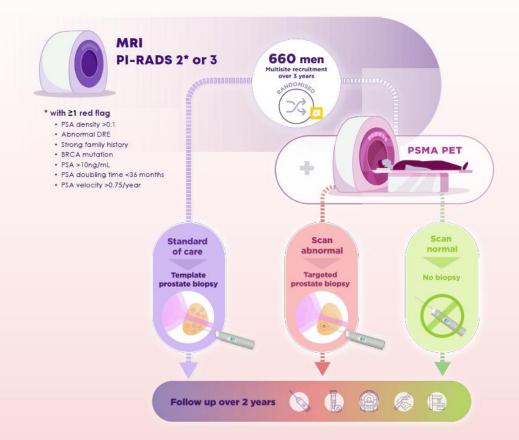
- reducing unnecessary biopsies and
- · limiting to targeted biopsies.





Additive value of PSMA PET

for men with negative or equivocal MRI to diagnose significant prostate cancer



personal use only and may not be

ASCO Genitourinary Cancers Symposium



No pattern

PRIMARY Score



Diffuse transition zone (Pattern A) Focal peripheral zone (Pattern D)





PRIMARY Scores

PRIMARY Scores 3, 4 and 5 = abnormal

OBJECTIVES

Co-primary endpoints



Difference between arms in clinically significant prostate cancer, defined as Gleason Score 3+4(≥10%)=7, Grade Group 2 or higher

Percentage of participants who avoid transperineal prostate biopsy

Measure impact on



Patient Reported Outcomes (PROs)

Reduce overdiagnosis and complications



CURRENT STATUS

- Enrolment commenced March 2022
- 123/660 participants recruited as of January 27th, 2023
- 5 activated Australian centres (St-Vincent's Hospital Sydney) Peter MacCallum Cancer Centre; Royal Brisbane and Women's Hospital; Cabrini Health Malvern; Royal Adelaide Hospital)











To be continued...

The PRIMARY study analysis utilized a minimum PSMA SUVmax cut-off [4.0] with expert reader analysis, finding a sensitivity of 90% with a specificity of 50% for csPCa. However, this method is not valid across unharmonized PET cameras and with variable PSMA ligands.

PSMA peptides- SUVmax variable

Same receptor but:

Variable binding affinity

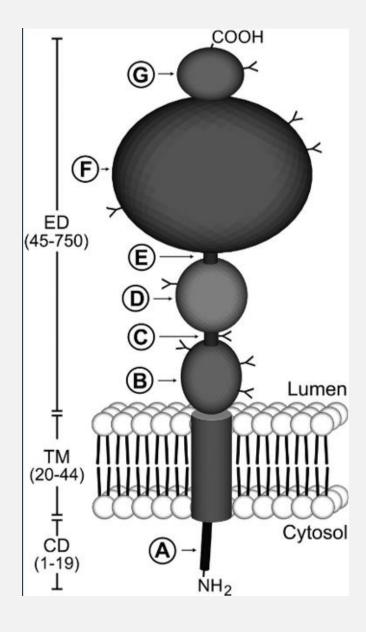
Variable half lives

Variable injected quantity

Variable time between injection and imaging

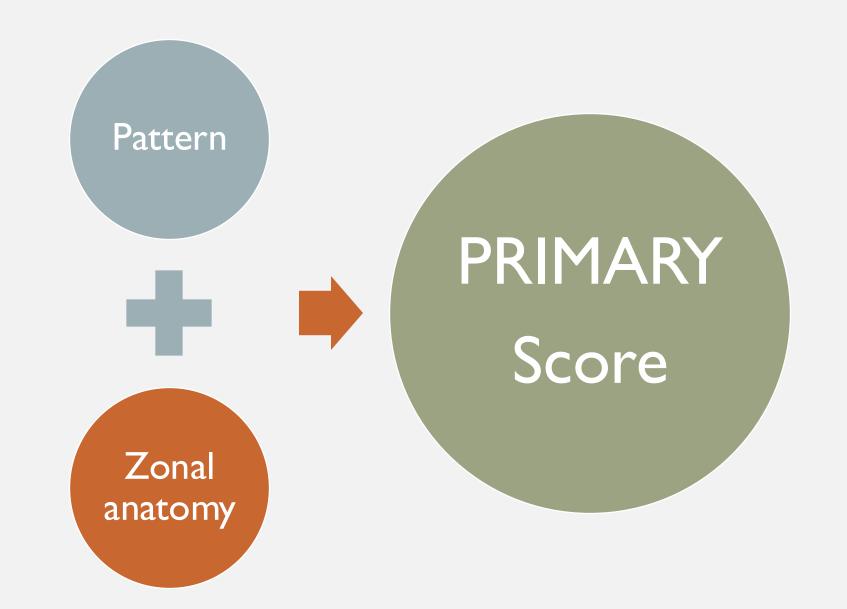
SUV max variability significant at low levels

Is there a better way to read PSMA PET?



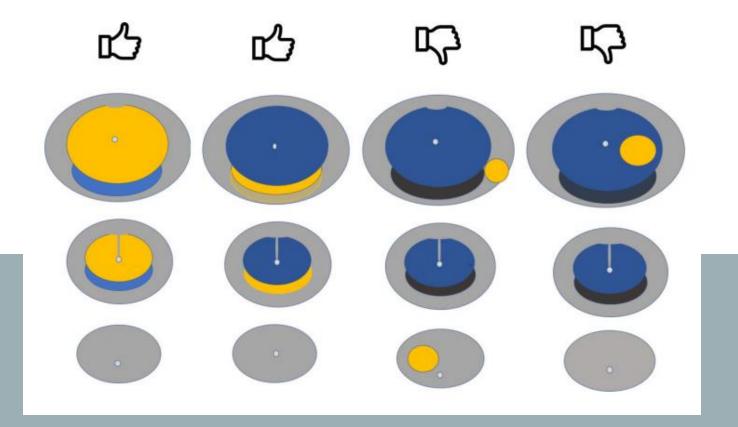


PRIMARY score



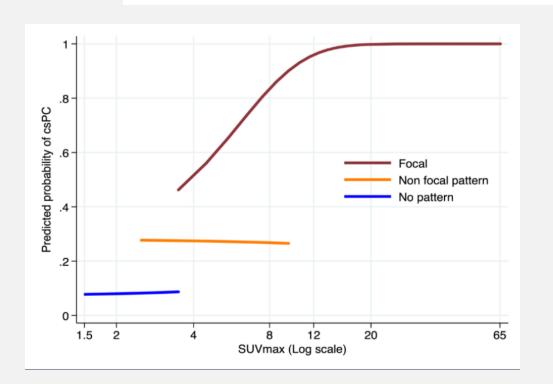
The PRIMARY Score: Using intra-prostatic PSMA PET/CT patterns to optimise prostate cancer diagnosis.

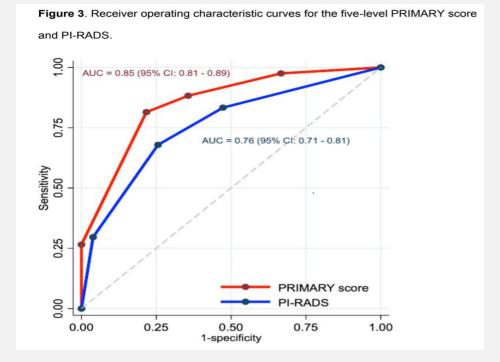
Louise Emmett^{1,2,3}, Nathan Papa⁴, James Buteau^{5,6}, Bao Ho¹, Victor Liu¹, Matthew Roberts⁷, James Thompson⁸, Dan Moon⁹, Gemma Sheehan-Dare¹, Omar Alghazo⁹, Shikha Agrawal¹, Declan Murphy⁹, Phillip Stricker^{10,11}, Thomas A. Hope¹², Michael S. Hofman^{5,6,13}

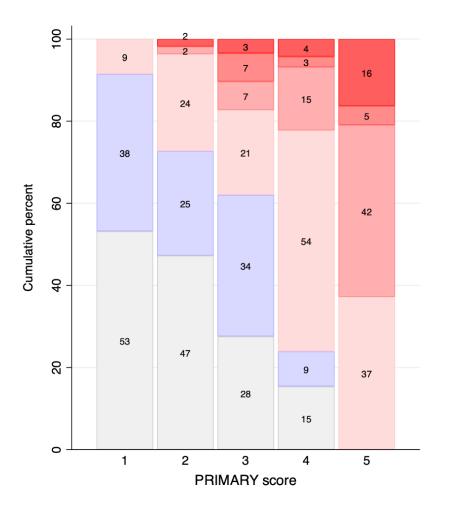


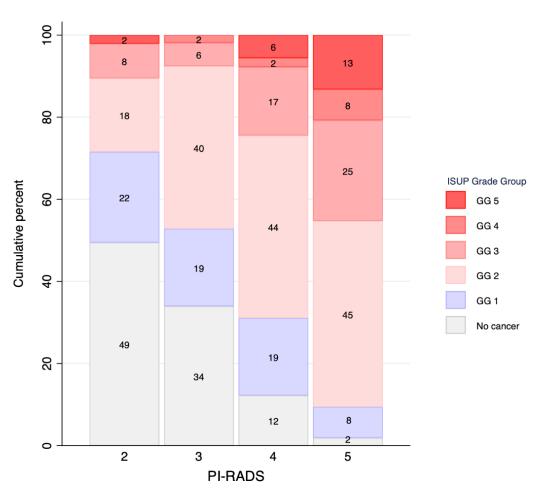
PRIMARY score	PET	PET/CT
1 No pattern Low grade activity		o Ans
2A Diffuse transition zone	**	o Ans o
2B Symmetrical central zone	*	o Ans o
3 Focal transition zone		9 SUV 0
4 Focal peripheral zone		9 SUV 0
5 Intense uptake SUVmax ≥12	4	9 SUV 0

	PRIMARY SCORE	n	% csPCa
1	No dominant intra-prostatic pattern on PSMA. Low grade activity.	47	8.5
2	Diffuse transition zone activity or symmetrical central zone activity that does not extend to the prostate margin on CT.	55	27
3	Focal TZ activity significantly above background TZ activity.	29	38
4	Focal PZ activity (no minimum intensity)	117	76
5	PSMA SUVmax > 12	43	100

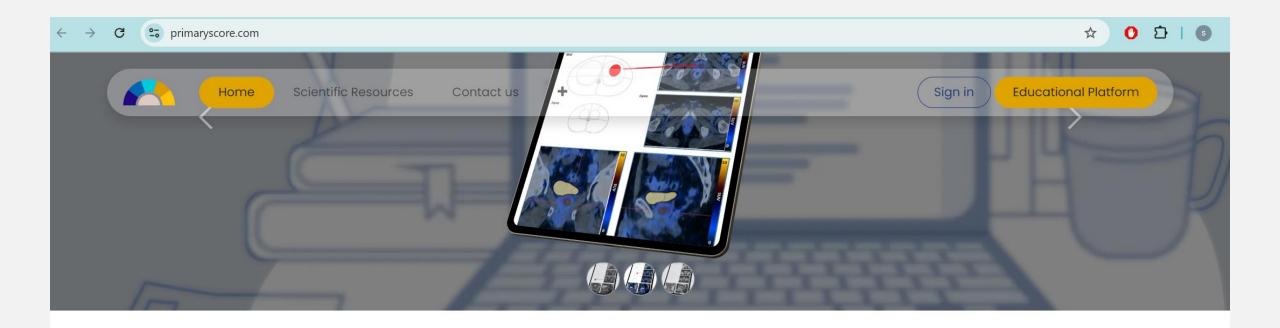








PRIMARY SCORE VS GG



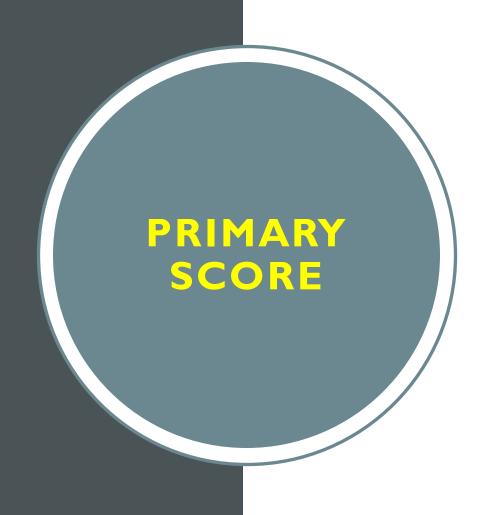
PRIMARY score

The PRIMARY score is a 5-category scale developed to identify clinically significant intraprostate malignancy (csPCa) on 68Ga-prostatespecific membrane antigen (PSMA) PET/CT (68Ga-PSMA PET) using a combination of anatomic site, pattern, and intensity.

This scoring system incorporating intraprostatic patterns and intensity on 68Ga-PSMA PET/CT shows potential as an accurate method for diagnosing csPCa and should be considered when PSMA PET is undertaken for this purpose.

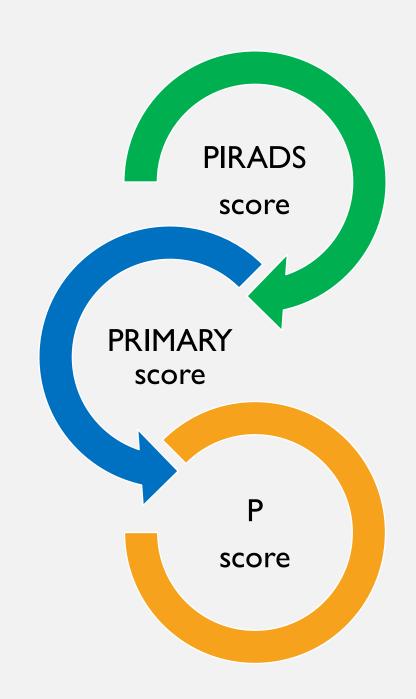
Learn more





- Reporting by pattern rather than intensity has higher specificity while maintaining sensitivity for PSMA PET alone.
- Kappa scores for inter-reader variability above that reported for PI-RADS.
- Needs to be validated in a low prevalence pre-biopsy population
- Not expected to replace PI-RADS (PRIMARY: an MRI triaged population).
- May further improve PSMA + MRI combined results.





P- SCORE

Beyond Prostate Imaging Reporting and Data
System: Combining Magnetic Resonance Imaging
Prostate Imaging Reporting and Data System and
Prostate-Specific Membrane Antigen-Positron
Emission Tomography/Computed Tomography
PRIMARY Score in a Composite (P) Score for More
Accurate Diagnosis of Clinically Significant Prostate
Cancer

Louise Emmett, Nathan Papa, Thomas A. Hope, Wolfgang Fendler,
Jeremie Calais, Irene Burger, Matthias Eiber, Francesco Barbato,
Daniel Moon, William Counter, Nikeith John, Alan Xue,
Anthony Franklin, James Thompson, Kris Rasiah, Mark Frydenberg,
John Yaxley, James Buteau, Shikha Agrawal, Bao Ho, Andrew Nguyen,
Victor Liu, Jonathan Lee, Henry Woo, Edward Hsiao,
Thomas Sutherland, Elyse Perry, Phillip Stricker, Michael S. Hofman,
Veeru Kasivisvanathan, Matthew Roberts, and Declan Murphy

View fewer authors X

Pages: 299–309 | Published Online: 05/17/2024

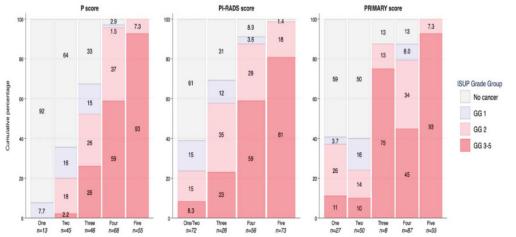
https://doi.org/10.1097/JU.0000000000004010

Combining MRI <u>P</u>I-RADS and <u>P</u>SMA-PET/CT <u>P</u>RIMARY score in a composite (P) score for more accurate diagnosis of clinically significant <u>P</u>rostate cancer.

Why This Study?

The MRI PI-RADS score is standard of care for clinically significant prostate cancer (csPCa) diagnosis. The PRIMARY-score (PSMA-PET/CT) also has high diagnostic accuracy for csPCa. This study aimed to develop a combined (P) score for csPCa detection (ISUP ≥ 2) incorporating separately read PI-RADS and PRIMARY scores, with external validation.

	PI-RADS			
PRIMARY	1/2	3	4	5
1			3	3
2	2		3	3
3	3			
4	3			
5	5	5	5	5



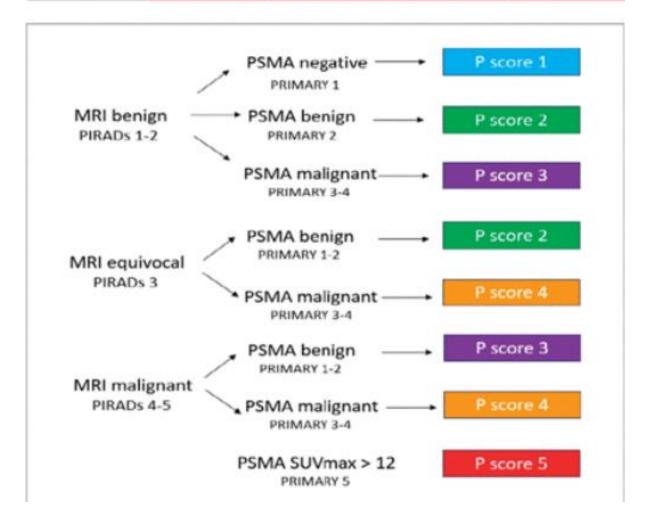
P Score	Sensitivity	NPV	
ISUP 2	94%	85%	
ISUP 3	99%	98%	

CONCLUSION:

The P-score improves accuracy for csPCa over both PI-RADS and PRIMARY scores. It should be considered when PSMA-PET is undertaken for diagnosis.

P SCORE

PRIMARY	PI-RADS			
	1/2	3	4	5
1	1	2	3	3
2	2	2	3	3
3	3	4	4	4
4	3			
5	5	5	5	5



P SCORE

P Score 1-5 \rightarrow 0%, 20%, 52%, 96% and 100% for csPCa

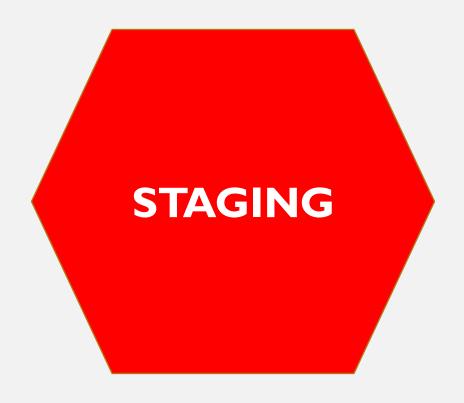
AUC for P score 0.93 > PI-RADS 0.89 and Primary score 0.84

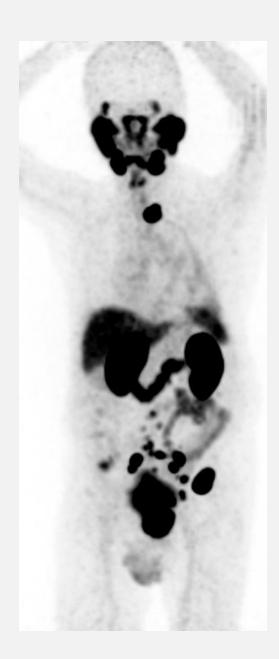
Splitting scores at 1/2 (negative) and 3/4/5 (positive): P score sensitivity 94% vs PI-RADS 89% and Primary score 86%

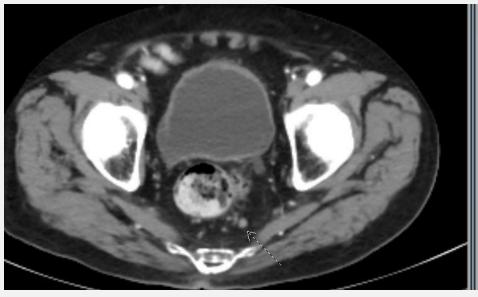
For ISUP >= 3, P score sensitivity 99% vs PIRADS 94% and Primary score 92%

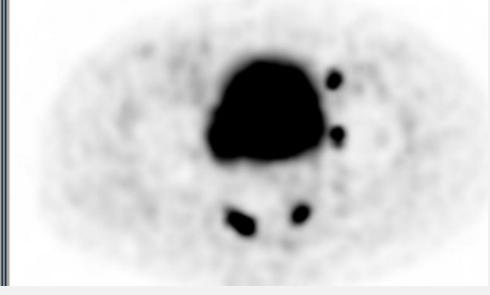
An SUV max > 12 (P score 5) ISUP >= 2 in all cases with 93% ISUP >= 3

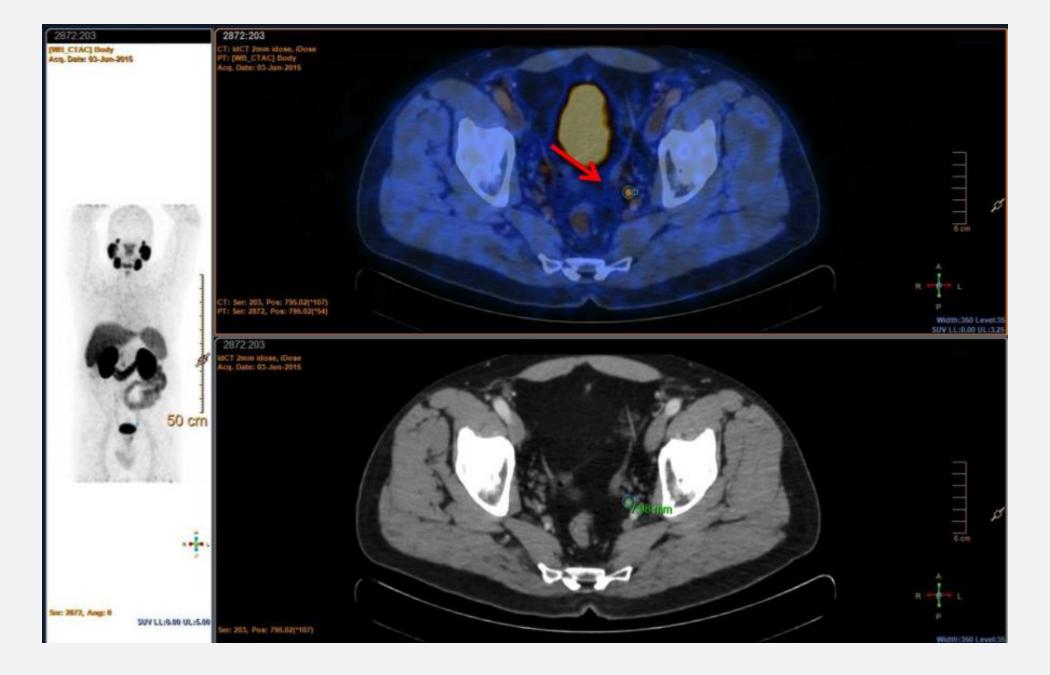
P score is easily calculated and improves csPCa dectection over both Pl-RADS and Primary scores. It should be considered when PSMA PET is undertaken for diagnosis.











Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study

Prof Michael S Hofman, MBBS 🔌 🖾 • Nathan Lawrentschuk, MBBS • Roslyn J Francis, MBBS • Colin Tang, MBBS •



Multicentre, two-arm, randomised study, 302 men with biopsy-proven prostate cancer and high-risk features



PSMA PET-CT is a suitable replacement for conventional imaging, providing superior accuracy!

	CT + Bone Scan	PSMA PET/CT
Accuracy	65% [60–69];p<0·0001	92% [88–95] ; p<0 0001
Sensitivity	38% [24–52]	85% [74–96]
Specificity	91% [85–97]	98% [95–100]
Pelvic nodal metastases	59%	91%
Distant metastases	74%	95%
Equivocal findings	23% [17–31]	7% [4–13]
First line imaging management change	15% [10–22];p=0.008	28% [21–36]; _p =0 ·008
Second line imaging management change	5%	27%
Radiation	19·2 mSv; p<0·001	8 ·4 mSv; p<0 ·00 I



Full Paper

⁶⁸Ga-HBEDD PSMA-11 PET/CT staging prior to radical prostatectomy in prostate cancer patients: Diagnostic and predictive value for the biochemical response to surgery

Rohan Nandurkar, ¹, Pimmeke van leeuwen, MD, PhD^{2,3}, Phillip Stricker, MBBS, FRACS^{2,4}, Henry Woo, DMedSc, FRACS, MBBS⁵, Rajdeep Kooner, MBBS, FRACS⁴, Carlo Yuen, MBBS, FRACS⁴, Gordon O'Neill, MBBS, FRACS⁴, David Ende, MBBS, PhD, FRACS⁴, Thomas Cusick, BMedSci, MRes², Bao Ho, MBBS⁶, Adam Hickey, BSci⁶ and Louise emmett, MBChB, MD, FRACP^{2,6}

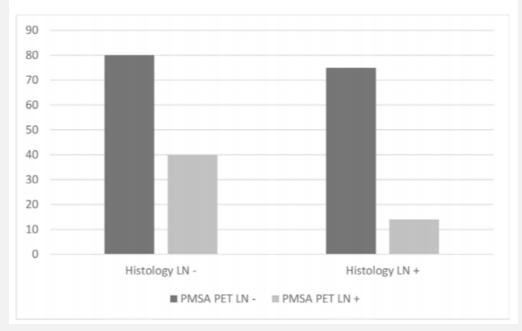
142 males, staging PSMA prior RP. SR (surgical response = PSA<0.03)

- 97.9% +ve intra-prostatic disease on PSMA → 82.9% SR
- 14.1% +ve extra-prostatic disease on PSMA → 28.6% SR
- PSMA superior in predictive value for SR than Gleason score, preop PSA or pT stage.

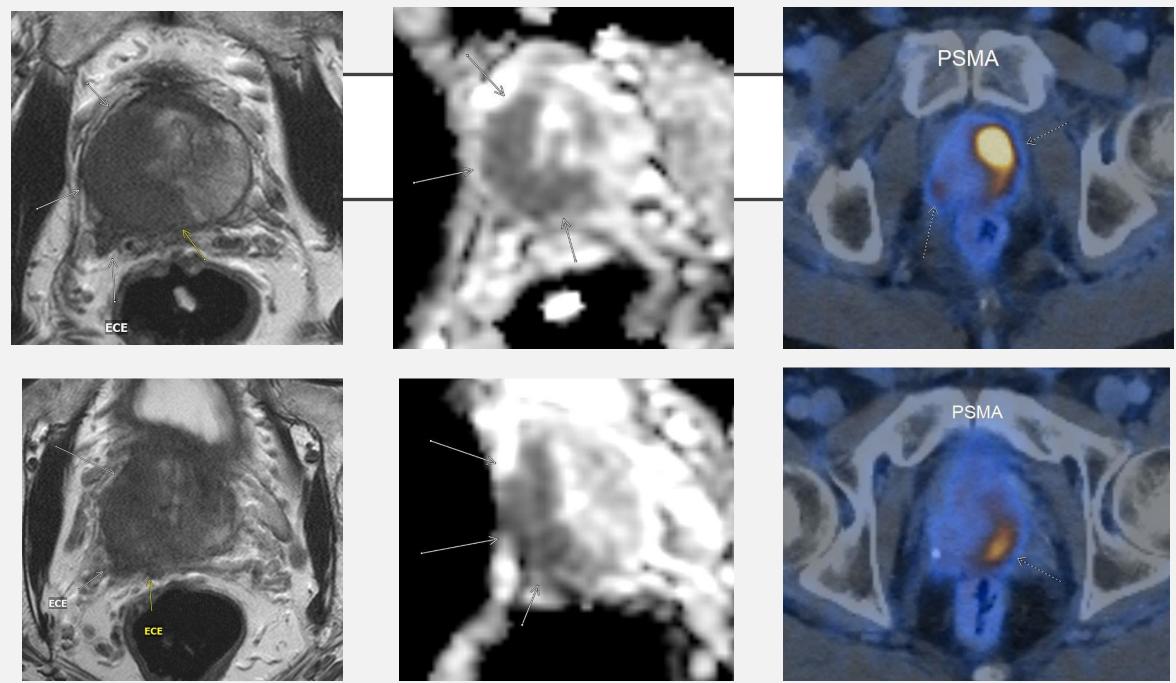
Extra-prostatic disease on staging pre-operative PSMA PET is independently predictive of a poor surgical response to RP

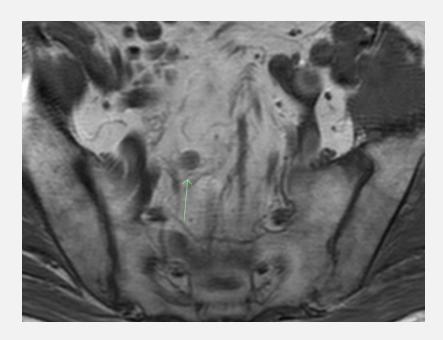
 \rightarrow need for a multimodality treatment approach.

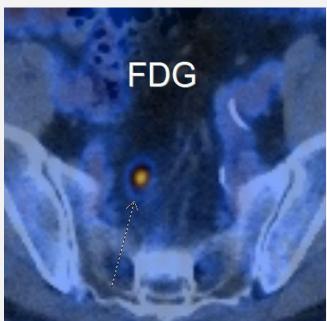
Figure 1. Comparison of PSMA PET positivity and histology positivity for pelvic lymph nodes and associated SR rates. LN,lymph nodal; PET,positron emission tomography; PSMA, prostate-specificmembrane antigen.

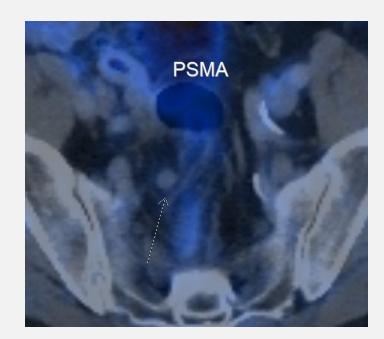


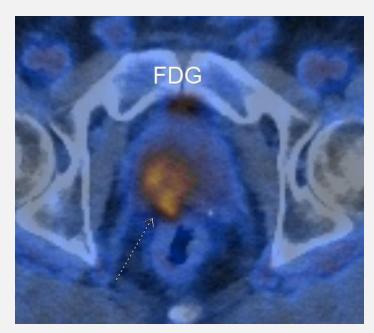
Images provided courtesy of St Vincent's Public Hospital, Sydney



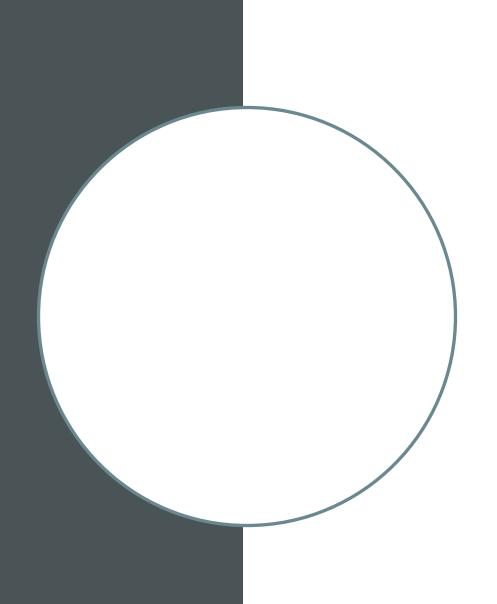








BIOCHEMICAL RECURRENCE



Salvage Radiotherapy treatment (SRT) to prostatic fossa +/pelvic nodes is the only potential curative Rx option in BCR
setting

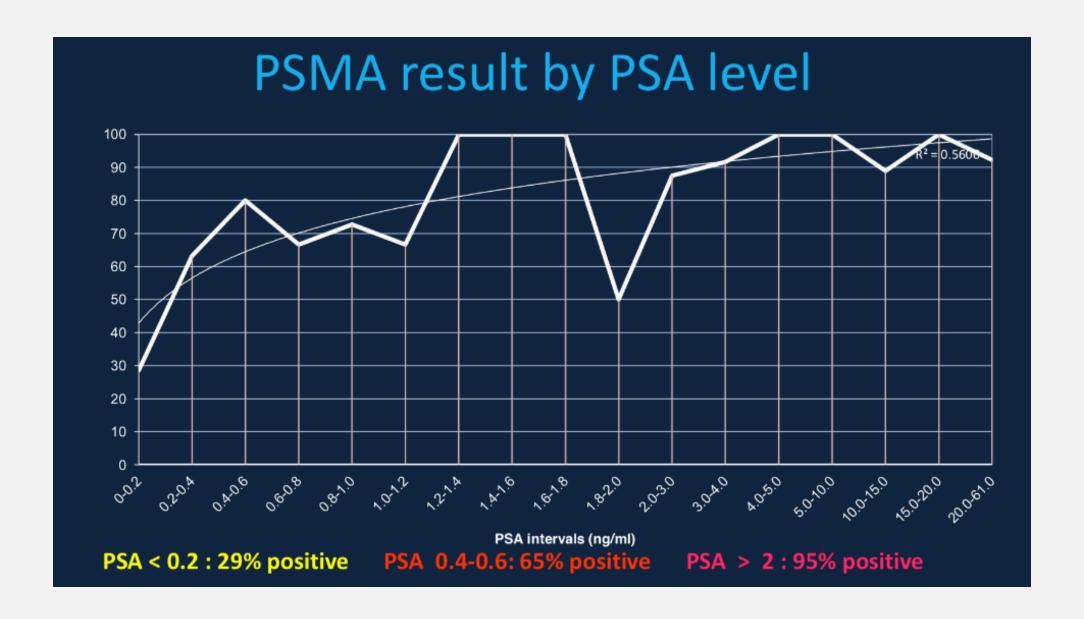
- 5-yr progression-free survival rate post SRT 56% (71% in pre-RT PSA <0.2 to 18% with PSA > 1.5) without ADT.
 - Low volume recurrent PC benefit the MOST from SRT

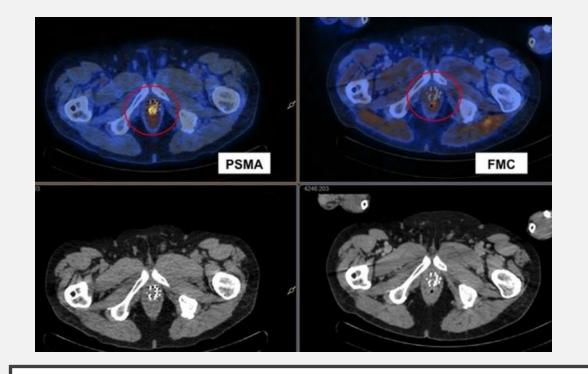
Prospective Comparison of ¹⁸F-Fluoromethylcholine Versus ⁶⁸Ga-PSMA PET/CT in Prostate Cancer Patients Who Have Rising PSA After Curative Treatment and Are Being Considered for Targeted Therapy

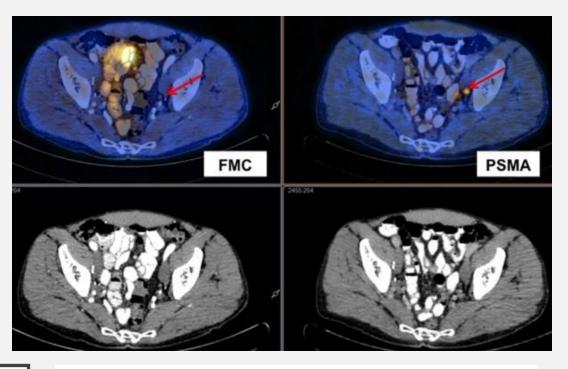
Joshua J. Morigi^{1,2}, Phillip D. Stricker^{3,4}, Pim J. van Leeuwen^{3,4}, Reuben Tang^{1,5}, Bao Ho¹, Quoc Nguyen^{3,4}, George Hruby⁶, Gerald Fogarty³, Raj Jagavkar³, Andrew Kneebone⁶, Adam Hickey¹, Stefano Fanti², Lisa Tarlinton¹, and Louise Emmett^{1,5}

 Prospectively compare the detection rates and management impact of 68-Ga-PSMA PET/CT vs 18Ffluoromethylcholine PET/CT in setting of low but detectable PSA relapse after curative treatment, being considered for targeted therapy.

PSA level (ng/mL)	Choline	PSMA	\boldsymbol{P}
<0.5	12.5% (2/16)	50% (8/16)	0.03
0.5-2.0	36% (5/14)	71% (10/14)	0.02
>2.0	63% (5/8)	88% (7/8)	0.18
Total	32% (12/38)	66% (25/38)	<0.001

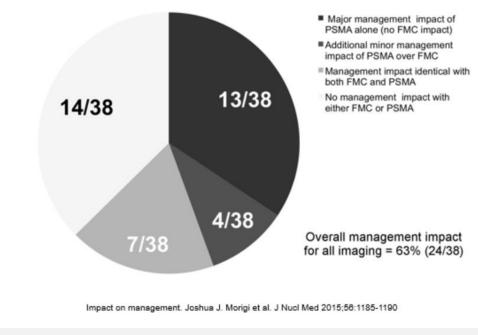






68GA-PSMA PET/CT: SIGNIFICANTLY
HIGHER DETECTION RATE & HAD AN
IMPACT ON MANAGEMENT IN MANY
PATIENTS.

J Nucl Med. 2015 Aug;56(8):1185-90.



Prospective, Multisite, International Comparison of ¹⁸F-Fluoromethylcholine PET/CT, Multiparametric MRI, and ⁶⁸Ga-HBED-CC PSMA-11 PET/CT in Men with High-Risk Features and Biochemical Failure After Radical Prostatectomy: Clinical Performance and Patient Outcomes.

Emmett L1, Metser U2, Bauman G3, Hicks RJ4, Weickhardt A5, Davis ID6, Punwani S7, Pond G8, Chua S9, Ho B1, Johnston E7, Pouliot F10, Scott AM5.

- Prospective multisite international (Australia, Canada and UK)
- Rising PSA post RP, high risk features, negative/equivocal conventional imaging
- 18F-FCH (91/91), Pelvic MRI (88/91), PSMA (31/91-Australia): all imaging performed within 2 wks
- Positive disease → SRT. Treatment response to SRT = reduction of PSA >50% without ADT

Detection	Pelvic MRI	Choline	PSMA
Recurrence	28% (25/88)	32% (29/91)	42% (13/31)

Detection	Pelvic MRI	Choline	PSMA
PF	21.5%	13%	19%
Extra-PF	8%	19%	32%

	Pelvis MRI	Choline	PSMA
Change in Management	24%	46%	Additional 23% over Choline

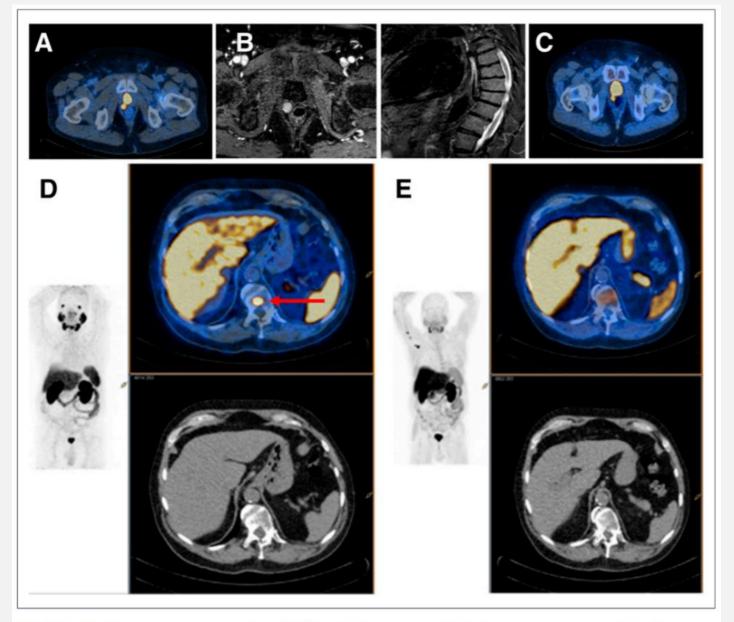


FIGURE 2. Man with a rising PSA (0.29 ng/mL) 5 y after RP. Imaging demonstrates PF recurrence on PSMA (A), MRI (B), and ¹⁸F-FCH (C). Solitary PSMA-avid (D), ¹⁸F-FCH (E) and MRI-negative focus in thoracic spine (red arrow) was confirmed as true-positive (repeat imaging and targeted treatment response).

Treatment Outcomes from ⁶⁸Ga-PSMA PET/CT—Informed Salvage Radiation Treatment in Men with Rising PSA After Radical Prostatectomy: Prognostic Value of a Negative PSMA PET

Louise Emmett, Pim J. van Leeuwen, Rohan Nandurkar, Matthijs J. Scheltema, Thomas Cusick, George Hruby, Andrew Kneebone, Thomas Eade, Gerald Fogarty, Raj Jagavkar, Quoc Nguyen, Bao Ho, Anthony M. Joshua and Phillip Stricker

Journal of Nuclear Medicine December 2017, 58 (12) 1972-1976; DOI: https://doi.org/10.2967/jnumed.117.196683

PSMA PET:

- independently predictive of a treatment response to SRT
- stratifies men into a high treatment response to SRT (negative or fossa-confined PSMA PET) vs men with a poor response to SRT (nodes or distant disease on PSMA PET).
- A negative PSMA PET predicts a high response to salvage fossa radiotherapy!

Comparison of Clinical Variables Between Men with Treatment Response to SRT and Men Who Did Not Have PSA Response to SRT					
Variable	All patients	Treatment response to SRT	No Treatment response to SRT	P	
PSA at PSMA PET	0.28 ± 0.19	0.24 ± 0.15	0.35 ± 0.25	0.01	
PSMA PET result					
Negative/local	63/99	52/63	11/63	0.002	
Lymph nodes/distant	36/99	19/36	17/36		
pT stage at RP					
T2	27	19/27	8/27	NS	
T3	65	47/65	18/65		
Gleason score					
6–7	72	53/72	19/72	NS	
8–9	27	18/27	9/27		
Surgical margins					
Positive	35	25/35	10/35	NS	
Negative	58	42/58	16/58		
Radiation therapy					
Fossa alone	49	38/49	11/49	0.007	
Fossa + nodes	44	32/44	12/44		
Distant SBRT	6	1/6	5/6		

3-Year Freedom from Progression After ⁶⁸Ga-PSMA PET/CT—Triaged Management in Men with Biochemical Recurrence After Radical Prostatectomy: Results of a Prospective Multicenter Trial

Louise Emmett, Reuben Tang, Rohan Nandurkar, George Hruby, Paul Roach, Jo Anne Watts, Thomas Cusick, Andrew Kneebone, Bao Ho, Lyn Chan, Pim J. van Leeuwen, Matthijs J. Scheltema, Andrew Nguyen, Charlotte Yin, Andrew Scott, Colin Tang, Michael McCarthy, Karen Fullard, Matthew Roberts, Roslyn Francis and Phillip Stricker Journal of Nuclear Medicine June 2020, 61 (6) 866-872; DOI: https://doi.org/10.2967/jnumed.119.235028

Could PSMA PET/CT findings impact long term outcome?

260 pts – 38 months follow up

PSMA highly predictive of FFP at 3 yrs following SBRT for BCR

 81% in negative/PF only disease vs 45% in extra-PF disease (p<0.0001)

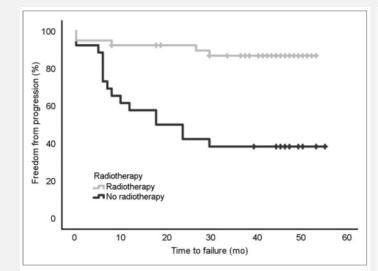


FIGURE 3. FFP in men with negative scan results who underwent sRT vs. men who were observed over 3 y (P < 0.0001).

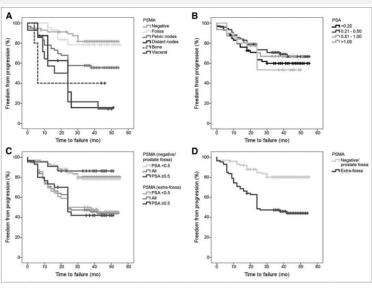
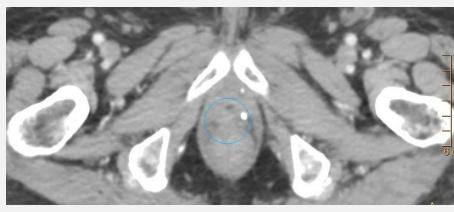
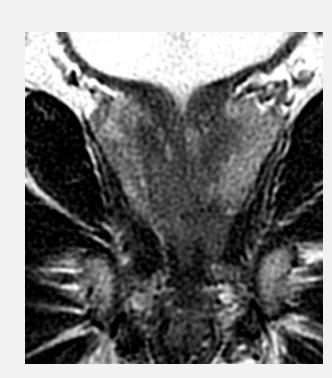


FIGURE 2. Kaplan-Meier curves for FFP based on PSMA PET (A), PSA (ng/mL) at PSMA PET (B), PSMA PET (negative/fossa-confined vs. outside fossa) stratified for both PSA and PSMA PET (C), and PSMA PET (negative/fossa-confined vs. outside fossa) (D).

VESICOURETHRAL ANASTOMOSIS

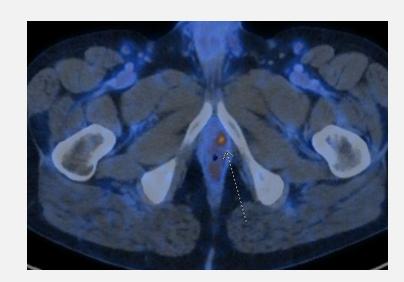


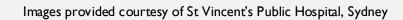








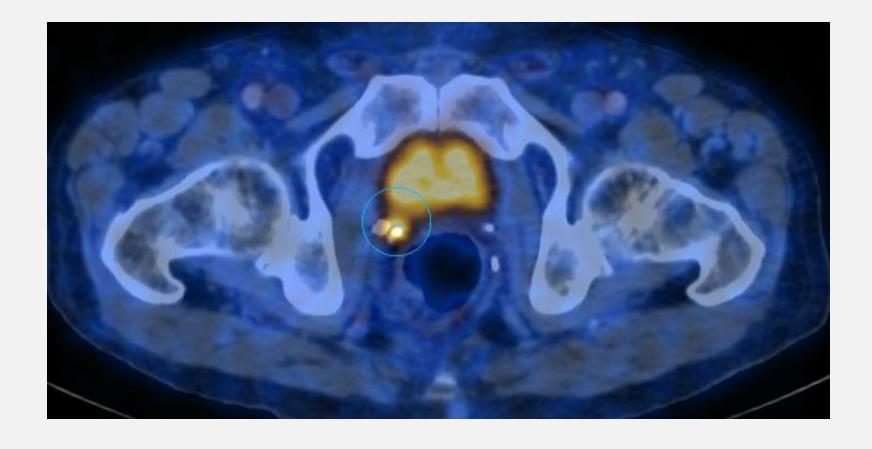


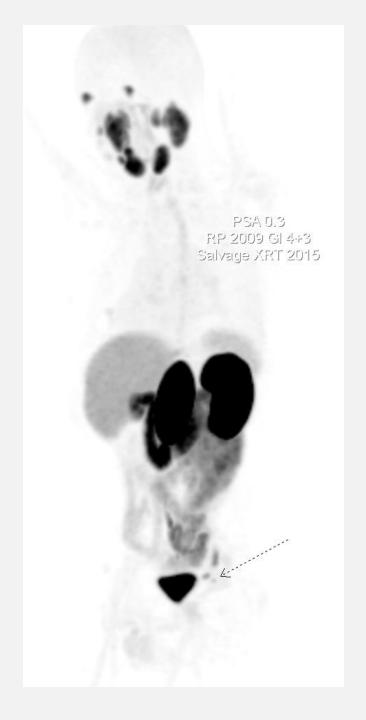


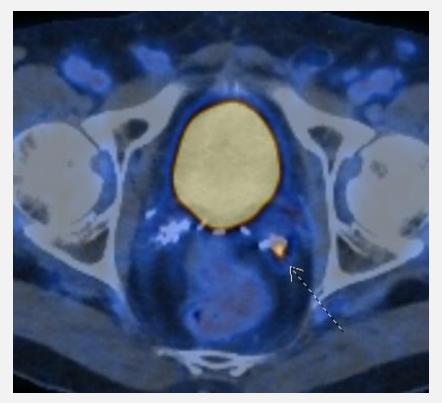


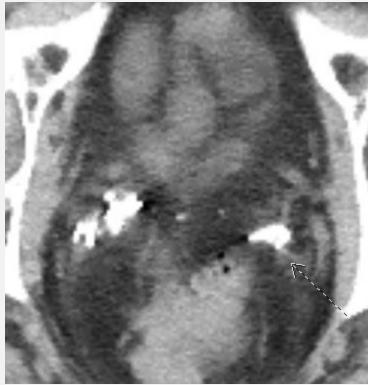


SEMINAL VESICLE BEDS

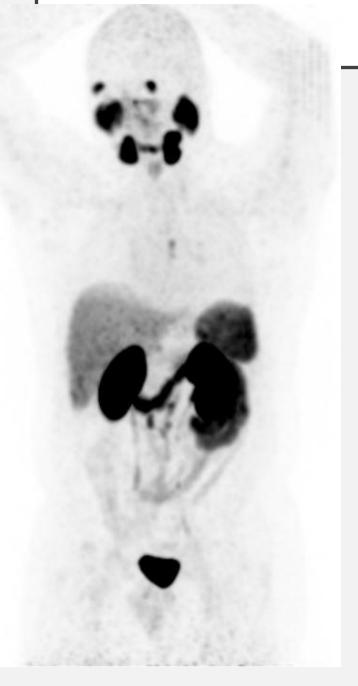


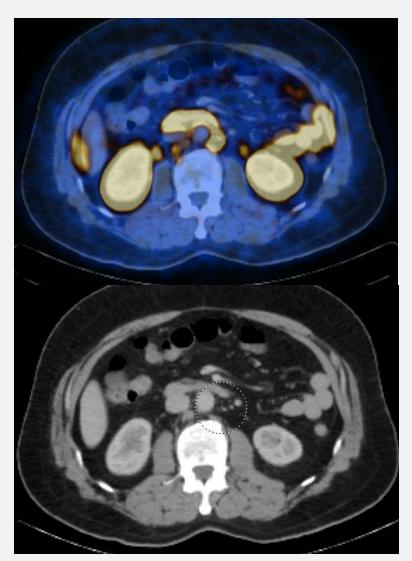


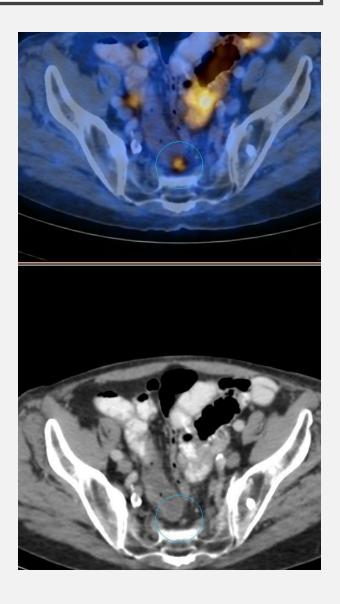




SMALL LYMPH NODES

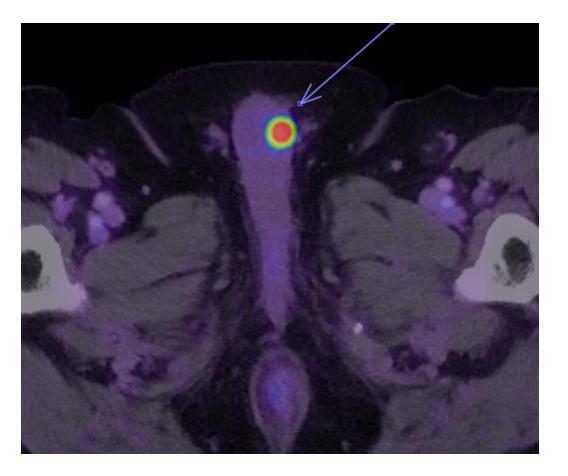




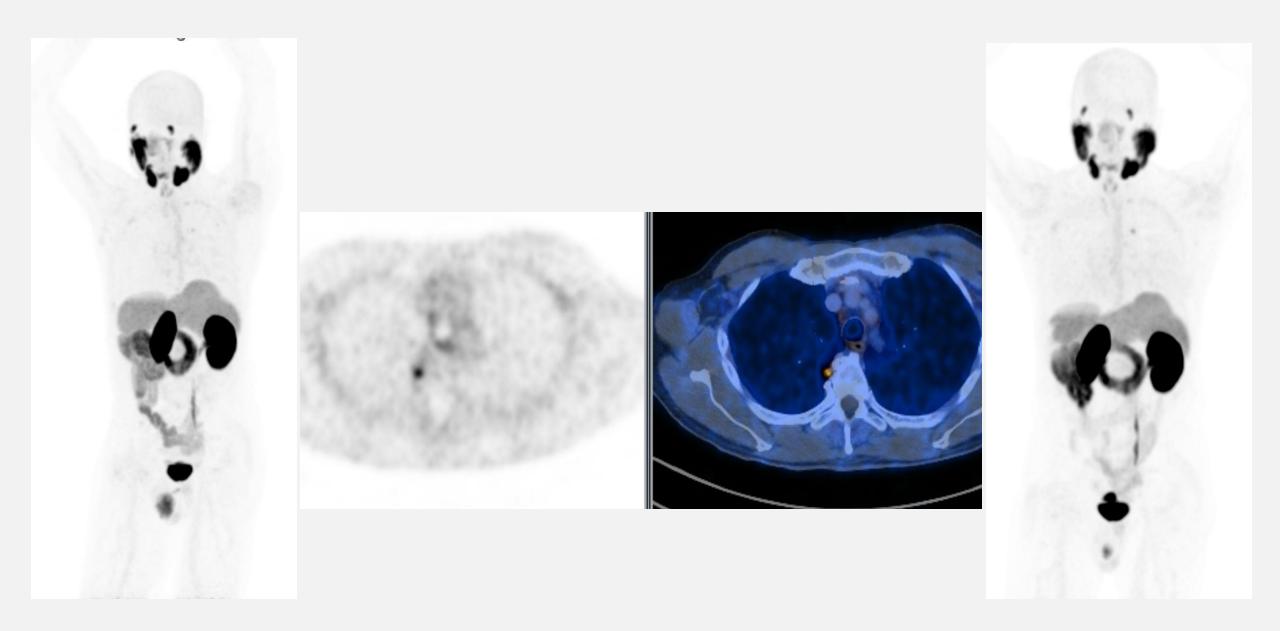


Images provided courtesy of St Vincent's Public Hospital, Sydney





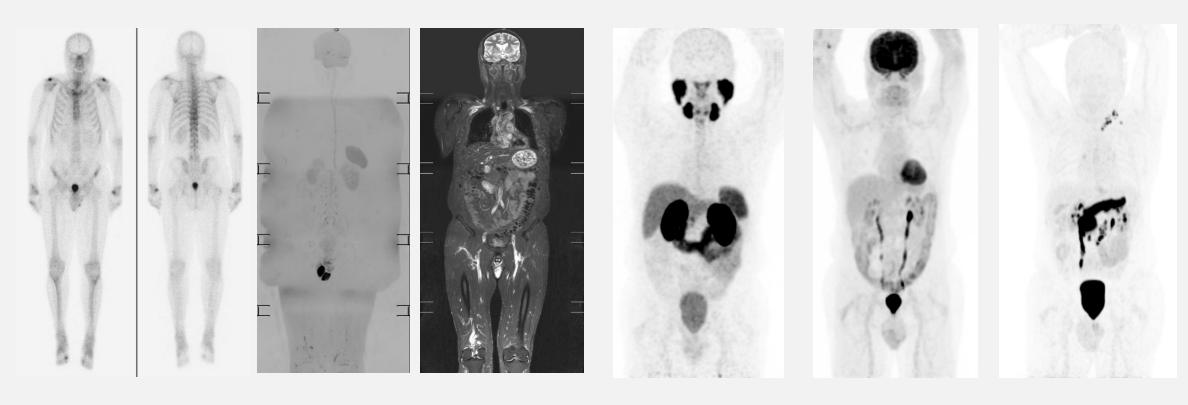
PENILE URETHRAL RECURRENCE PSA 0.27



Images provided courtesy of St Vincent's Public Hospital, Sydney

WHAT ABOUT BCR IN THE SETTING OF NEGATIVE SERIAL PSMA PET ??

- Gastrin-releasing peptide receptor (GRPR) is overexpressed in prostate cancer, particularly in well-differentiated lower grade carcinomas in contrast to the absence or low receptor density in non-neoplastic prostatic tissue including benign hyperplastic prostate.
- Significant inverse correlations GRPR vs increasing Gleason score/ PSA value / tumour size
- Bombesin (BBN) is a 14-amino-acid amphibian homolog of the mammalian gastrin-releasing peptide.
 - Bombesin can be radiolabelled with isotopes of copper for both diagnostic and therapeutic purposes with the use of different chelators such as SarAR, forming compounds such as 64 Cu-SAR-BBN.
 - Dual potential in diagnosis and therapy application



Specimen:

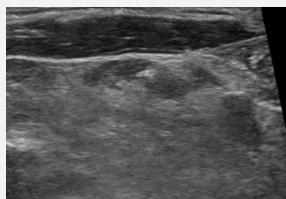
1. FNA Left Cervical Lymph Node

Clinical Information:

L cervical (supraclav.) node FNA. Cu64 PET positive PSMA FDG PET negative. Increased PSA $\,$

DIAGNOSTIC SUMMARY:

FNA Left Cervical Lymph Node: Malignant; metastatic acinar adenocarcinoma in keeping with prostate origin



Images provided courtesy of St Vincent's Public Hospital, Sydney



NEW TECHNOLOGIES



NEW GENERATION OF PET SCANNERS

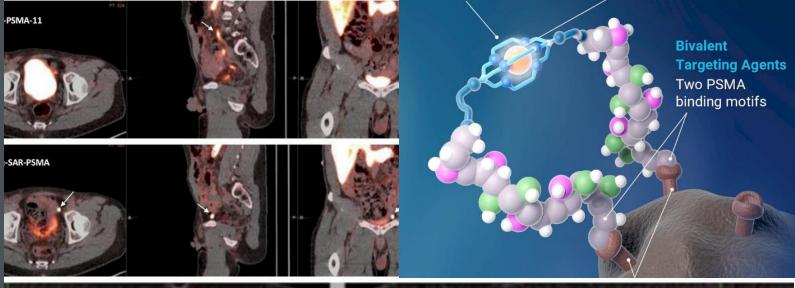
Digital PET technology vs Analog PET system:

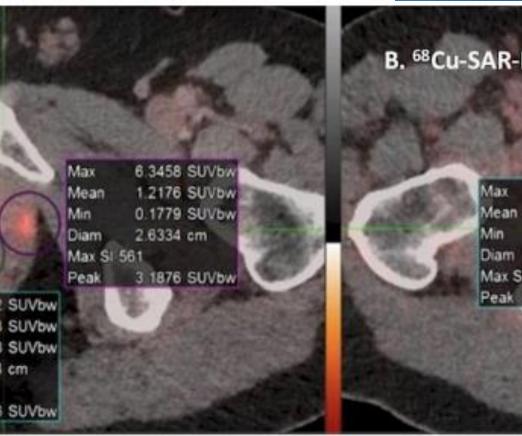
- Digital photon-counting technique
- Shorter scan time
- Reducing the patient's radiation dose
- Higher image quality
- Detect even smaller lesions

64CU-SAR-BISPSMA

• 64Cu-SAR-bisPSMA:

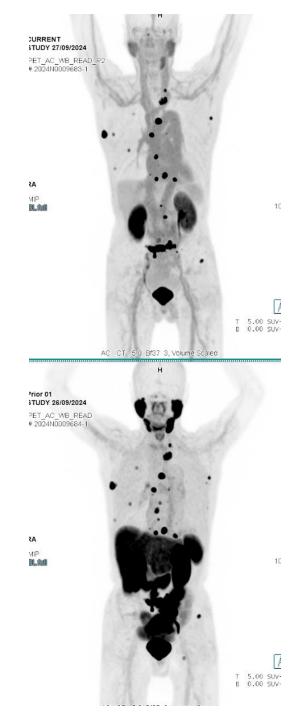
- The targeting moiety having two PSMAtargeting functional groups → increased tumor uptake and retention
- Copper-64 isotope has a longer half-life of 12.7 hours, longer shelf-life, greater flexibility for patient scheduling, and the ability to image at later time points, which has previously been shown to detect additional lesions
- ⁶⁴Cu has a shorter positron range (0.56 mm), leading to improved scan resolution
- Safe and effective.
- Detect a greater number of lesions with higher uptake when compared to ⁶⁸Ga-PSMA-11







GA68 PSMA R2



THANK YOU FOR YOUR ATTENTION!





New Diagnostic Imaging Medicare Benefits Schedule (MBS) items 61563 and 61564

Last updated: 18 March 2022

- From 1 July 2022, two new items will be introduced for prostate-specific membrane antigen (PSMA) positron
 emission tomography (PET) study for patients with prostate cancer.
- These items will allow for a PSMA PET study for the initial staging of intermediate to high-risk patients with prostate cancer and for the restaging of patients with recurrent prostate cancer.
- These items will assist patients with prostate cancer to receive the most appropriate treatment pathway.

What are the changes?

In the 2021-22 Budget the Government announced that from 1 July 2022 two new PSMA PET scans for patients with prostate cancer will commence:

Item 61563

- Whole body PSMA PET study performed for the initial staging of intermediate to high-risk prostate adenocarcinoma, for a previously untreated patient who is considered suitable for locoregional therapy with curative intent.
- Medicare benefits are payable for a maximum of one service in the patient's lifetime.

Item 61564

- Whole body PSMA PET study performed for the restaging of recurrent prostate adenocarcinoma, for a patient who
 has undergone prior locoregional therapy and is considered suitable for further locoregional therapy to determine
 appropriate therapeutic pathways and timing of treatment initiation.
- This item can be claimed by patients with a prostate specific antigen (PSA) increase of 2ng/ml above the nadir after radiation therapy; or failure of PSA levels to fall to undetectable levels; or rising PSA serum after a radical prostatectomy.
- Medicare benefits are payable for a maximum of two services in the patient's lifetime.

Whole body PSMA PET study items 61563 and 61564 **are not** to be used for surveillance nor for assessment of patients with suspected (as opposed to confirmed) prostate adenocarcinoma or disease recurrence.

Whole body PET studies should be used as an alternative rather than additional to conventional CT scanning. Diagnostic CT items cannot be claimed with a PET item where the purpose of the CT is for attenuation correction or anatomical correlation. CT item 61505 is the correct item to be claimed in these circumstances. Further information is at **Attachment A**.

63541 - item number for DETECTION OF CANCER

The patient is **suspected** of developing prostate cancer:

- a) On the basis of a digital rectal examination; **OR**
- b) In the circumstances mentioned below.
 - For a person **70 years or older**, at least two PSA tests performed within an interval of 1-3 months have a PSA concentration of greater than 5.5 µg/L, and the free/total PSA ratio is less than 25% **OR**
 - For a person **under 70 years**, at least two prostate specific antigen (PSA) tests are performed within an interval of 1-3 months have a PSA concentration of greater than 3.0 ng/ml, and the free/total PSA ratio is less than 25%, or the repeat PSA exceeds 5.5 µg/L **OR**
 - For a person under 70 years, whose risk of developing prostate cancer based on relevant family
 history is at least double the average risk, at least two PSA tests performed within an interval of 1-3
 months have a PSA concentration greater than 2.0 ng/ml, and the free/total PSA ratio is less than
 25%, or the repeat PSA exceeds 5.5 μg/L.
 - Relevant family history is a first degree relative who has or has had prostate cancer or is suspected of carrying a BRCA 1 or BRCA 2 mutation.

Benefits are payable on one occasion only in any 12 month period.

63543 - item number for ACTIVE SURVEILLANCE

The patient is:

- a) Under active surveillance following a confirmed diagnosis of prostate cancer by biopsy histopathology;
 AND
- b) Not undergoing, or planning to undergo, treatment for prostate cancer.

Benefits are payable at the time of diagnosis of prostate cancer, 12 months following diagnosis and then every third year thereafter (or at any time if there is a clinical concern, including PSA progression).

Note: This item is used for **monitoring low risk patients** who have been diagnosed with prostate cancer and who have **not been already treated or are not planning or undergoing treatment**.