What is the value of mpMRI in monitoring men on active surveillance?

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Disclosure

No relevant disclosures

Active Surveillance vs Watchful Waiting

Active Surveillance	Watchful Waiting
increasing acceptance	“small” niche
planned monitoring	passive observation
well defined selection criteria	limited life-expectancy
identification of PCa progression	identification of signs/symptoms
curative intent	palliative intent

Active Surveillance vs Watchful Waiting

Active Surveillance	Watchful Waiting
increasing acceptance	“small” niche
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well defined selection criteria	limited life-expectancy
identification of PCa progression	identification of signs/symptoms
curative intent	palliative intent

Active Surveillance

"… aim to maintain the opportunity of curing more aggressive disease via structured monitoring (eg, with PSA testing and repeat prostate biopsies), which attempts to identify any change in disease risk (eg, an increase in Gleason score) that would merit definitive treatment."

Filson CP, Marks LS, Litwin MS.CA Cancer J Clin. 2015 Jul-Aug;65(4):265-82.

Rationale for AS

- Overdiagnosis (and overtreatment)
  - 25% to 60% of men with PCa
  - (or 200,000 to 500,000 men worldwide)
- Up to 80% of cancers detected in men with PSA < 10 ng/ml are indolent or incidental.

Draisma G. J Natl Cancer Inst. 2003;95(12):868-78
Etzioni R. J Natl Cancer Inst. 2002;94(13):981-90.

Pepe P & Aragona F. Prostate Cancer Prostatic Dis. 2010;13(4):316-9
Eggener SE et al. J Urol. 2009;181(4):1635-41
Klotz L. AUA 2010 Annual Meeting; San Francisco

Annals of Internal Medicine | ORIGINAL RESEARCH

Observation Versus Initial Treatment for Men With Localized, Low-Risk Prostate Cancer

A Cost-Effectiveness Analysis

Julia H. Hayes, MD; Daniel A. Ollendorf, MPH; Steven D. Pearson, MD, MSc; Michael J. Barry, MD; Philip W. Kantoff, MD; Pablo A. Lee, BS; and Pamela M. McMahon, PhD

AS is dominant at age 65 or more.

Definitive Pathology at Radical Prostatectomy Is Commonly Favorable in Men Following Initial Active Surveillance

eau European Association of Urology

Sung Kyu Hong[a,b,*], *Itay A. Sternberg*[a], *Gal E. Keren Paz*[a], *Philip H. Kim*[a], *Karim A. Touijer*[a,c], *Peter T. Scardino*[a,c], *James A. Eastham*[a,c]

[a] *Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA;* [b] *Department of Urology, Seoul National University Bundang Hospital, Seongnam, Korea;* [c] *Department of Urology, Weill Medical College of Cornell University, New York, NY, USA*

Favorable pathology after delayed surgery

Adverse pathology not different after primary or delayed surgery

BJUI BJU INTERNATIONAL

Surgical management after active surveillance for low-risk prostate cancer: pathological outcomes compared with men undergoing immediate treatment

Marc A. Dall'Era*, Janet E. Cowan†, Jeffrey Simko‡, Katsuto Shinohara†, Benjamin Davies§, Badrinath R Konety¶, Maxwell V. Meng†, Nannette Perez†, Kirsten Greene† and Peter R. Carroll†

AS may have slightly lower PCa-specific survival, but with significant benefits in terms of quality of life.

Clinical Cancer Research

Cancer Therapy: Clinical

Prostate Cancer Mortality following Active Surveillance versus Immediate Radical Prostatectomy

Jing Xia[1], Bruce J. Trock[4], Matthew R. Cooperberg[6], Roman Gulati[1], Steven B. Zeliadt[2], John L. Gore[3], Daniel W. Lin[3], Peter R. Carroll[6], H. Ballentine Carter[5], and Ruth Etzioni[1]

AS Inclusion Criteria

- Very low risk to low risk
- Various strategies (PRIAS, UCSF, University of Toronto, and more)

	clinical stage	PSA (ng/ml)	PSA density (ng/ml per g)	Gleason score	# + cores	% single core involvement
PRIAS	T1/T2	≤ 10	≤ 0.2	≤ 6	≤ 2	-
UCSF	T1/T2	≤ 10	-	≤ 6	< 1/3 all cores	≤ 50%
U of T	T1/T2	≤ 15	-	≤ 3+4	≤ 3	≤ 50%

Typical AS Protocol

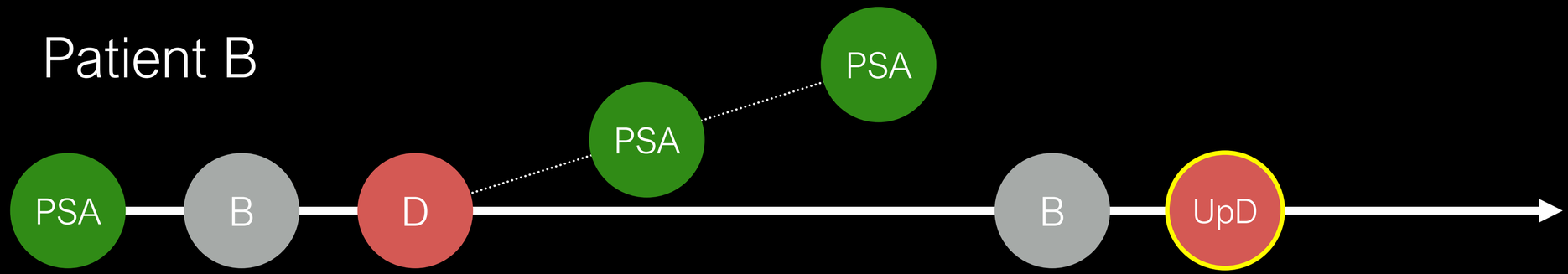
Patient A

TRUS-guided

every 3-6 months

TRUS-guided, per protocol
at 12 to 24 months
every 12-36 months

Patient B



TRUS-guided

TRUS-guided, cause

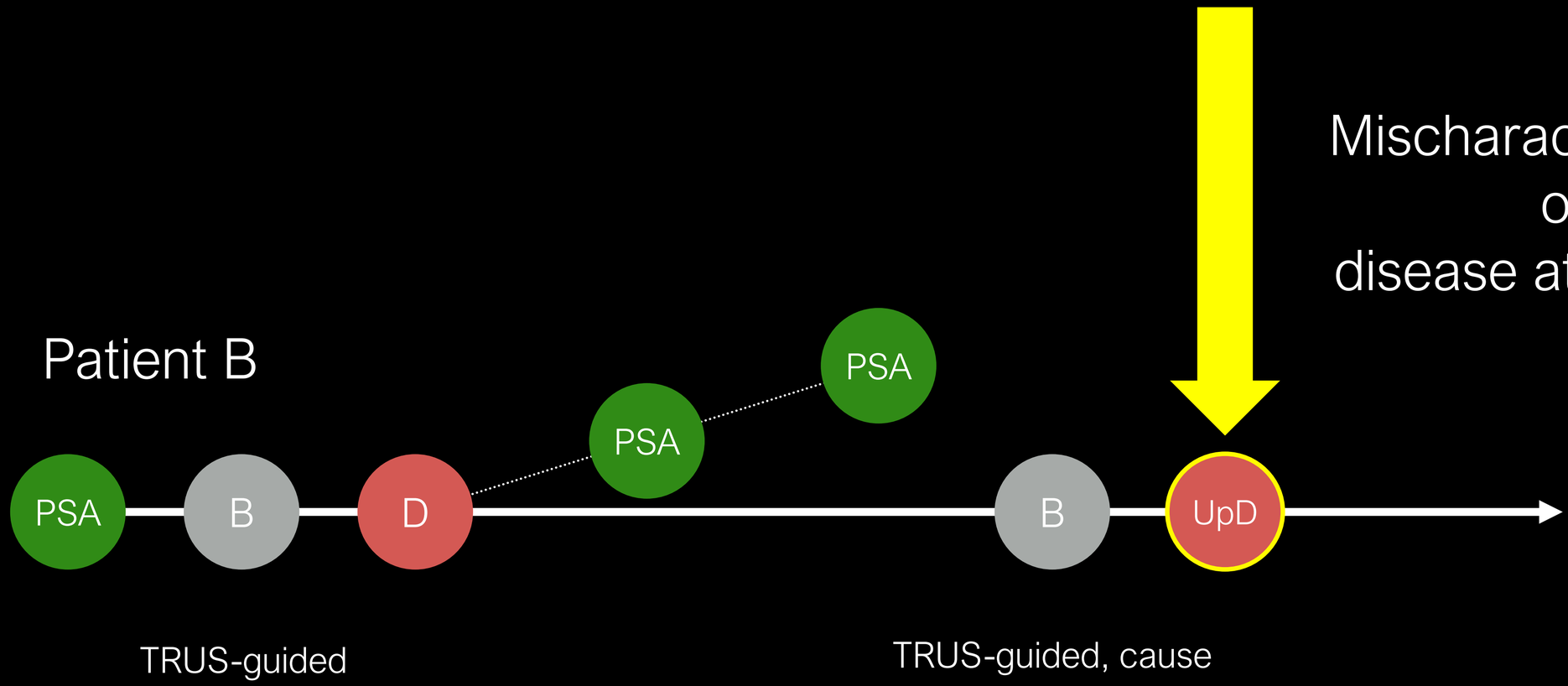
Limitation of AS

15% to 50% of men switch to definitive therapy in 2 years.

75% protocol-based recommendations
10%-15% due to anxiety

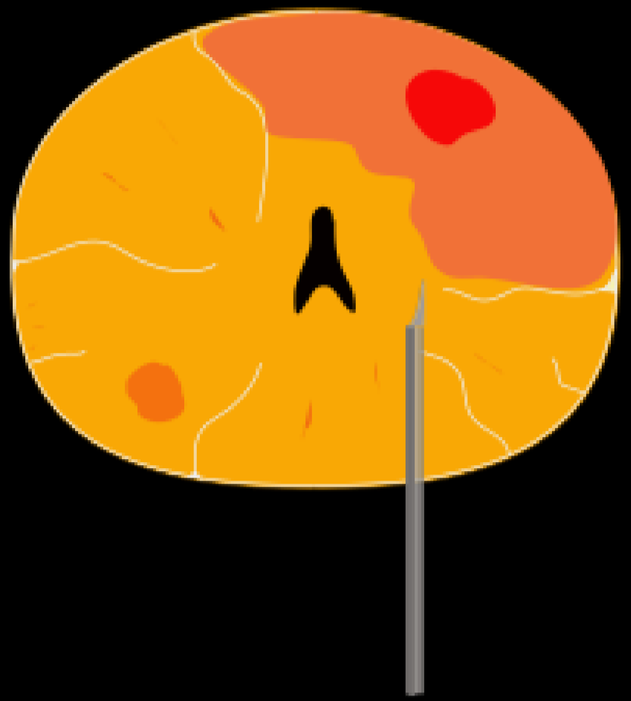
Bul M. Eur Urol. 2012 Aug;62(2):195-200.
Kinsella N. Transl Androl Urol 2018;7(1):83-97
van den Bergh RC. BJU Int. 2010 Apr;105(7):956-62.
Drost FJH. Transl Androl Urol 2018;7(1):98-105

Switch to Definitive Therapy



Limitations of TRUS-guided Biopsy

False-negative result

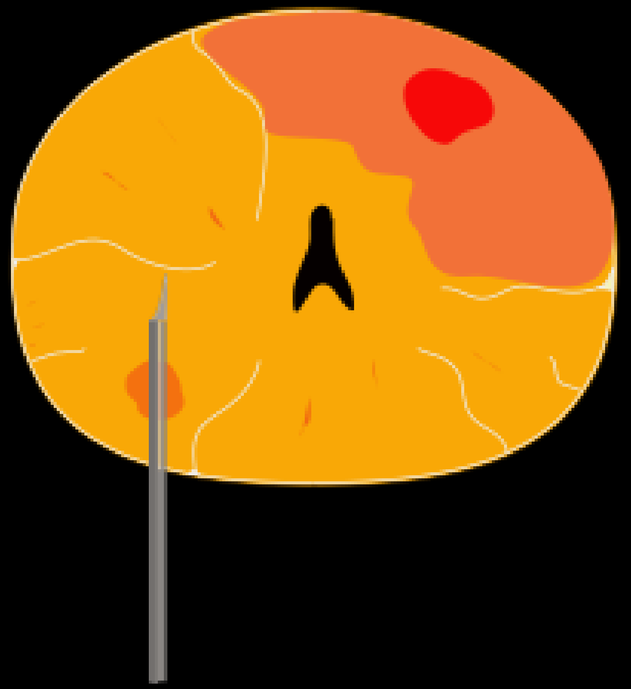


Roehl KA. J Urol. 2002;167(6):2435-9.

Underestimation of
Gleason and volume

Freeland SJ. Urology. 2007;69(3):495-9.

Sampling of
non dominant tumor



Berglund RK. J Urol 2008;180(5):1964-7

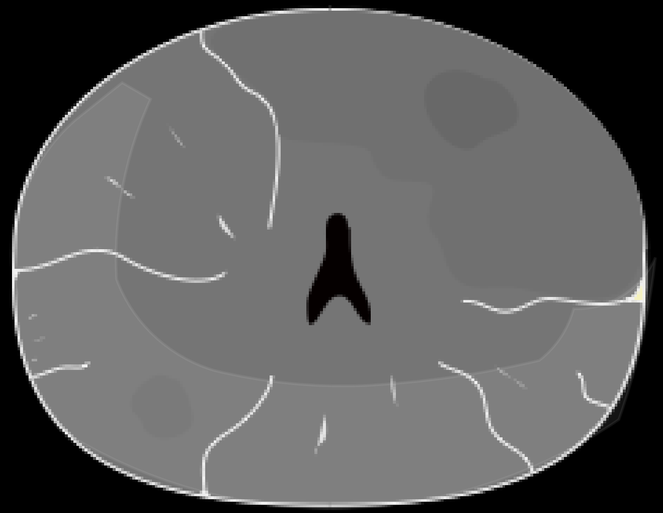
Images courtesy of Jelle O. Barentsz

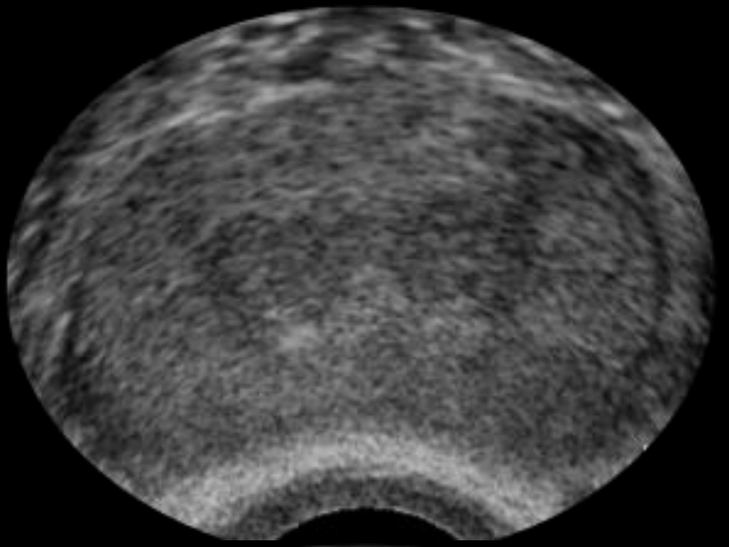
To see better …

… we need MRI glasses!

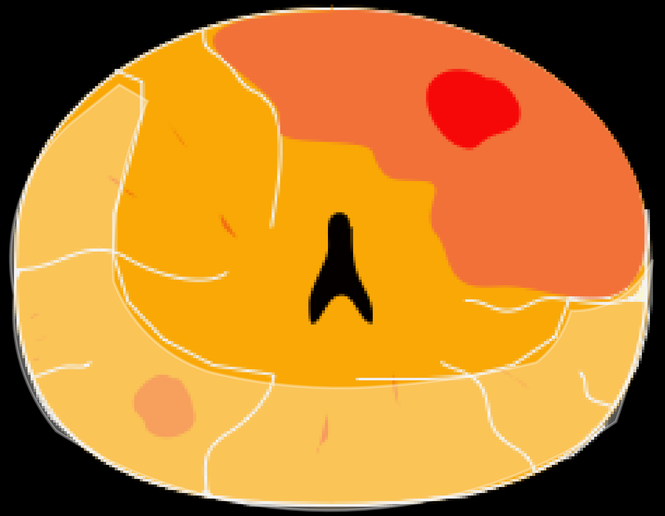
Comparison of TRUS and MRI

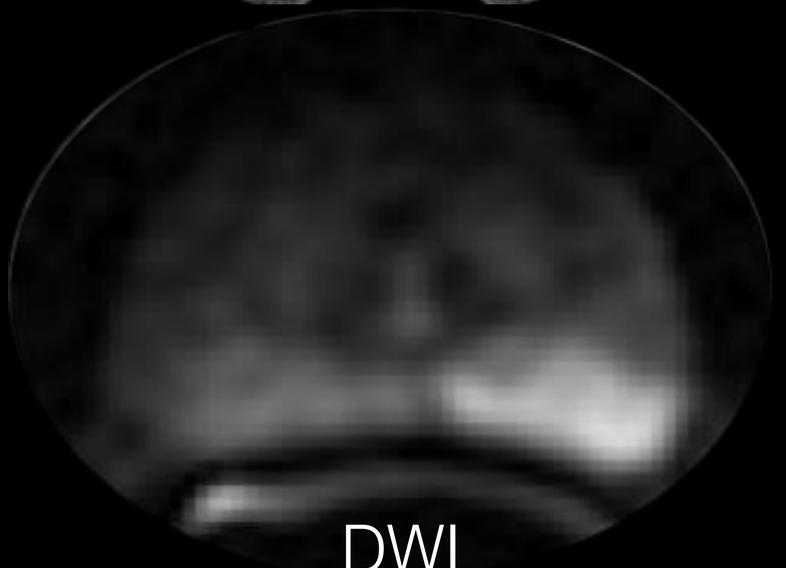
Soft tissue resolution





Functional sequences



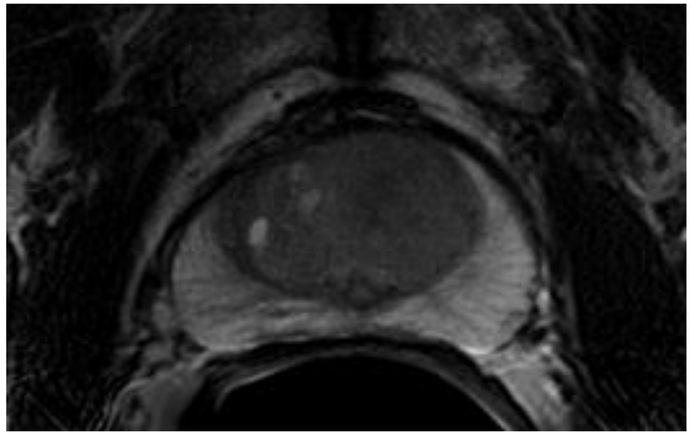


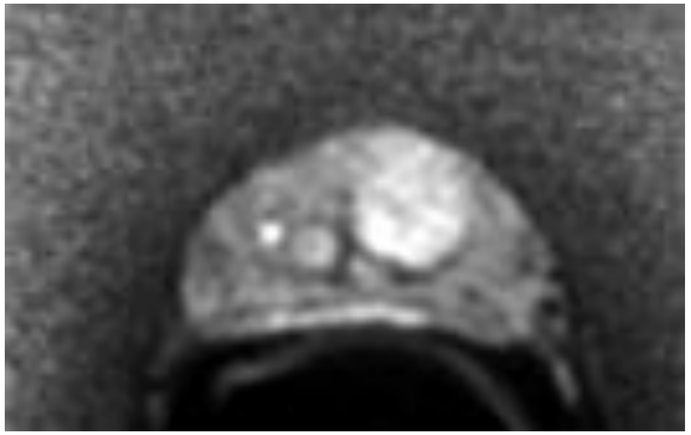
DWI

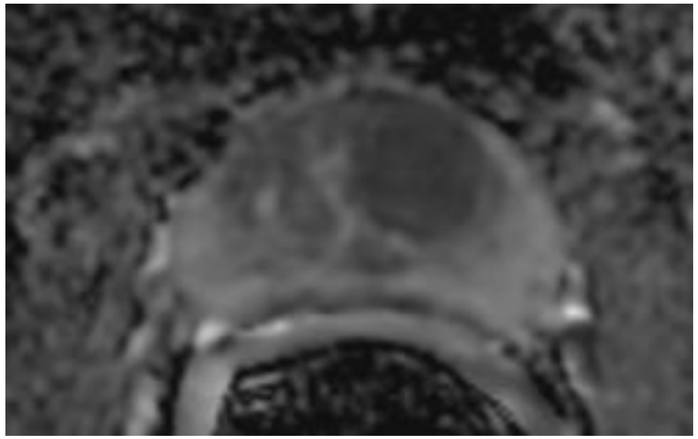
Target the tumor, not the gland

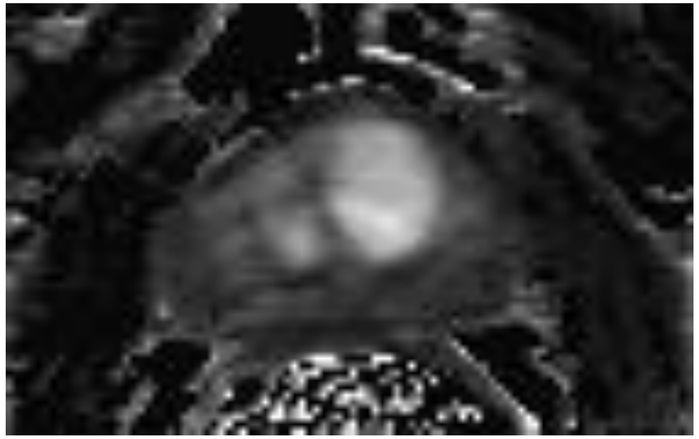
“MRI has now become the investigation of choice for all men with suspected prostate cancer; it has completely radicalized and changed our paradigm.”

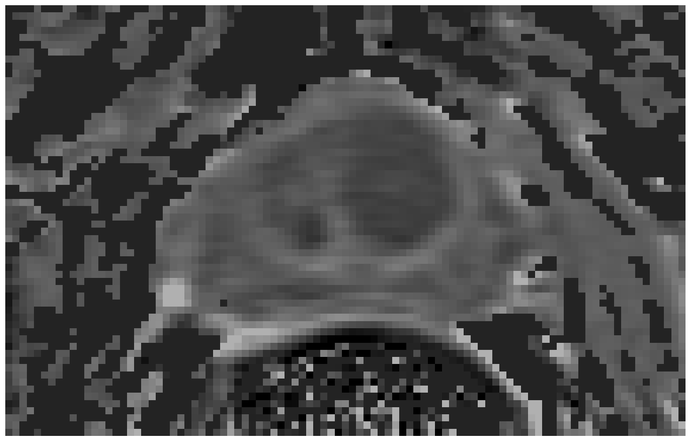
Morgan Pokorny, MD, urologist, Australia

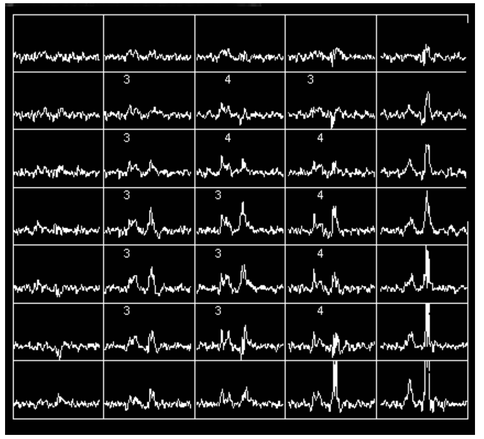








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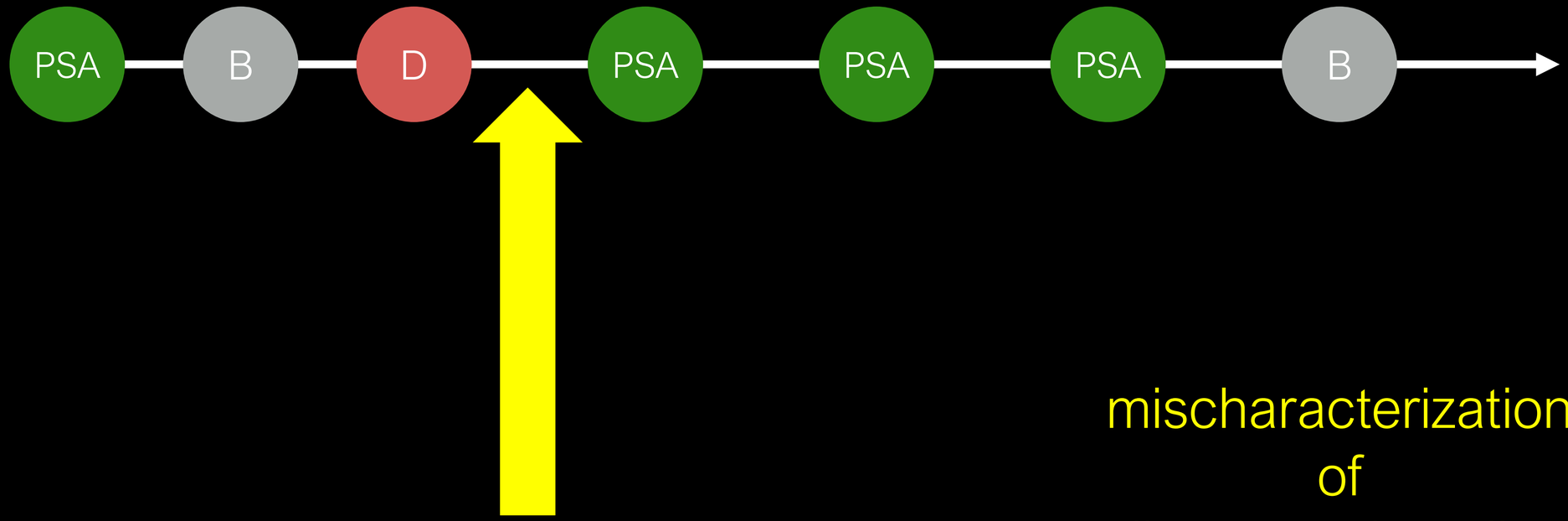
AS Protocol with MRI



confirm candidacy
targeted-biopsy

mischaracterization
of
disease at baseline

Confirmatory Biopsy

- Common practice prior to enrollment
- NCCN, AUA, e SAR recommend MRI after a negative biopsy if PSA continues to raise (diagnosis).
- Why not use MRI to confirm a diagnosis of low-grade PCa, specially if clinical assessment suggests intermediate of high-risk?

Rosenkrantz AB, Verma S, Choyke P, et al. Prostate MRI and MRI-targeted biopsy in patients with a prior negative biopsy: A Consensus Statement by AUA and SAR. J Urol, 2016;196:1613-8.

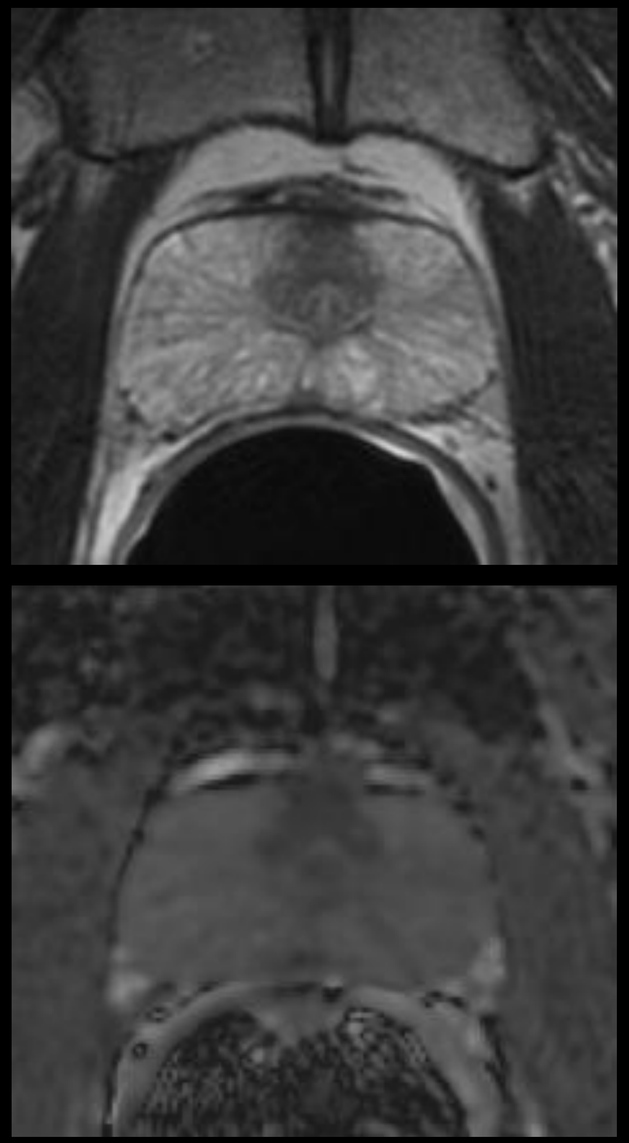
NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer Early Detection. Version 2.2018 — April 5, 2018.

baseline
MRI

Baseline MRI after TRUS-guided biopsy proven PCa
Goal - risk stratification

Patients with negative MRI are unlikely to have clinically significant disease.

NPV 75% - 90%



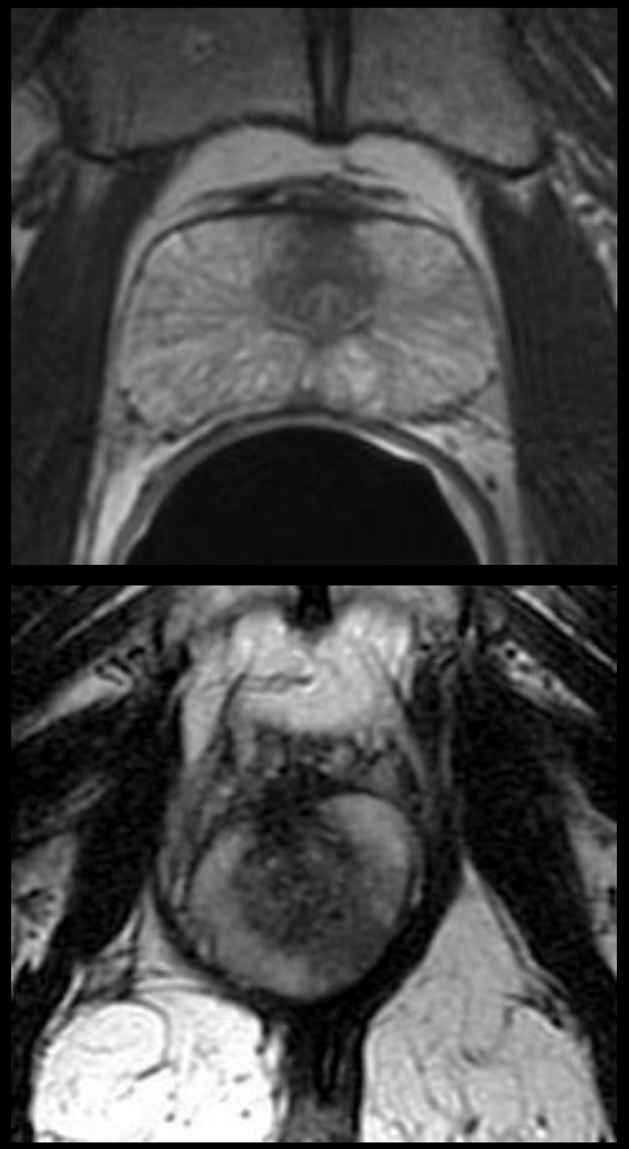
Garcia-Reyes K. J Urol. 2018 Mar;199(3):699-705.
Vargas HA. J Urol. 2012; 188(5): 1732-1738.
Somford DM. J Urol. 2013 Nov;190(5):1728-34.
Itatani R. Eur J Radiol. 2014 Oct;83(10):1740-5.
Petrillo A. J Magn Reson Imaging. 2014;39(5):1206-12.

baseline
MRI

Baseline MRI after TRUS-guided biopsy proven PCa
Goal - risk stratification

Patients with negative MRI are less likely to have clinically significant disease on confirmatory biopsy.

Negative MRI 12% vs positive MRI 35% (RR ≈ 3.0)



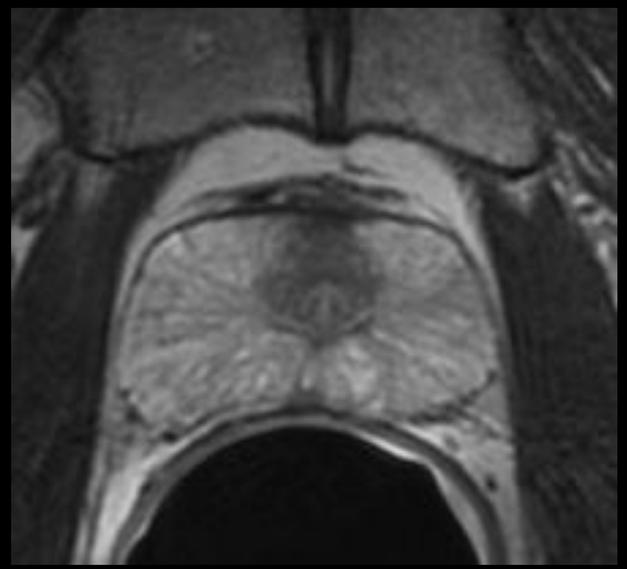
Schoots IG. BJU Int 2018; 122:946–958.

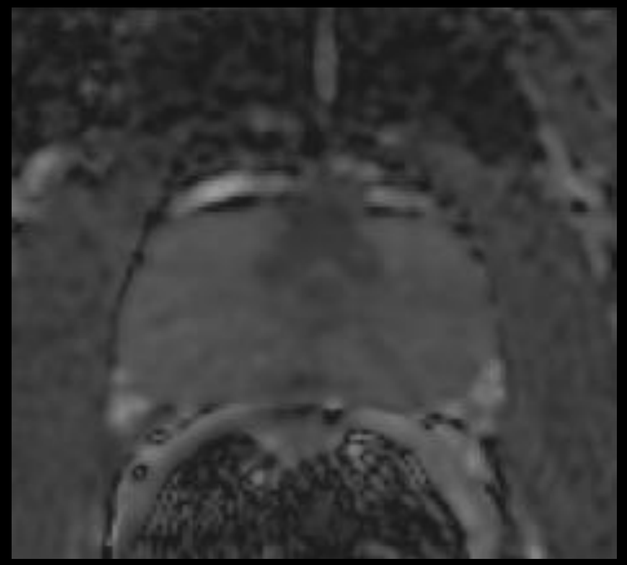
baseline
MRI

Baseline MRI after TRUS-guided biopsy proven PCa
Goal - risk stratification

Negative MRI does not exclude clinically significant disease.

NPV 75% - 90%





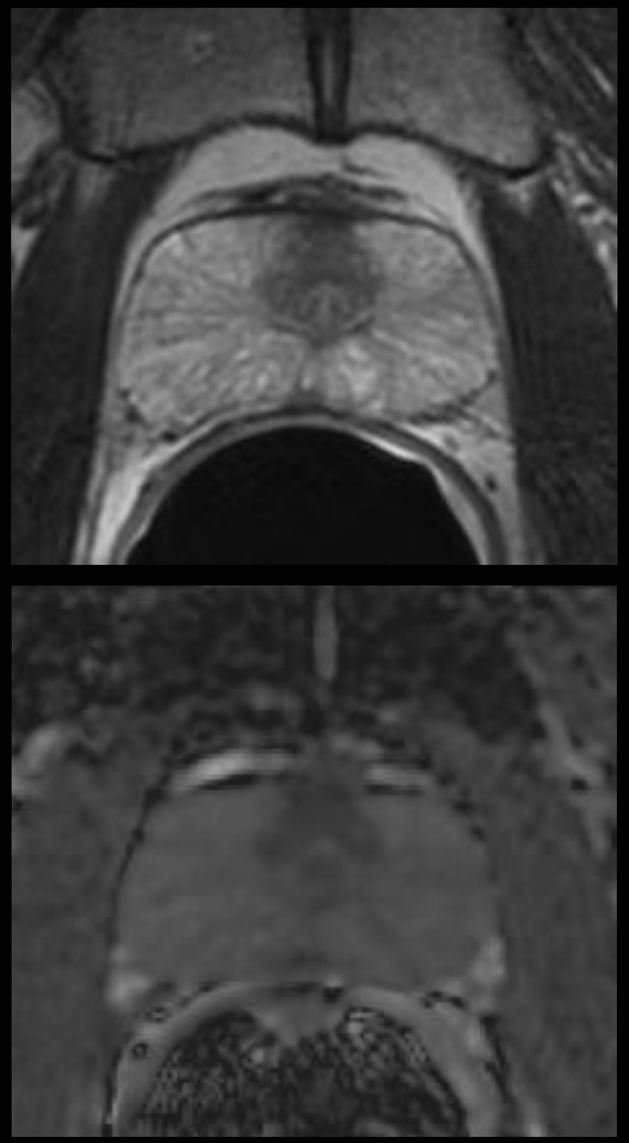
Garcia-Reyes K, Westphalen AC et al. J Urol. 2018 Mar;199(3):699-705.
Vargas HA. J Urol. 2012; 188(5): 1732-1738.
Somford DM. J Urol. 2013 Nov;190(5):1728-34.
Itatani R. Eur J Radiol. 2014 Oct;83(10):1740-5.
Petrillo A. J Magn Reson Imaging. 2014;39(5):1206-12.

baseline
MRI

Baseline MRI after TRUS-guided biopsy proven PCa
Goal - risk stratification

Negative MRI does not exclude clinically significant disease.

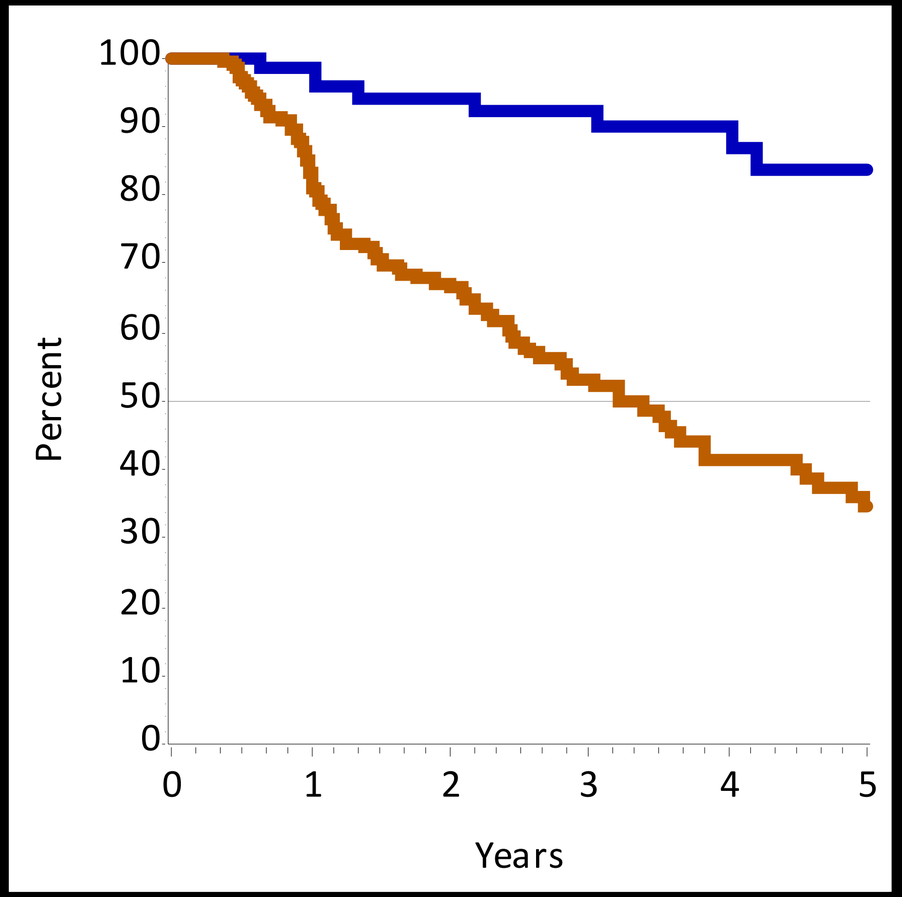
Incorporation of PSAD improves risk stratification



Chu CE, Westphalen AC, et al. Eur Urol. 2020 Oct;78(4):515-517.
Washington SL, Westphalen AC, et al. AJR Am J Roentgenol 2020 Mar;214(3):574-578.
Westphalen AC, Fazel F, et al. Int Braz J Urol. Jul-Aug 2019;45(4):713-723.

baseline
MRI

Gleason Upgrade-Free Survival at UCSF

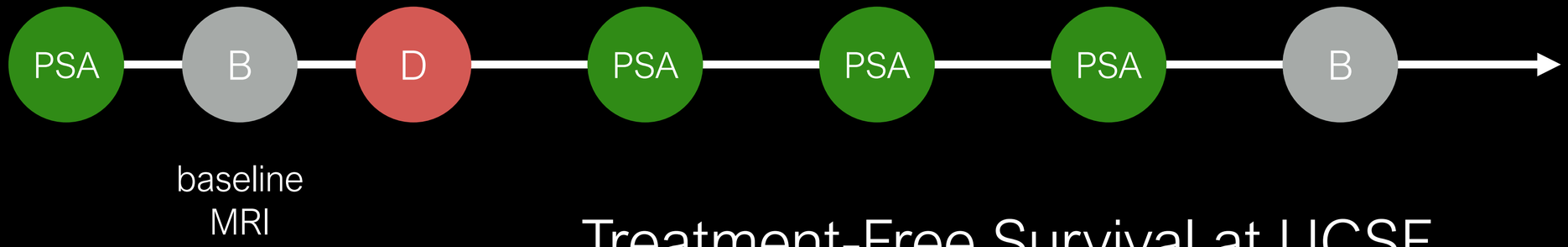


negative MRI

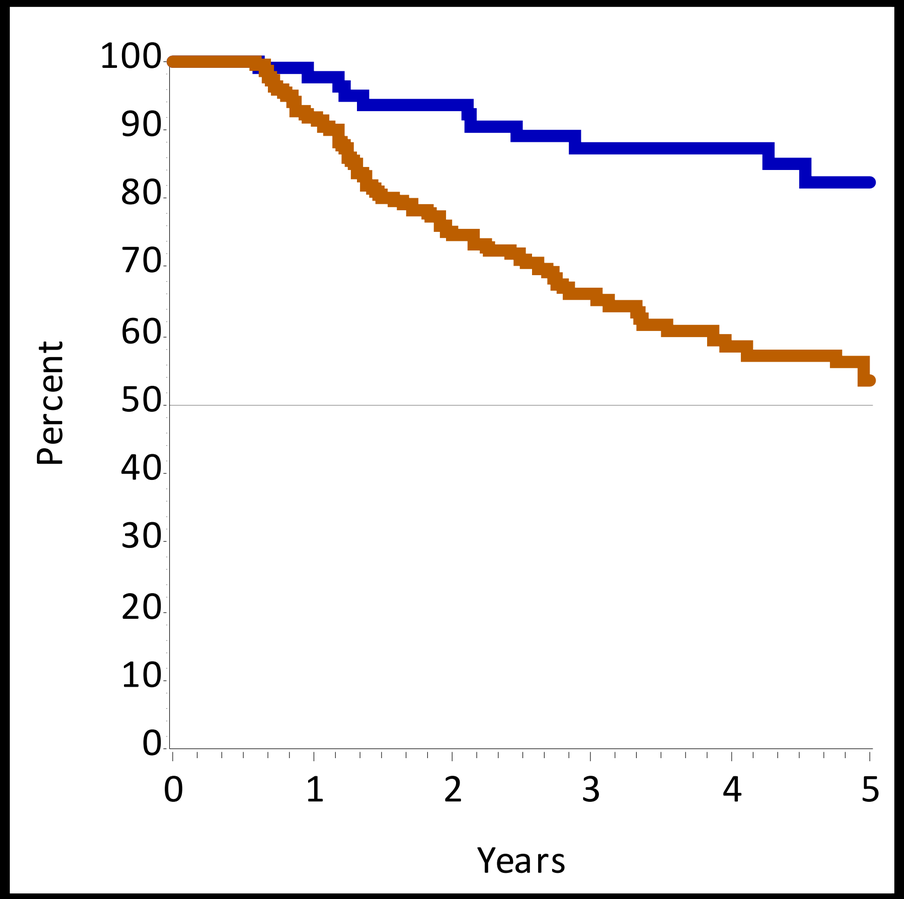
positive MRI

3y: 92% vs. 53% (P < 0.001)

5y: 84% vs. 35% (P < 0.001)



Treatment-Free Survival at UCSF



negative MRI

positive MRI

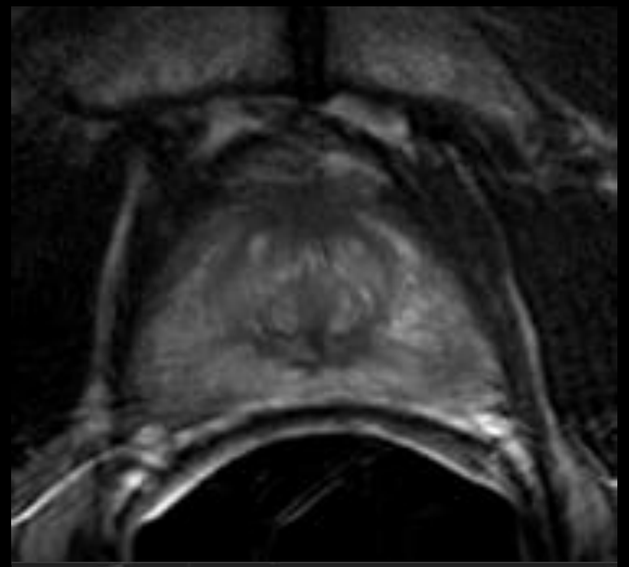
3y: 87% vs. 66% (P < 0.001)

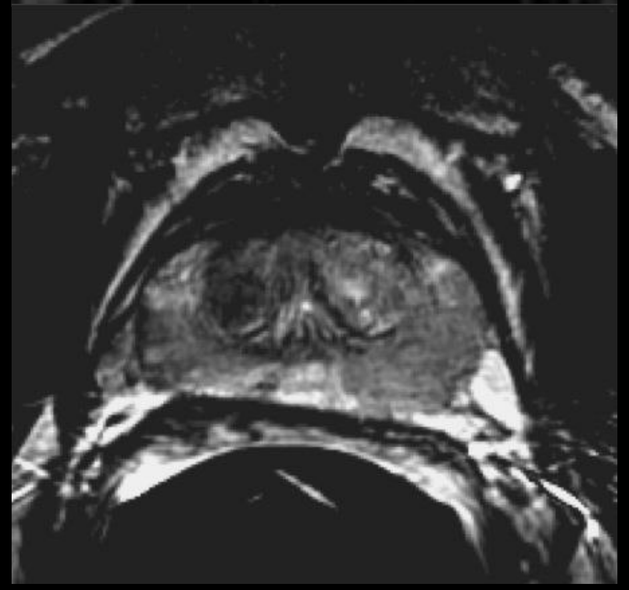
5y: 83% vs. 54% (P < 0.001)

Skip the confirmatory biopsy if MRI is negative?

What if MRI is positive?

baseline
MRI



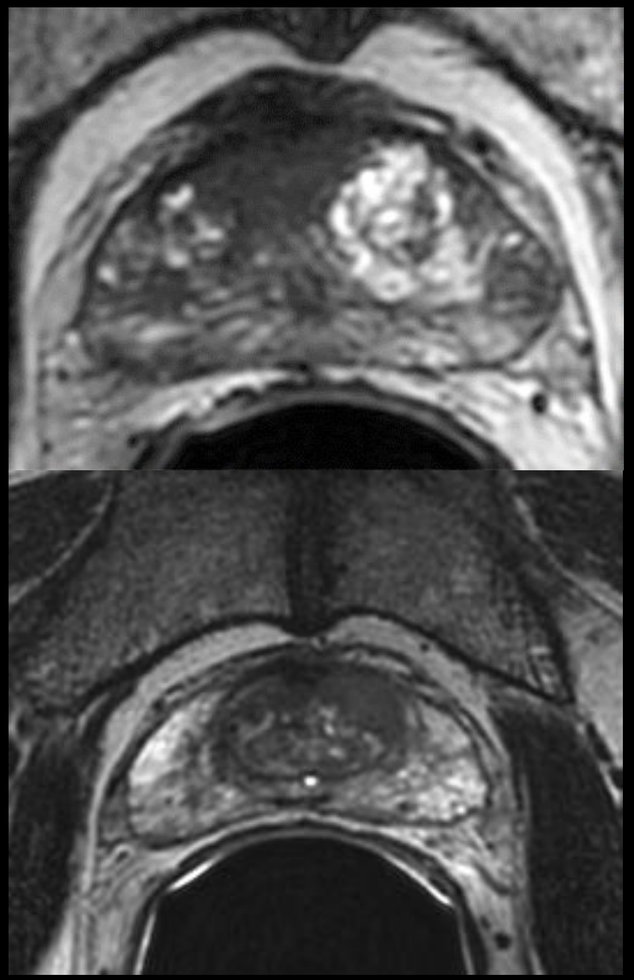


Visible tumor size predicts tumor grade

Size threshold = 1 cm axial diameter
Group 1 - small PCa: Gleason ≤ 6 (80%) Gleason ≥ 7 (20%)
Group 2 - large PCa: Gleason ≤ 6 (61%) Gleason ≥ 7 (39%)

Lee DH. J Urol. 2013 Oct;190(4):1213-7.

baseline
MRI



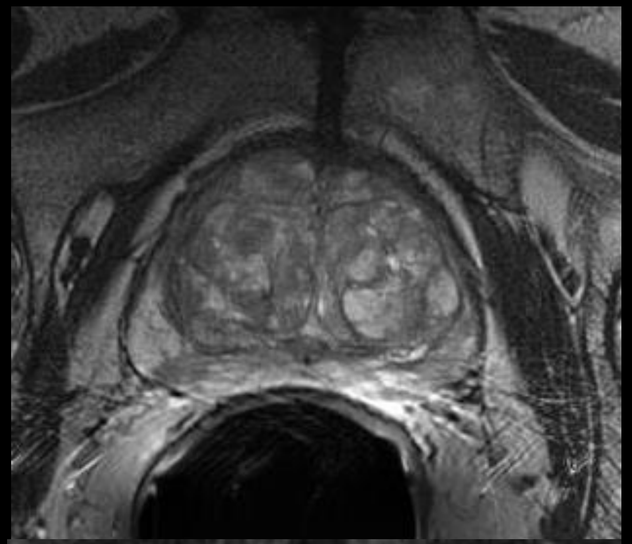
Visible tumor size predicts tumor grade

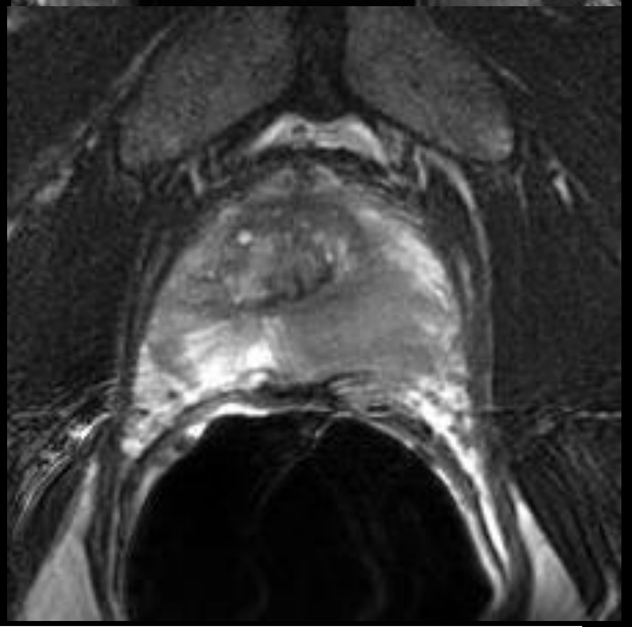
Size threshold = 1 cm axial diameter

80% reclassified outside AS criteria

Margel D. J Urol. 2012 April; 187(4):1247–1252

baseline
MRI



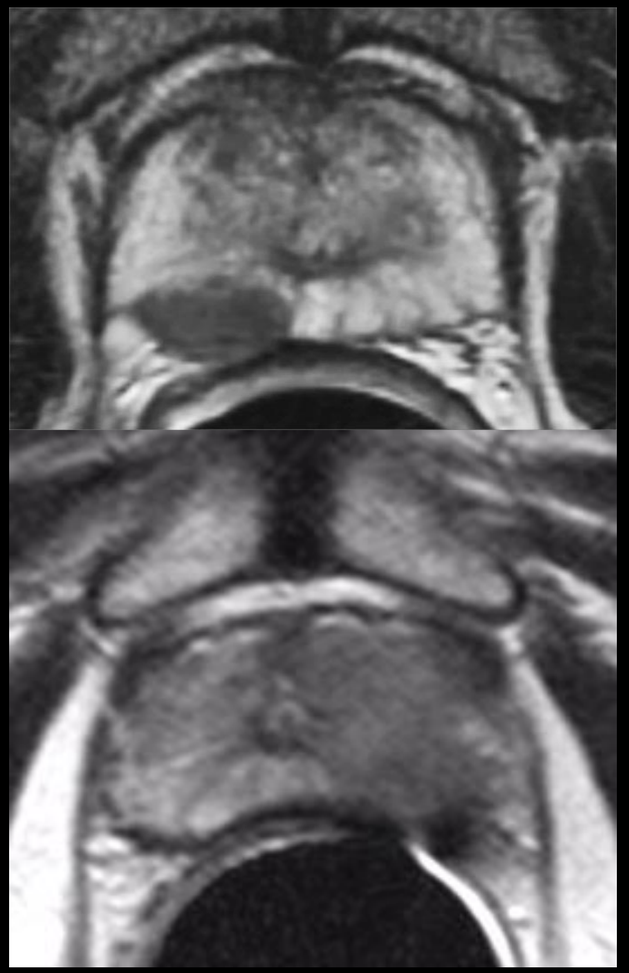


Visible tumor size predicts EPE

15 mm / 20 mm (LAD) threshold
All OR > 7.5
Independent of PSA, GS, clinical stage, D'Amico

Baco E. J Urol. 2014; doi: 10.1016/j.juro.2014.08.084.

baseline
MRI

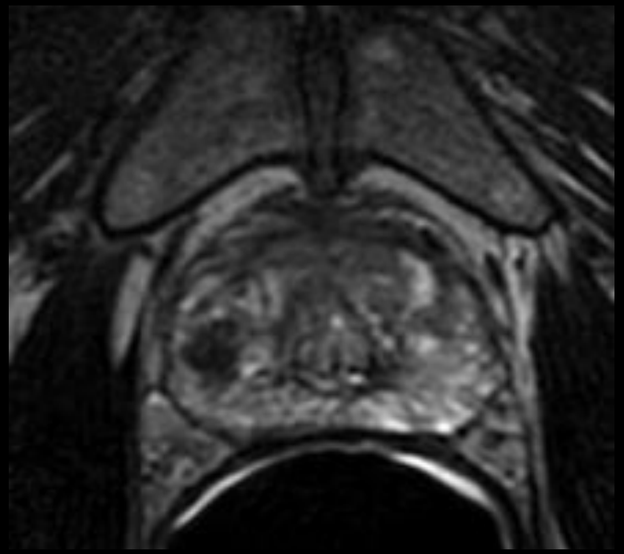


Extent of capsular contact predicts ECE

20 mm capsular contact threshold
sensitivity = 79%, specificity = 85%
NPV = 88%, PPV = 76%

Baco E. J Urol. 2014; doi: 10.1016/j.juro.2014.08.084.

baseline
MRI

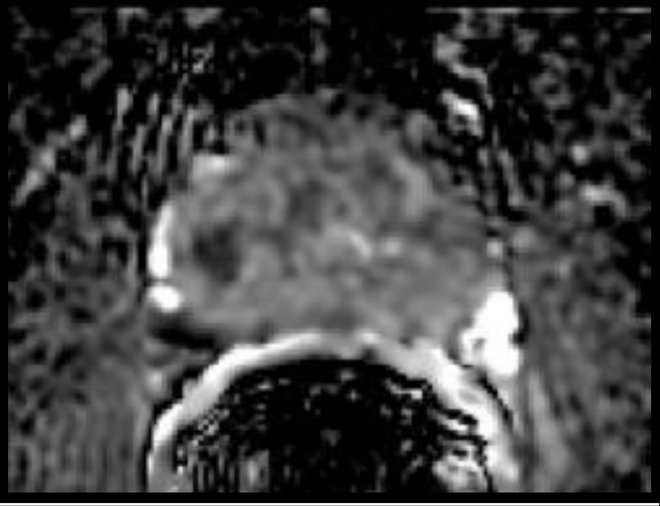


ADC values predict tumor grade

<u>Mean ADC value</u>

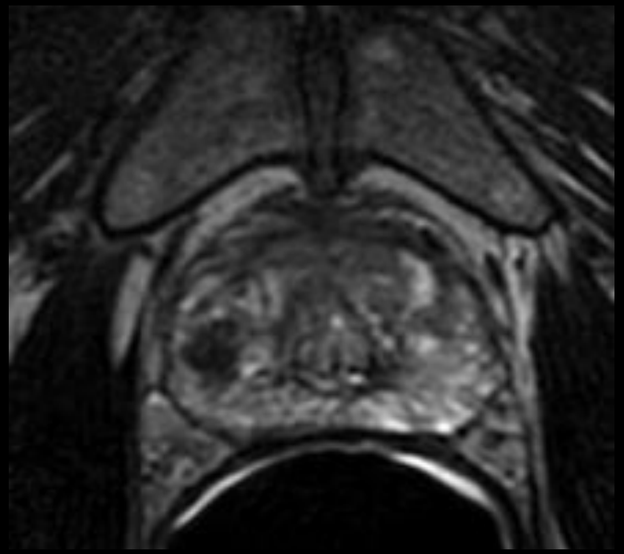
Gleason ≤ 6: 1.09 × 10^{-3} mm^2/s (SD, 0.25)

Gleason ≥ 7: 0.84 × 10^{-3} mm^2/s (SD, 0.35)



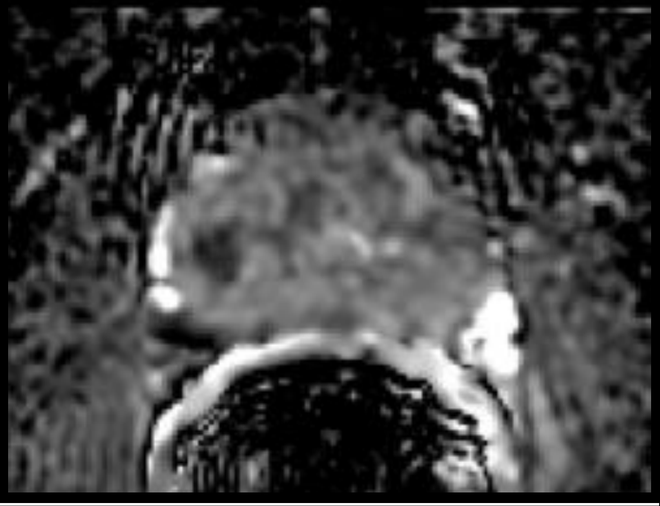
Somford DM. Invest Radiol. 2013 Mar;48(3):152-7.

baseline
MRI



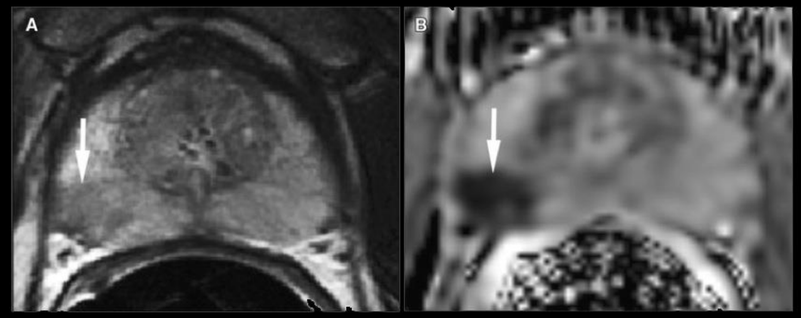
Baseline ADC values predict outcome of men under AS

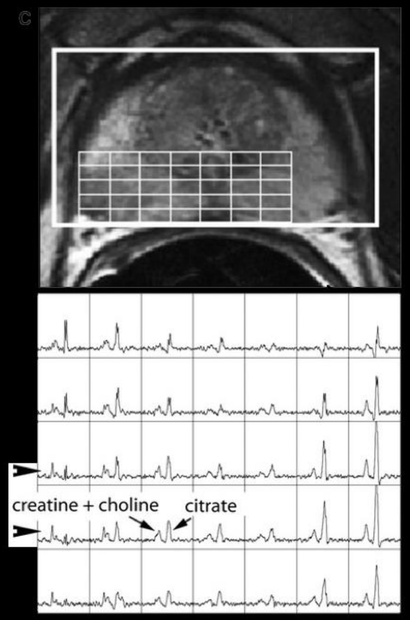
Median ADC value = 0.97 x 10-3mm2/s (IQR 0.88-1.17)
Below median values predict progression to definitive treatment at an early time-point and adverse histology



Henderson DR. Eur Urol. 2016 Jun;69(6):1028-33.

baseline
MRI





Baseline MRI predicts outcome of men under AS.

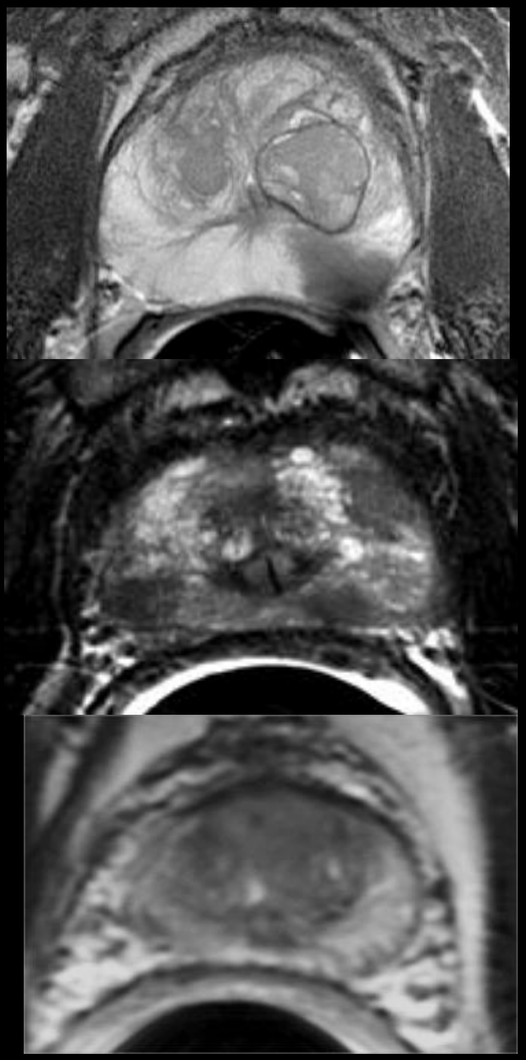
T2 and DWI independently predicted tumor upgrading (HR≅2.5)

The probability of upgrading gets higher as the number of positive MR sequences increases (83% if 3 parameters).

Flavell RR. Abdom Imaging. 2014 Oct;39(5):1027-35.

Fradet V. Radiology. 2010 Jul;256(1):176-83.

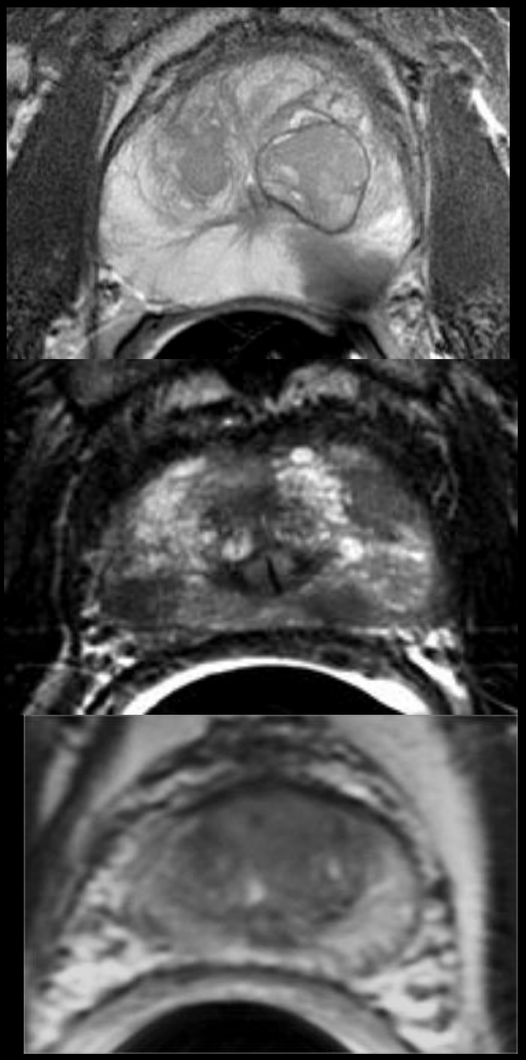
baseline
MRI



Degrees of suspicion on MRI correlates with the risk of csPCA

Filson CP et al. Cancer. 2016;122: 884-92.
Mertan FV et al. J Urol, 2016;196:690-6.
Barkovich EJ, Shankar PR, **Westphalen AC.** AJR. 2019 Apr;212(4):847-854.
Westphalen AC et al. Radiology. 2020 Jul;296(1):76-84.

baseline
MRI



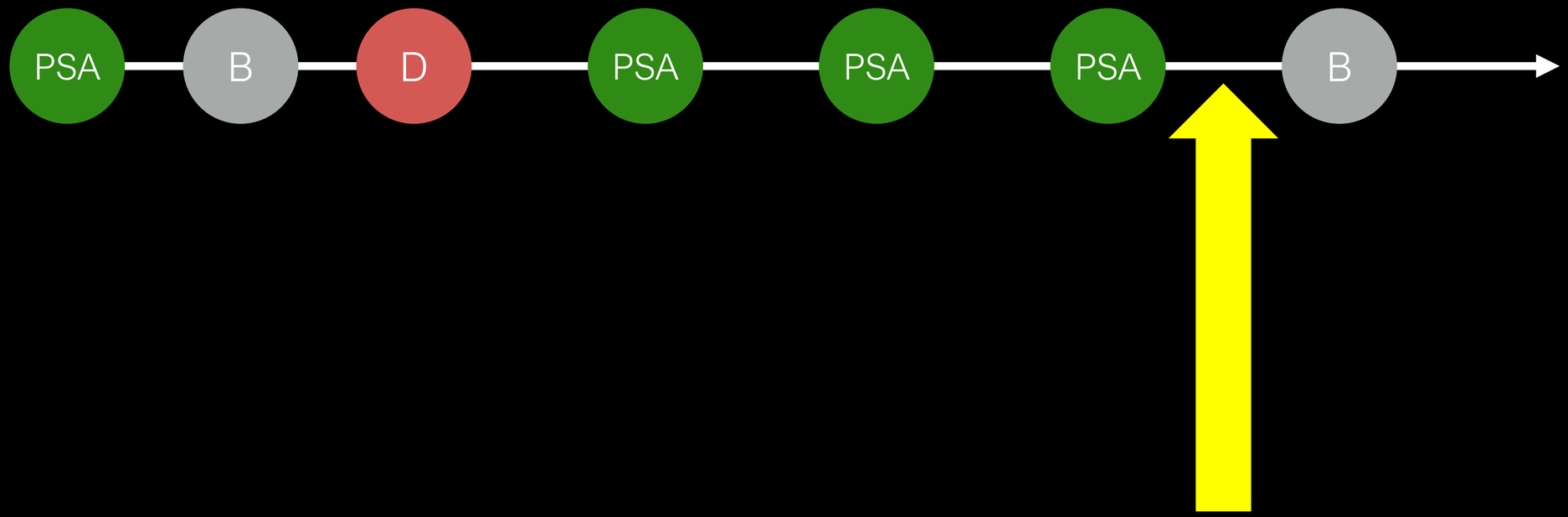
PI-RADS scores predict outcome of men under AS.

Scores 4 and 5 associated with upgrading and therapy change

Eineluoto JT. Plos One 2017; 12(12): e0189272.

MR-targeted confirmatory biopsy

AS Protocol with MRI



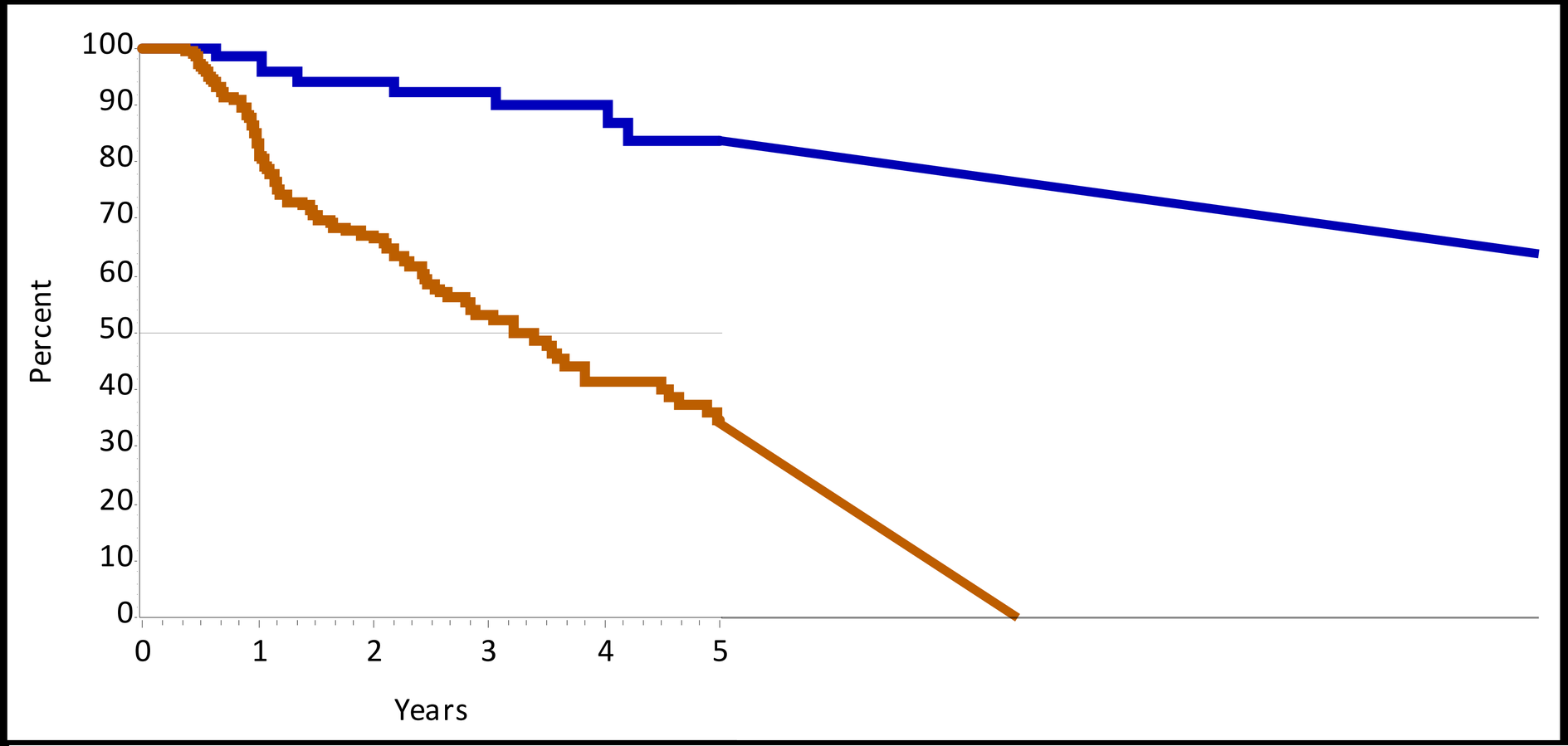
every 12 plus months

Possible scenarios

- Negative baseline MRI – negative F/U MRI
- Negative baseline MRI – positive F/U MRI
- Positive baseline MRI – stable or less worrisome F/U MRI
- Positive baseline MRI – more worrisome F/U MRI

baseline
MRI

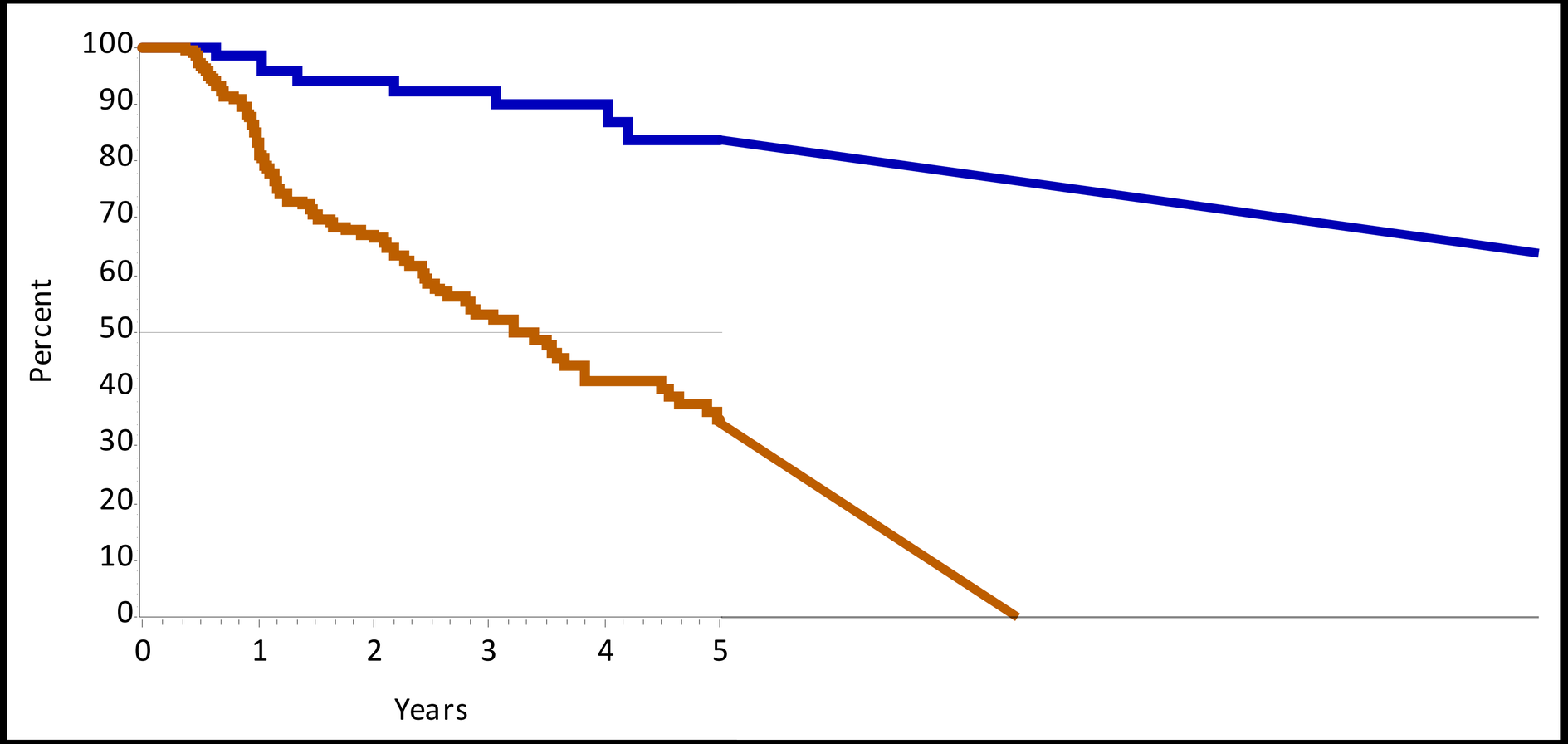
Gleason Upgrade-Free Survival at UCSF



negative F/U MRI
postpone?

baseline
MRI

Gleason Upgrade-Free Survival at UCSF



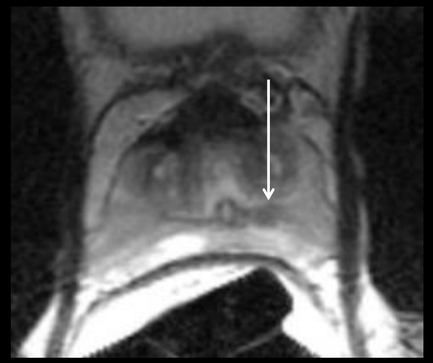
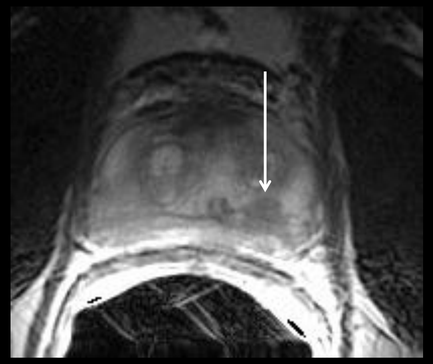
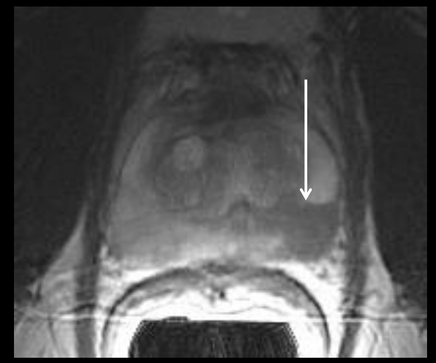
negative MRI
postpone?

newly positive MRI
targeted biopsy

Possible scenarios

- Negative baseline MRI – negative F/U MRI
- Negative baseline MRI – positive F/U MRI
- Positive baseline MRI – stable or less worrisome F/U MRI
- Positive baseline MRI – more worrisome F/U MRI

- Some data suggest changes in MRI predict cancer upgrading and allow timely curative treatment.

baseline  6 years  1 year 

Vos LJ. World J Radiol 2016; **8**: 410.
Habibian DJ. AJR Am J Roentgenol 2017; **208**: 564.

European Radiology (2020) 30:6042–6051
https://doi.org/10.1007/s00330-020-06997-1

UROGENITAL

Check for updates

Multiparametric magnetic resonance imaging can exclude prostate cancer progression in patients on active surveillance: a retrospective cohort study

T. Ullrich[1,2] · C. Arsov[3] · M. Quentin[1] · F. Mones[1] · A. C. Westphalen[2] · D. Mally[3] · A. Hiester[3] · P. Albers[3] · G. Antoch[1] · L. Schimmöller[1]

Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE)

1. Resolution of previous features suspicious on MRI
2. Reduction in volume and/or conspicuity of feature suspicious for PCa
3. Stable MRI appearance
4. Significant increase in size and/or conspicuity of features suspicious for PCa
5. Definite radiologic stage progression, i.e. new EPE

European Association of Urology

Platinum Priority Brief Correspondence

Editorial by James Thompson, Amer Amin and Phillip Stricker on pp. 518–519 of this issue

Multiparametric Magnetic Resonance Imaging Alone is Insufficient to Detect Grade Reclassification in Active Surveillance for Prostate Cancer

Carissa E. Chu[a], Peter E Lonergan[a], Samuel L. Washington[a], Janet E Cowan[a], Katsuto Shinohara[a], Antonio C. Westphalen[a,b], Peter R. Carroll[a], Matthew R Cooperberg[a,c,]*

PI-RADS v2

PI-RADS 1 – Very low (csPCa is highly unlikely to be present)
PI-RADS 2 – Low (csPCa is unlikely to be present)
PI-RADS 3 – Intermediate (the presence of csPCa is equivocal)
PI-RADS 4 – High (csPCa is likely to be present)
PI-RADS 5 – Very high (csPCa is highly likely to be present)

No standardized imaging criteria to determine mpMRI tumor progression.

Change on serial MRI at UCSF

n= 57

71.9% low CAPRA risk (0-2)

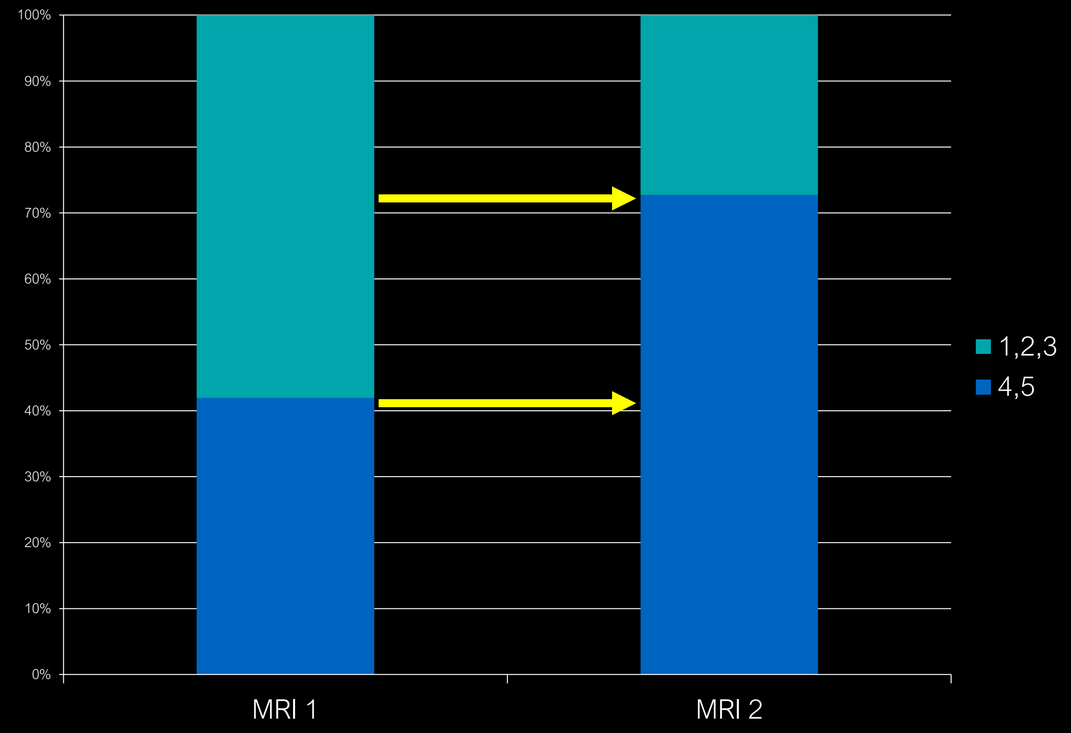
28.1% intermediate (3-5)

84% Gleason 3+3

16% Gleason 3+4

median time between studies 24.8 months (IQR 19-31)

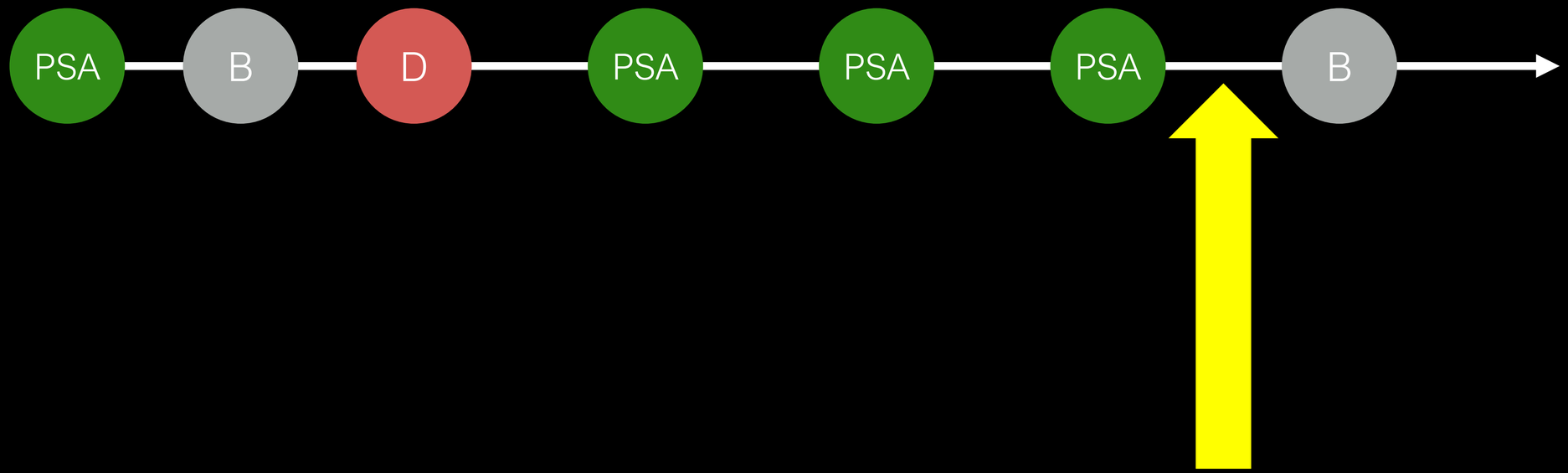
index lesion PI-RADS unchanged in 94% of men



Increase from P1-3 to P4-5 likely associated with upgrade at follow-up biopsy (OR 2.68, 95% CI 0.80-8.98, p=0.11)

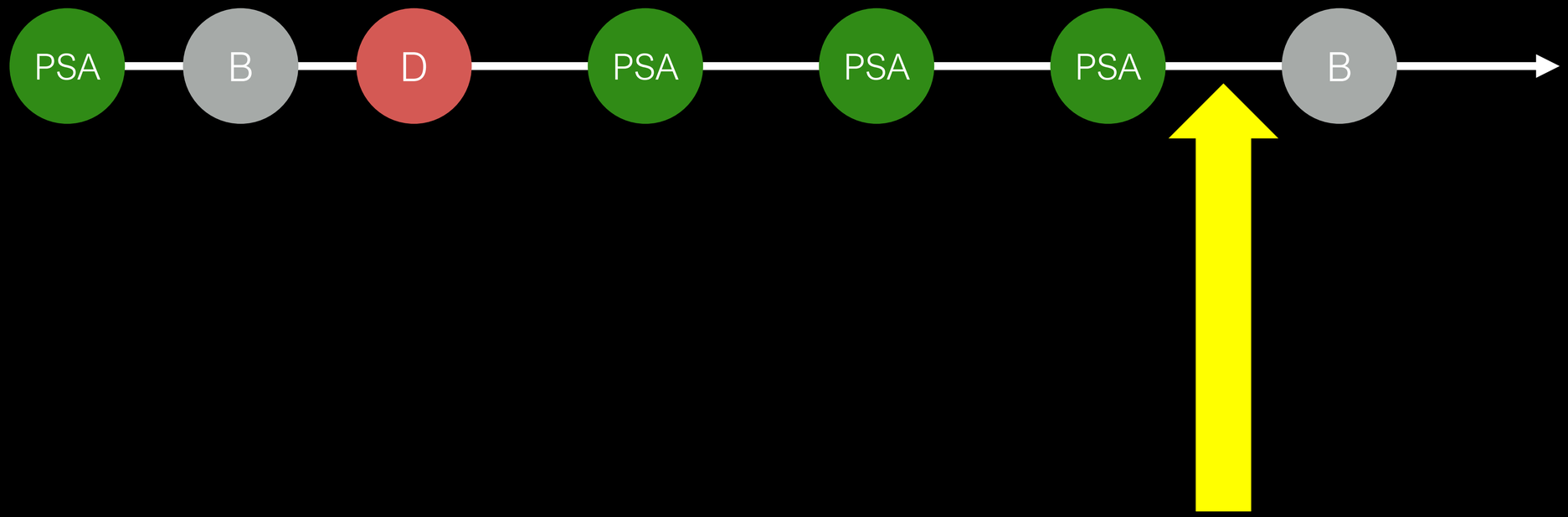
Equivalent to PRECISE category 4

AS Protocol with MRI



every 12 plus months
less conspicuous findings (PRECISE 2)
stable MRI appearance (PRECISE 3)
postpone biopsy? targeted biopsy?

AS Protocol with MRI



every 12 plus months
progression (PRECISE 4/5)
targeted biopsy

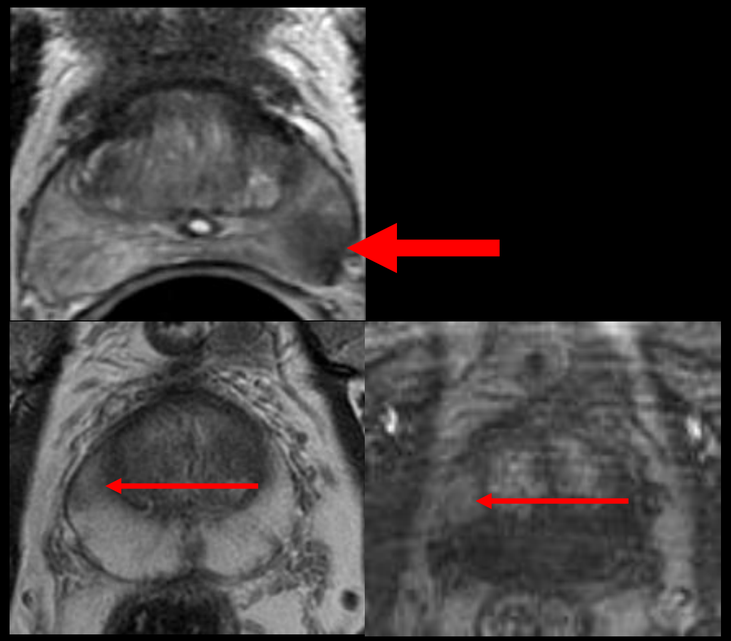
Teaser - not all PI-RADS 4 are the same

- PZ - circumscribed, homogenous, moderately hypointense focus/mass confined to the prostate and < 1.5 cm in greatest dimension.

- TZ – lenticular or non circumscribed, homogeneous, moderately hypointense, confined to the prostate and < 1.5 cm in greatest dimension.

DWI	T2W	DCE	PI-RADS
1	Any*	Any	1
2	Any	Any	2
3	Any	–	3
		+	4
4	Any	Any	4
5	Any	Any	5

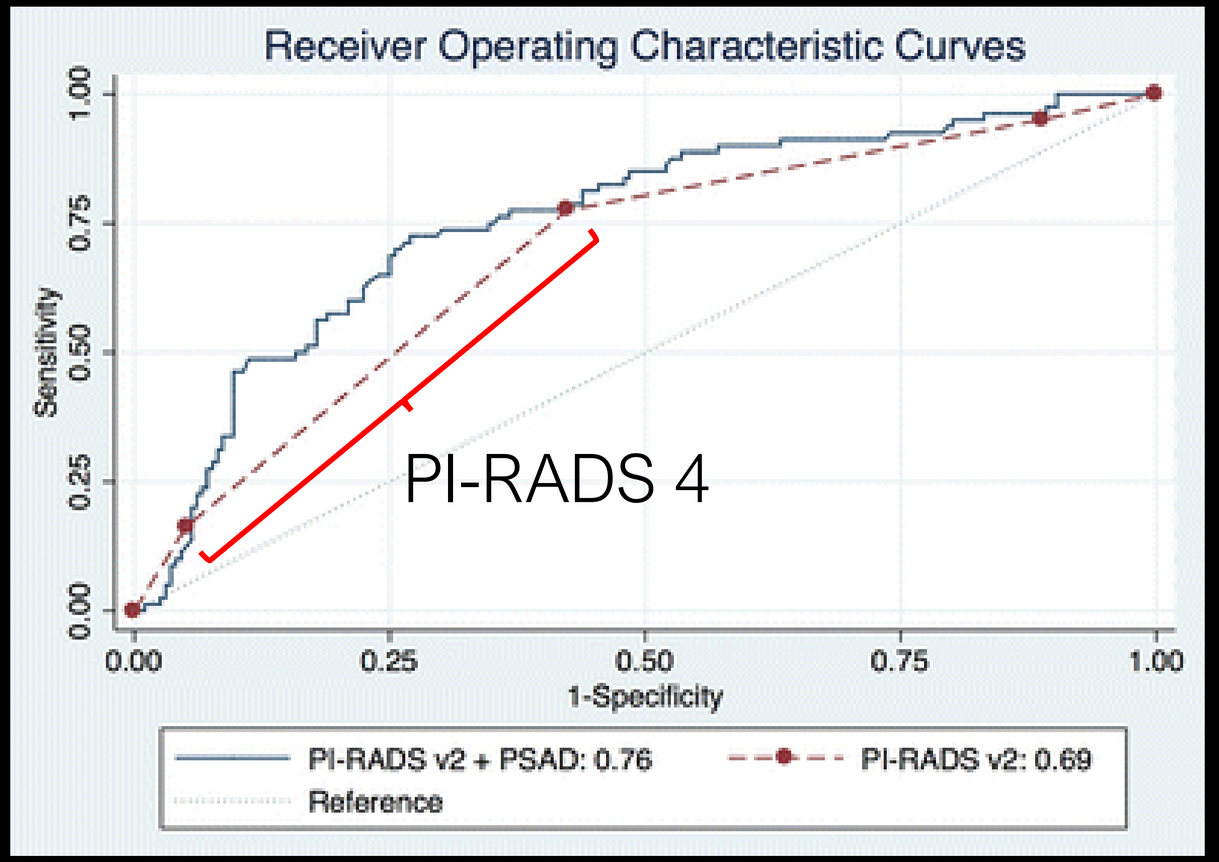
T2W	DWI	DCE	PI-RADS
1	Any*	Any	1
2	≤3	Any	2
	≥4	Any	3
3	≤4	Any	3
	5	Any	4
4	Any	Any	4
5	Any	Any	5



PI-RADS 4

Rate of csPCa 2x higher if PSAD ≥ 15

PI-RADS 4 and PSAD ≥ 0.15 = PI-RADS 5



Jordan E, Westphalen AC, et al. Abd Radiol 2017, 42(11): 275-2731

Complications of TRUS-guided Biopsy

acute prostatitis - 1% to 3% (≅ 20% resistant to common antibiotics)

hospitalization (within 30 days) - 1 to 4%

TRUS-guided biopsy - 12 to 16 cores

Can fewer cores adequately assess the disease?

Song W. 2014 Nov;84(5):1001-7.

Nam RK. J Urol. 2010 Mar;183(3):963-8.

Do we need systematic biopsy too?

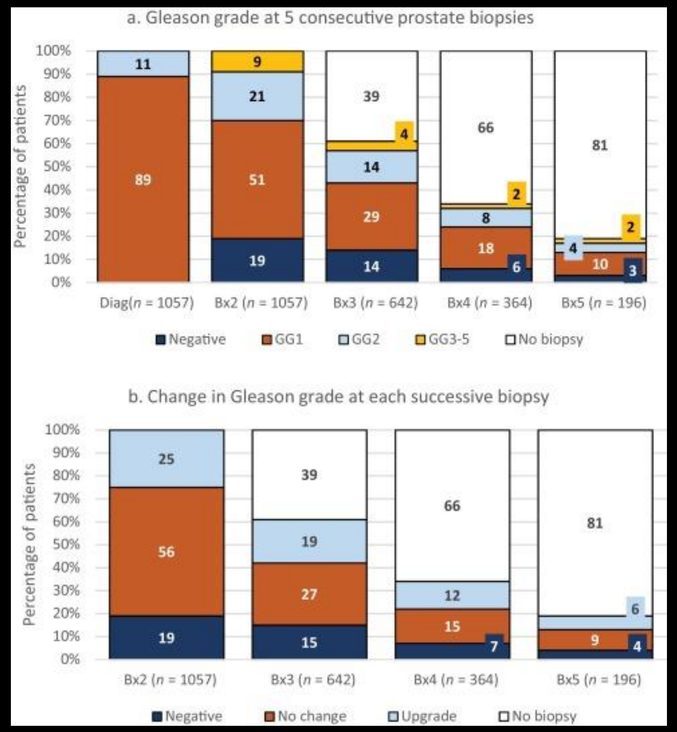
European Association of Urology

Prostate Cancer

Characteristics of Cancer Progression on Serial Biopsy in Men on Active Surveillance for Early-stage Prostate Cancer: Implications for Focal Therapy

Vittorio Fasulo [a,b,c], Janet E. Cowan [a,b], Martina Maggi [a,b,d], Samuel L. Washington III [a,b], Hao G. Nguyen [a,b], Katsuto Shinohara [a,b], Massimo Lazzeri [c], Paolo Casale [c], Peter R. Carroll [a,b,]*

[a] *Department of Urology, University of California, San Francisco, CA, USA;* [b] *UCSF—Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA;* [c] *Department of Urology, Humanitas Clinical and Research Center—IRCCS, Rozzano, Milan, Italy;* [d] *Department of Urology, Sapienza Rome University, Policlinico Umberto I, Rome, Italy*

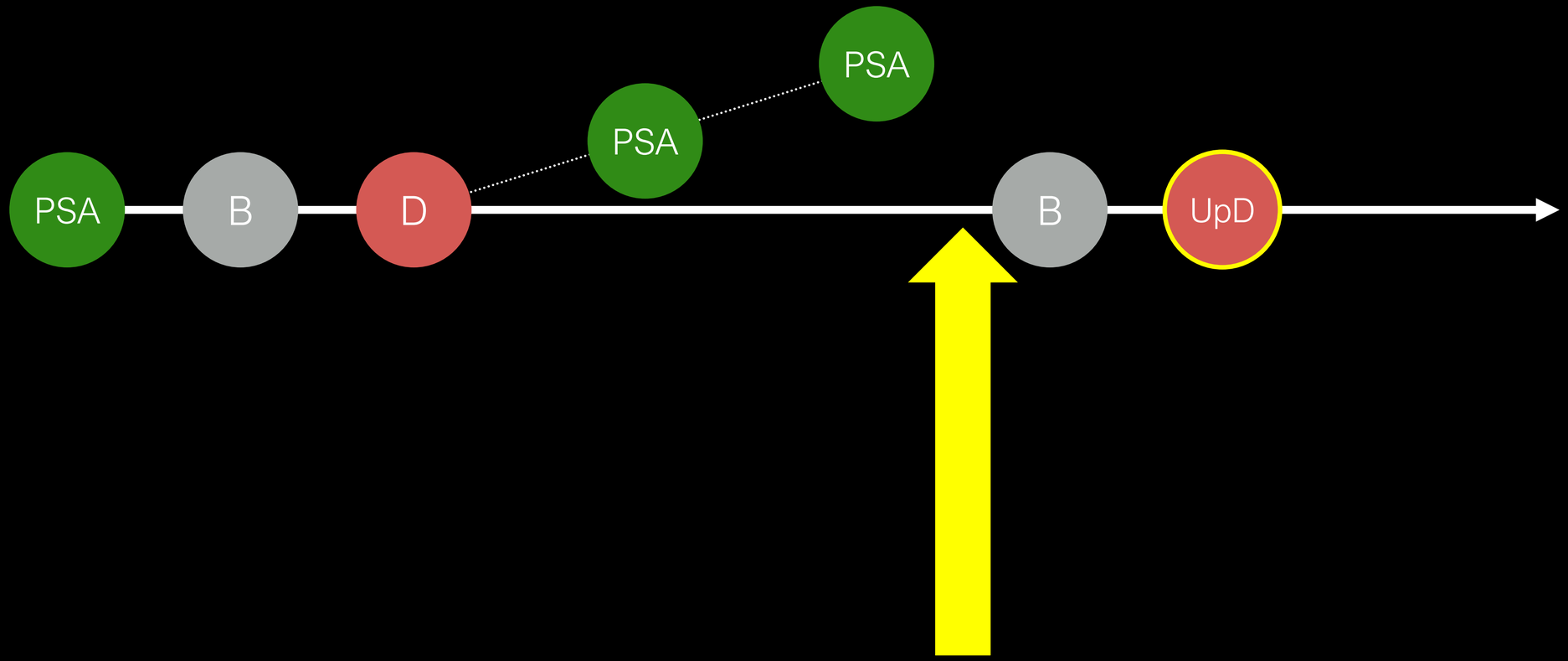


"Findings of serial biopsies in men with low or intermediate-risk disease on AS show that tumor location remains relatively stable overtime and that significant changes in grade and/or volume occur largely in the dominant tumor (ACW note, visible tumor on MRI). The combination of diagnostic and confirmatory biopsy findings better selects patients for FT than the use of the diagnostic biopsy alone."

"…mpMRI results were utilized to confirm DT location after diagnostic biopsy. Given that mpMRI adoption is now widespread and most men have undergone mpMRI fusion biopsy at diagnosis, it may be feasible to offer FT based on this information alone."

If FT may be feasible based on MRI and fusion biopsy alone, MRI targeted biopsy alone is probably enough in AS when f/u MRI is positive!

AS Protocol with MRI



clinically indicated
targeted biopsy

$64K Question

REVIEW

Can MRI replace serial biopsies in men on active surveillance for prostate cancer?

Caroline M. Moore[a,b], *Neophytos Petrides*[a,b], *and Mark Emberton*[a,b]

$64K Question

1. What is clinically significant disease on MRI? Visibility, conspicuity, size

2. What is progression on MRI? PRECISE categories

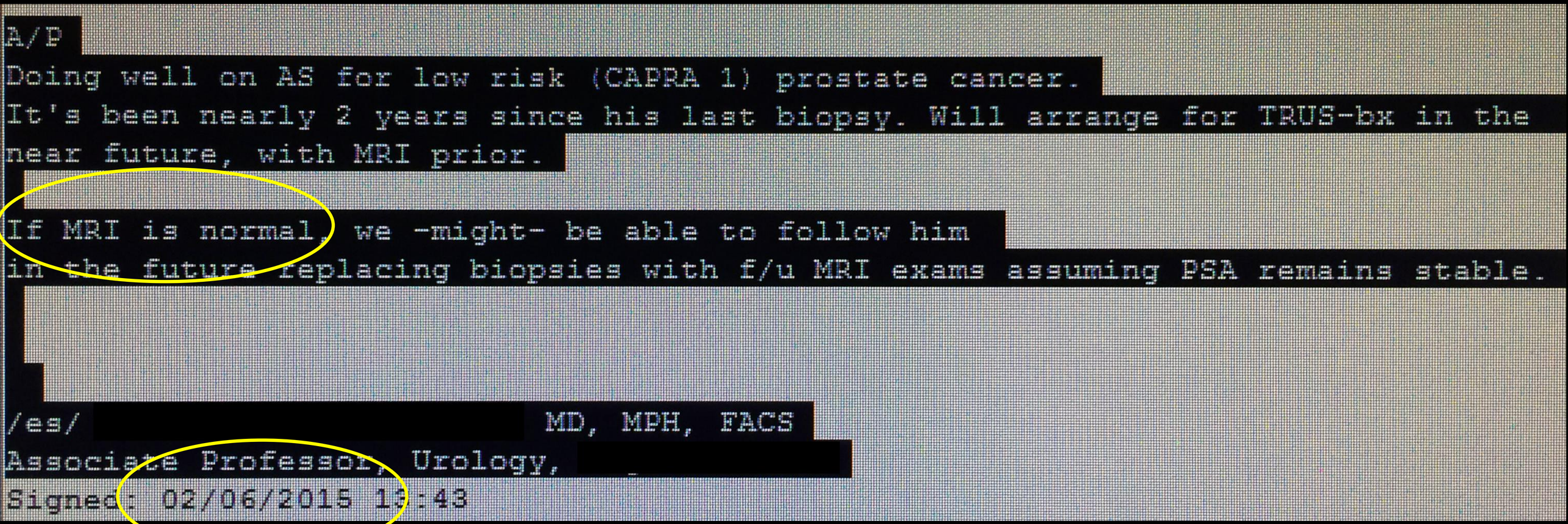
3. What is the significance of a csPCa diagnosed after a negative MRI?

Rais-Bahrami S. Diagn Interv Radiol. 2014 Jul-Aug;20(4):293-8.

$64K Question

The impact nonvisible (i.e. presumably small volume) high-grade lesions have on patients' outcomes is unknown.

Outcomes Studies


A/P
Doing well on AS for low risk (CAPRA 1) prostate cancer.
It's been nearly 2 years since his last biopsy. Will arrange for TRUS-bx in the near future, with MRI prior.
If MRI is normal, we -might- be able to follow him in the future replacing biopsies with f/u MRI exams assuming PSA remains stable.
/es/ MD, MPH, FACS
Associate Professor, Urology,
Signed: 02/06/2015 13:43

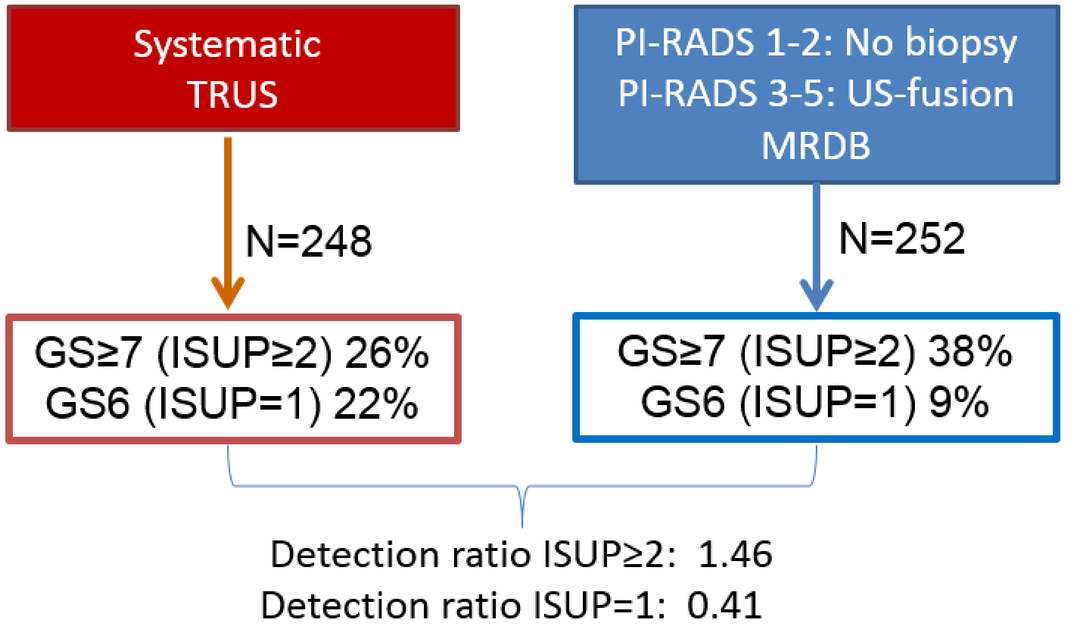
500 men with elevated PSA; 25 centers, International; Median age 64 yrs; Median PSA 6.7 ng/mL; 15% abnormal DRE; 1.5/3T; TRUS – 12 cores; positive mpMRI – MRDB

@ProfPadhani

PRECISION Population

Biopsy naive

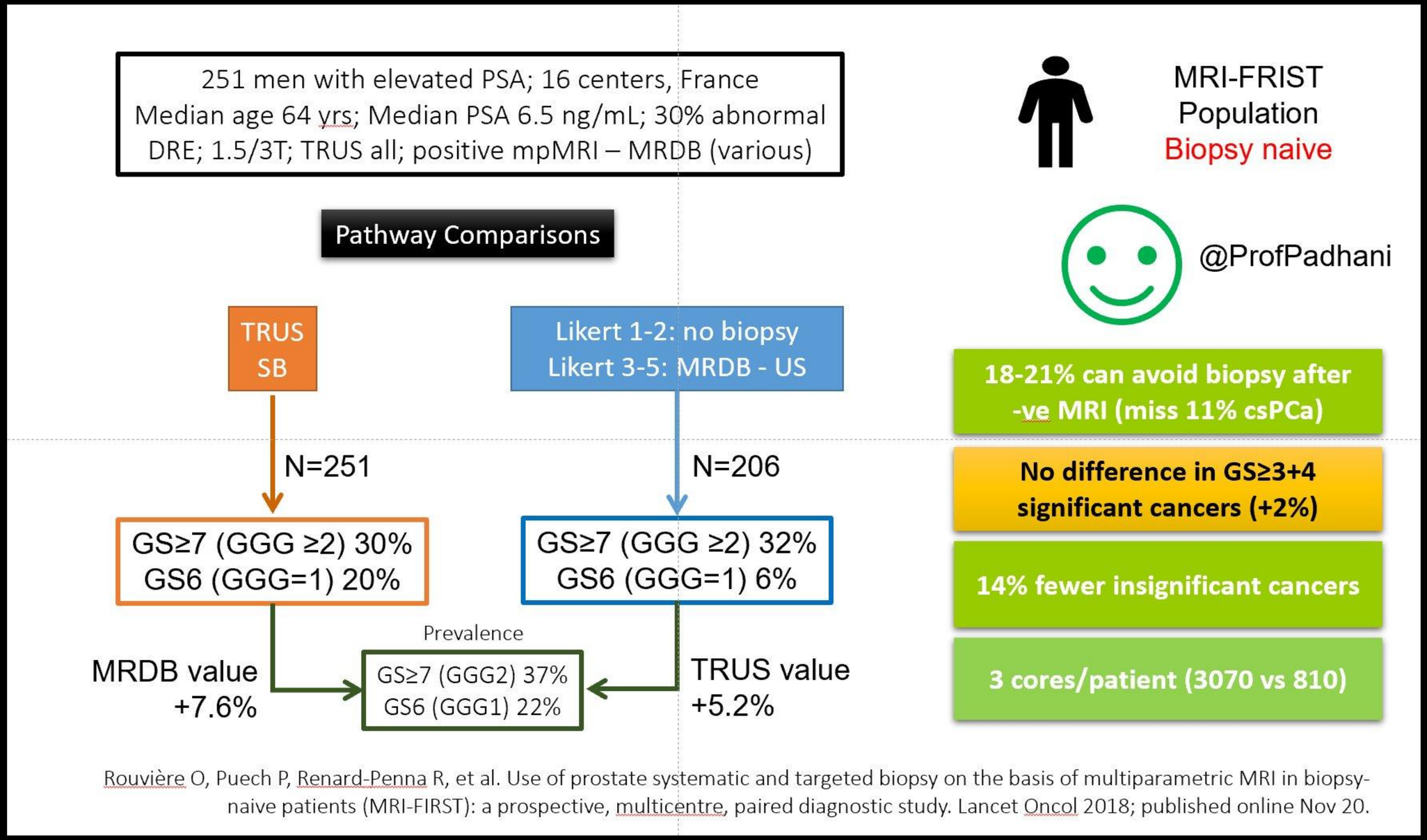
Randomized Control Trial Agreement Comparisons



MRI Pathway Benefits

- 28% avoid biopsy after negative mpMRI
- More GS≥3+4 significant cancers (+12%)
- 13% fewer insignificant cancers
- 4 cores/patient (2788 vs 967)

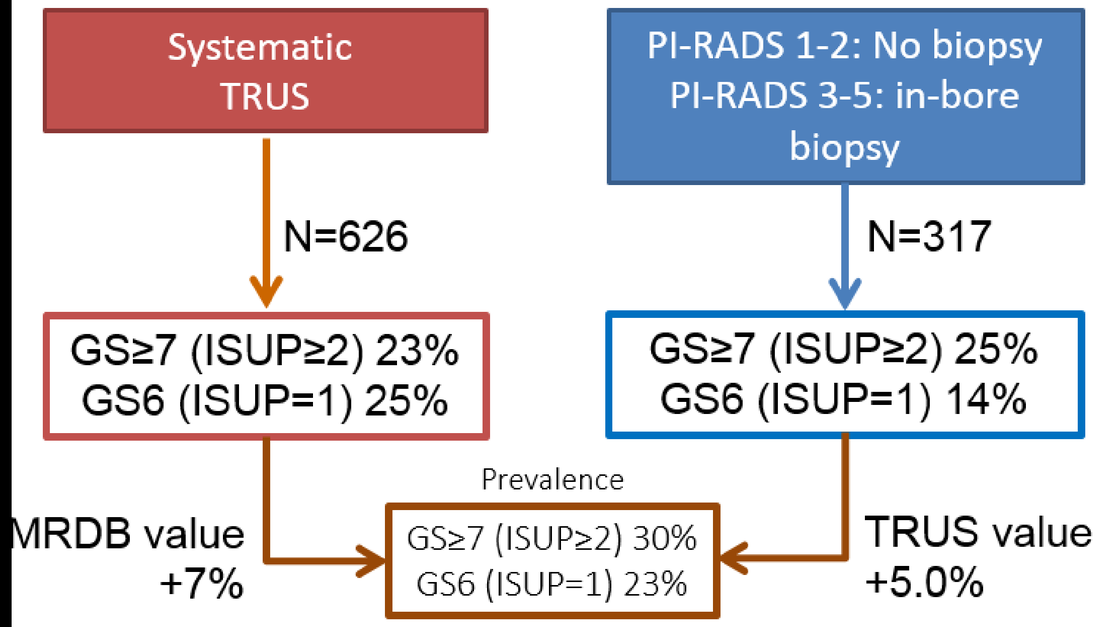
Kasivisvanathan V, et al. PRECISION Study Group Collaborators. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med. 2018; 378(19):1767-1777



Rouvière O, Puech P, Renard-Penna R, et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. Lancet Oncol 2018; published online Nov 20.

626 men with elevated PSA; 4 centers, Netherlands
Median age 65 yrs; Median PSA 6.4 ng/mL; 28% abnormal DRE; 3T all; TRUSGB all; positive mpMRI – MRDB (in-bore)

Head-to-Head Pathway Agreements



@ProfPadhani

4M Population

Biopsy naive

MRI Pathway Benefits

- 49% avoid biopsy after negative mpMRI (miss 3-4% csPCa)
- No difference in GS≥3+4 significant cancers (+2%) — Advantage PI-RADS 4
- 11% fewer insignificant cancers
- 3 cores/patient (7512 vs 849)

van der Leesta M, Cornelb E, Israëla B, et al. Head-to-head comparison of TRUS biopsy versus mpMRI with subsequent MR-guided biopsy in biopsy-naïve men with elevated PSA; a large prospective multicenter clinical study. Eur Urol 2019; 75:570-578.

@ProfPadhani

20 studies; 5219 patients; 67% +ve MRI cases
Systematic (8-15) all; MRI-TBx (2-7 cores) positive MRI

Systematic vs MRI-direct biopsy pathway comparisons
Patient Level Agreement Comparisons

Systematic Biopsy Pathway

MRI-Pathway
PI-RADS 1-2: No biopsy PI-RADS 3-5: MRDB

GS≥7 (ISUP≥2) 21.4%

GS≥7 (ISUP≥2) 23.4%

Targeted biopsy value +6.3% (4.8, 8.2)

Prevalence
GS≥7 (ISUP≥2) 27.7%

Systematic biopsy value +4.3% (2.6, 6.9)

Meta-analysis Population

Biopsy naive

MRI Pathway Benefits

- 33% (26-41) men avoid biopsy
- MRI pathway lowers ISUP=1 yields (DR=0.63 (0.54, 0.74))
- MRI pathway increases detection of ISUP≥2 (DR=1.05 (0.95, 1.16))
- MRI pathway increases detection of ISUP≥3 (DR=1.09 (0.94, 1.26))

DR = Detection Ratio of MRI versus systematic biopsy pathway

Drost FJH, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. Cochrane Database of Systematic Reviews 2019, Issue 4. Art. No.: CD012663.

UK National Institute for Health and Care Excellence (NICE)
National Comprehensive Cancer Network (NCCN)
AUA/ASTRO/SUO guideline

Sanda MG. J Urol 2017; 199: 683–90

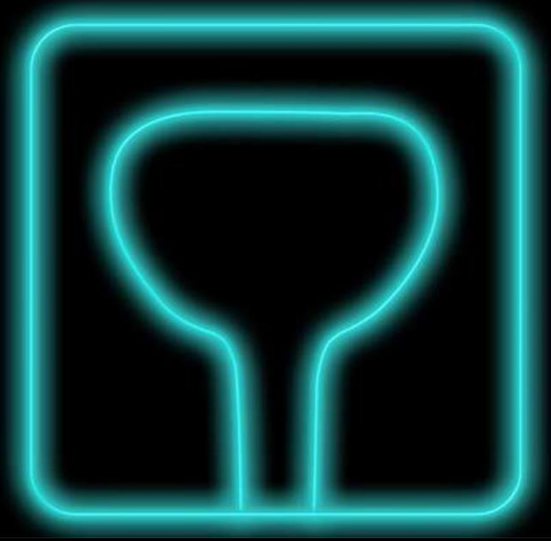
Prostate cancer: diagnosis and management NICE guideline. Published date: May 2019
NCCN Guidelines Version 2.2019 Prostate Cancer. Published date: April 2019

PI-RADS®

Prostate Imaging – Reporting and Data System

2019

Version 2.1



RADIOLOGIST

REST OF THE WORLD


9
6.1
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CREATIVE
BRAND
UNICATIONS
ADVERTISING
STRATEGY
FIRM
MARK


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European Urology

Platinum Priority – Prostate Cancer

Editorial by Axel Heidenreich on pp. 495–497 of this issue

Magnetic Resonance Imaging for the Detection, Localisation, and Characterisation of Prostate Cancer: Recommendations from a European Consensus Meeting

Louise Dickinson [a,b,c,], Hashim U. Ahmed [a,b], Clare Allen [d], Jelle O. Barentsz [e], Brendan Carey [f], Jurgen J. Futterer [e], Stijn W. Heijmink [e], Peter J. Hoskin [g], Alex Kirkham [d], Anwar R. Padhani [h], Raj Persad [i], Philippe Puech [j], Shonit Punwani [d], Aslam S. Sohaib [k], Bertrand Tombal [l], Arnauld Villers [m], Jan van der Meulen [c,n], Mark Emberton [a,b,c]*

EUROPEAN UROLOGY 59 (2011) 477–494

Eur Radiol (2012) 22:746–757
DOI 10.1007/s00330-011-2377-y

UROGENITAL

ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg · Richard Clements · Peter Choyke · Sadhna Verma · Geert Villeirs · Olivier Rouviere · Vibeke Logager · Jurgen J. Fütterer

Key Points

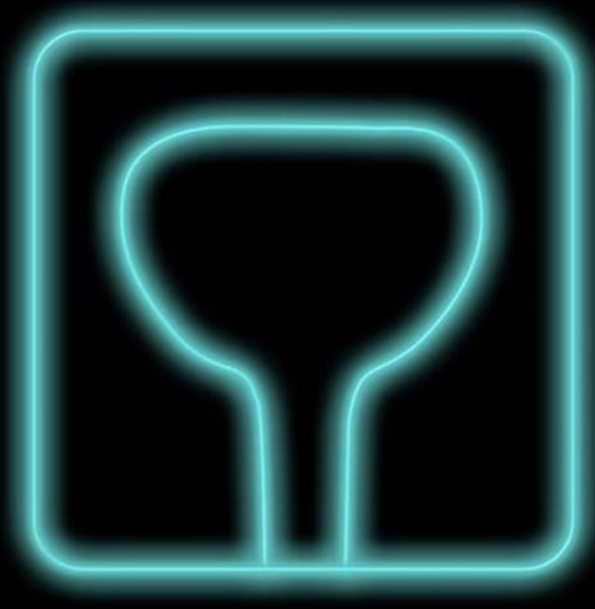
- *This report provides guidelines for magnetic resonance imaging (MRI) in prostate cancer.*
- *Clinical indications, and minimal and optimal imaging acquisition protocols are provided.*
- *A structured reporting system (PI-RADS) is described.*

Abstract The aim was to develop clinical guidelines for multi-parametric MRI of the prostate by a group of prostate MRI experts from the European Society of Urogenital Radiology (ESUR), based on literature evidence and consensus expert opinion. True evidence-based guidelines could not be formulated, but a compromise, reflected by "minimal" and "optimal" requirements has been made. The scope of these ESUR guidelines is to promulgate high quality MRI in acquisition and evaluation with the correct indications for prostate cancer across the whole of Europe and eventually outside Europe. The guidelines for the optimal technique and three protocols for "detection", "staging" and "node and bone" are presented. The use of endorectal coil vs. pelvic phased array coil and 1.5 vs. 3 T is discussed. Clinical indications and a PI-RADS classification for structured reporting are presented.

PI-RADS™

Prostate Imaging – Reporting and Data System

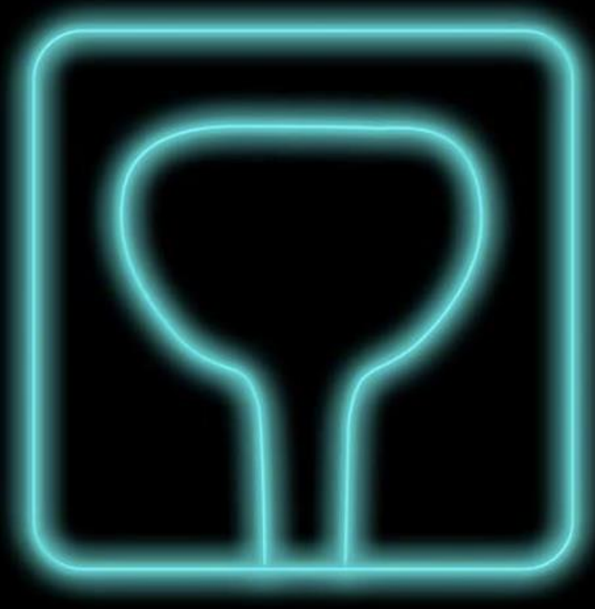
2015
version 2



PI-RADS®

Prostate Imaging – Reporting and Data System

2019
Version 2.1



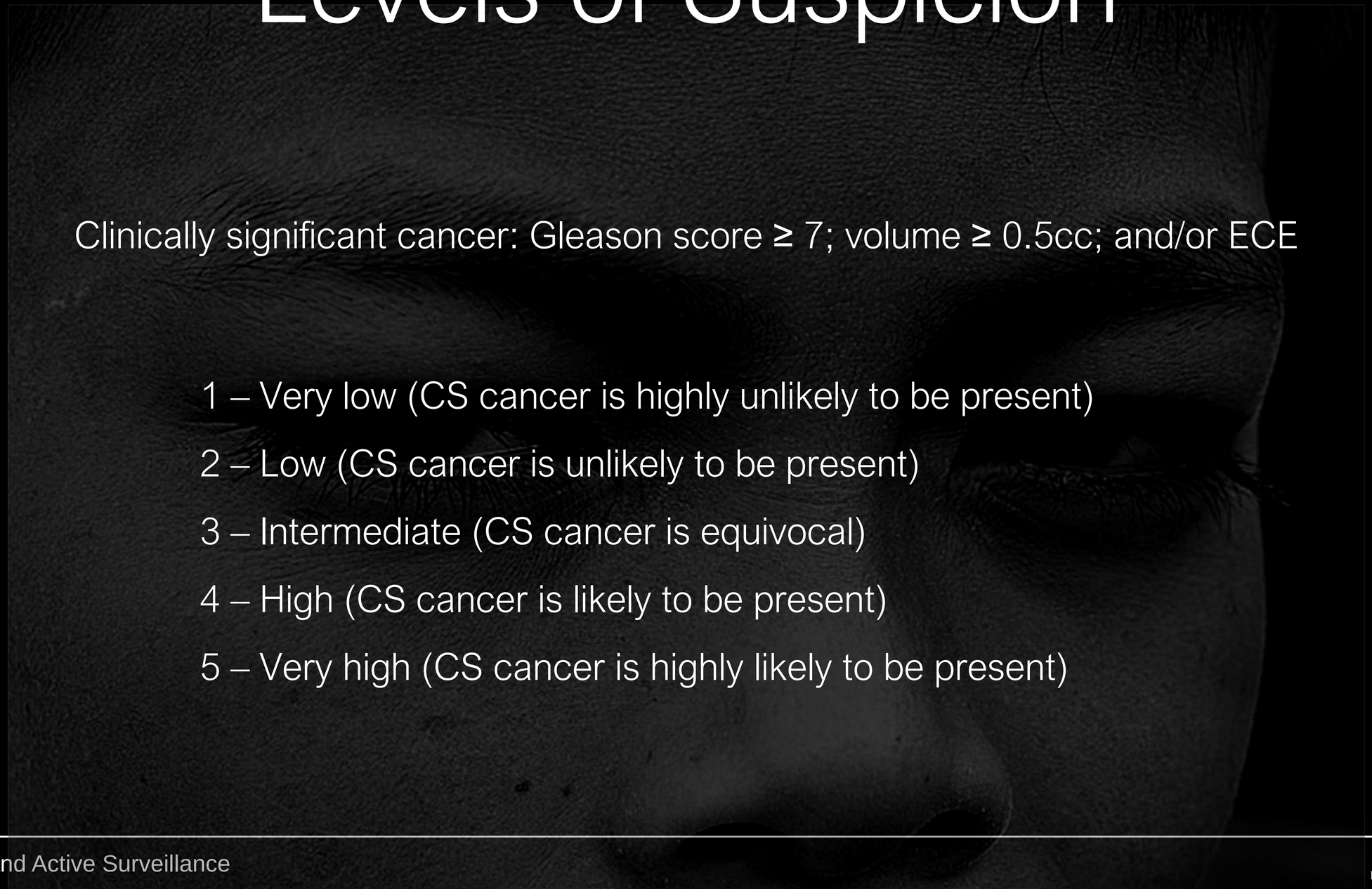
Goal: improve detection, localization, characterization, and risk stratification in patients with suspected cancer in

treatment naïve prostate glands.

Standardization and Quality

How reliable is the PI-RADS?

Levels of Suspicion



Clinically significant cancer: Gleason score ≥ 7; volume ≥ 0.5cc; and/or ECE

1 – Very low (CS cancer is highly unlikely to be present)

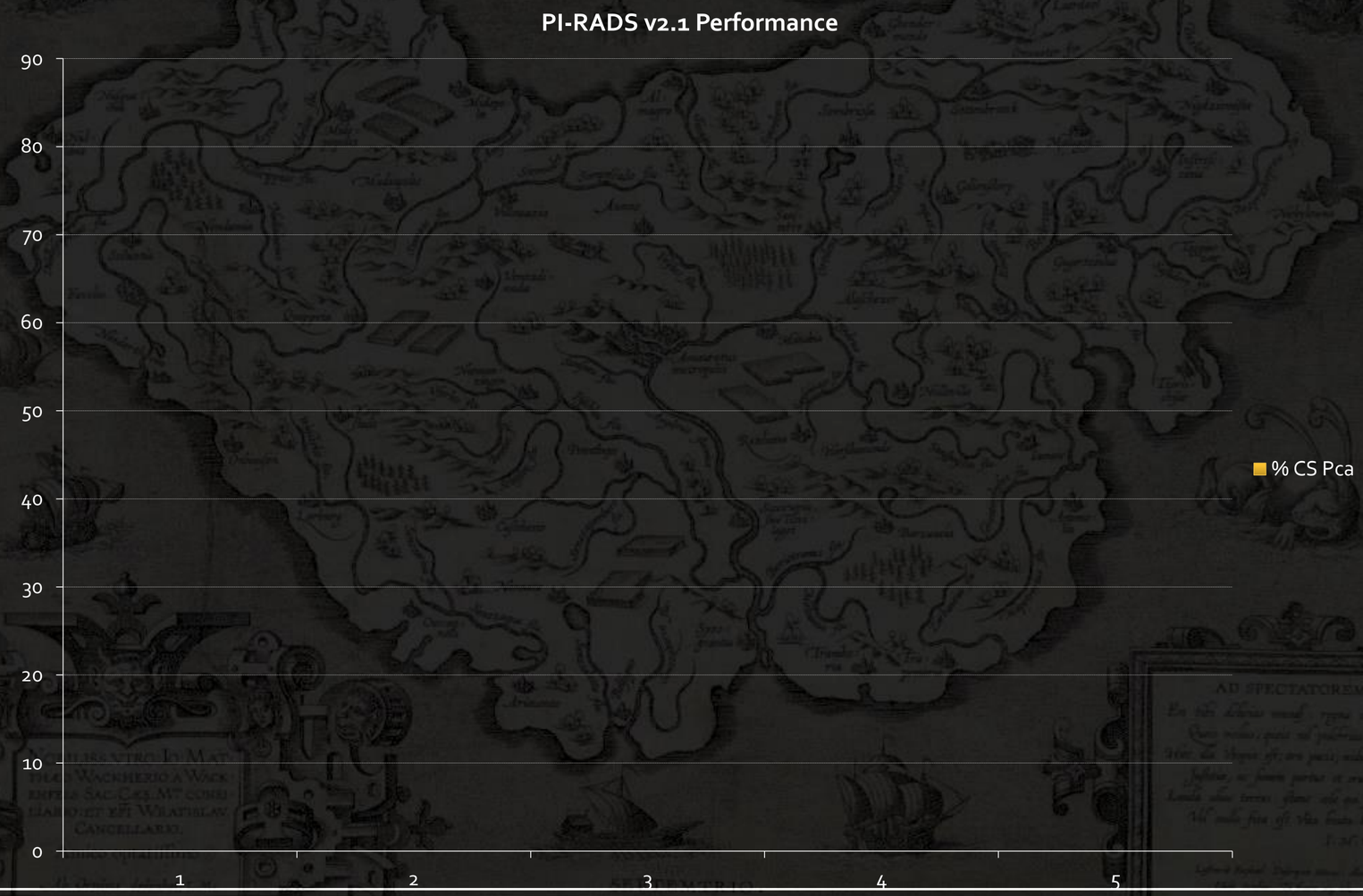
2 – Low (CS cancer is unlikely to be present)

3 – Intermediate (CS cancer is equivocal)

4 – High (CS cancer is likely to be present)

5 – Very high (CS cancer is highly likely to be present)

Levels of Suspicion



Levels of Suspicion

A Systematic Review of the Existing Prostate Imaging Reporting and Data System Version 2 (PI-RADSv2) Literature and Subset Meta-Analysis of PI-RADSv2 Categ... by Gleason Scores

Emil Jernstedt Barkovich[1]
Prasad R. Shankar[2]
Antonio C. Westphalen[3,4]

OBJECTIVE. The objective of this study wa... the methodologic heterogeneity of the current Pr... version 2 (PI-RADSv2) literature and estimate th... nosed across PI-RADSv2 categories.

MATERIALS AND METHODS. This study was a systematic review and meta-analysis and was performed in concordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Only English-language studies and studies published before April 1, 2018, were assessed. The primary outcome of the meta-analysis was the estimated percentage of patients with GS ≥ 3 + 4 within each individual PI-RADSv2...

CONCLUSION. The data available in the literature are highly heterogeneous and challenging to analyze because of variations in terminology, patient cohort selection, criteria, imaging parameters, and reference standards. In spite of this heterogeneity, our meta-analysis shows that PI-RADSv2 has good sensitivity when a score of ≥ 3 is considered as a positive test.

Keywords: multiparametric MRI (mpMRI), pr... imaging, Prostate Imaging Reporting and Da... (PI-RADS), Prostate Imaging Reporting and ... version 2 (PI-RADSv2)

doi.org/10.2214/AJR.18.20571

Received August 20, 2018; accepted after re... September 30, 2018.

TABLE 1: Prevalence of Prostate Cancer by Gleason Score (GS) and Prostate Imaging Reporting and Data System Version 2 (PI-RADSv2) Suspicion Score

PI-RADSv2 Score	GS 3 + 3	Clinically Significant Cancer			
		GS 3 + 4	GS 4 + 3	GS ≥ 8	
1 or 2	8.0 (2.1–13.9)	5.5 (0.7–10.3)	0.4 (0.0–1.4)	0.06 (0.0–1.1)	6.4
3	14.0 (9.4–18.7)	9.3 (4.3–14.1)	1.5 (0.05–3.0)	0.7 (0.0–1.6)	11.5
4	21.0 (13.0–28.9)	29.7 (13.9–45.5)	7.7 (3.4–12.0)	10.8 (5.7–15.9)	48.2
5	12.0 (5.3–18.7)	33.5 (8.0–59.0)	15.7 (6.4–25.1)	23.0 (8.2–37.9)	72.2

Note—Data are percentages with 95% CIs in parentheses; data are from the following studies: [6, 9, 11–14, 18–20, 22–25].

Original Research

Variability of the Positive Predictive Value of PI-RADS for Prostate MRI across 26 Centers: Experience of the Society of Abdominal Radiology Prostate Cancer Disease-focused Panel

Antonio C. Westphalen, Charles E. McCulloch, Jordan M. Anaokar, Sandeep Arora, Nimrod S. Barashi, Jelle O. Barentsz, Tharakeswara K. Bathala, Leonardo K. Bittencourt, ... See all authors

Table 2: PPVs of PI-RADS

PI-RADS version 2 Score	Estimated Overall PPV (%)		Confidence Interval (%)*	Interquartile Range (%)†
≥2 (*n* = 5030)	31		24, 39	27–44
≥3 (*n* = 4420)	35		27, 43	27–48
≥4 (*n* = 2958)	49		40, 58	34–65
2 (*n* = 610)	5	6.4	3, 7	0–14
3 (*n* = 1462)	15	11.5	11, 19	10–26
4 (*n* = 2071)	39	48.2	34, 45	25–55
5 (*n* = 887)	72	72.2	66, 77	61–82

Radiology

Andrew B. Rosenkrantz, MD
Luke A. Ginocchio, BS
Daniel Cornfeld, MD[2]
Adam T. Froemming, MD
Rajan T. Gupta, MD
Baris Turkbey, MD
Antonio C. Westphalen, MD, PhD
James S. Babb, PhD
Daniel J. Margolis, MD

Interobserver Reproducibility of the PI-RADS Version 2 Lexicon: A Multicenter Study of Six Experienced Prostate Radiologists[1]

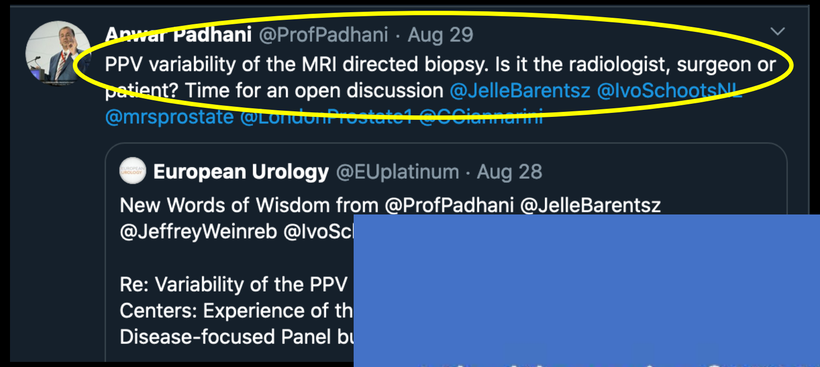
Feature	Session 1	Session 2	Sessions 1 and 2 Combined
Peripheral zone			
Focal (not indistinct) shape on DWI and ADC map	58.3 (70/120)	66.3 (159/240)	63.6 (229/360)
Markedly hyperintense on high-*b*-value DWI	41.7 (50/120)	50.8 (122/240)	47.8 (172/360)
Markedly hypointense on ADC map	42.5 (51/120)	51.7 (124/240)	48.6 (175/360)
Definite extraprostatic extension or invasive behavior on T2-weighted images	16.7 (20/120)	11.7 (28/240)	13.3 (48/360)
Early enhancement in region	75.0 (90/120)	67.1 (161/240)	69.7 (251/360)
Focal early enhancement	48.3 (58/120)	48.8 (117/240)	48.6 (175/360)
Early enhancement that correspond with finding on other sequences	50.8 (61/120)	53.3 (128/240)	52.5 (189/360)
≥15 mm	15.0 (18/120)	14.2 (34/240)	14.4 (52/360)
T2 score ≥3	75.8 (91/120)	83.3 (200/240)	80.8 (291/360)
T2 score ≥4	35.8 (43/120)	45.8 (110/240)	42.5 (153/360)
DWI score ≥3	67.5 (81/120)	76.7 (184/240)	73.6 (265/360)
DWI score ≥4	41.7 (50/120)	50.0 (120/240)	47.2 (170/360)
DCE positive	49.2 (59/120)	49.2 (118/240)	49.2 (177/360)
PI-RADS assessment category ≥3	67.5 (81/120)	76.7 (184/240)	73.6 (265/360)
PI-RADS assessment category ≥4	52.5 (63/120)	60.8 (146/240)	58.1 (209/360)
Transition zone			
Circumscribed (vs obscured) margins	62.5 (75/120)	57.9 (139/240)	59.6 (211/360)
Encapsulated	31.7 (38/120)	27.5 (66/240)	28.9 (104/360)
Heterogeneous (vs homogeneous)	60.8 (73/120)	64.2 (154/240)	63.1 (227/360)
Moderately hypointense	94.2 (113/120)	95.4 (229/240)	95.0 (342/360)
Lenticular shape	6.7 (8/120)	25.0 (60/240)	18.9 (68/360)
Definite extraprostatic extension or invasive behavior on T2-weighted imaging	12.5 (15/120)	17.9 (43/240)	16.1 (58/360)
Focal (vs indistinct) shape on DWI and ADC map	81.7 (98/120)	89.2 (214/240)	86.7 (312/360)
Markedly hyperintense on high-*b*-value DWI	53.3 (64/120)	62.1 (149/240)	59.2 (213/360)
Markedly hypointense on ADC map	55.0 (66/120)	70.0 (168/240)	65.0 (234/360)
≥15 mm	35.0 (42/120)	41.3 (99/240)	39.2 (141/360)
T2 score ≥3	71.7 (86/120)	76.7 (184/240)	75.0 (270/360)
T2 score ≥4	47.5 (57/120)	49.2 (118/240)	48.6 (175/360)
DWI score ≥3	80.8 (97/120)	92.1 (221/240)	88.3 (318/360)
DWI score ≥4	53.3 (64/120)	63.8 (153/240)	60.3 (217/360)
PI-RADS assessment category ≥3	71.7 (86/120)	76.7 (184/240)	75.0 (270/360)
PI-RADS assessment category ≥4	48.3 (58/120)	52.1 (125/240)	50.8 (183/360)
Peripheral and transition zones combined			
PI-RADS assessment category ≥3	69.6 (167/240)	76.7 (368/480)	74.3 (535/720)
PI-RADS assessment category ≥4	50.4 (121/240)	56.5 (271/480)	54.4 (392/720)

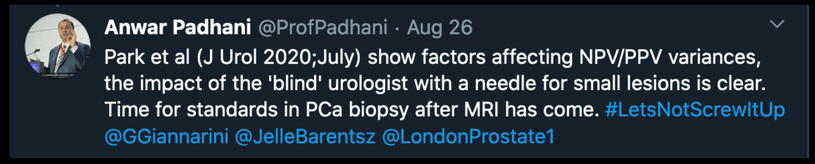
	κ Value			Percent Agreement			
Feature	Session 1	Session 2	Overall	Session 1 (%)	Session 2 (%)	*P* Value*	Overall (%)
PZ							
Focal (vs indistinct) shape on DWI and ADC map	0.630	0.611	0.619	82.0	82.5	.853	82.3
Markedly hyperintense on high-*b*-value DWI	0.524	0.535	0.535	76.7	76.7	>.999	79.1
Markedly hypointense on ADC map	0.611	0.533	0.562	81.0	76.7	.139	71.8
Definite extraprostatic extension or invasive behavior on T2-weighted images	0.281	0.289	0.289	80.0	85.3	.043	84.9
Early enhancement in region	0.163	0.305	0.266	68.0	69.2	.722	68.8
Focal early enhancement	0.385	0.470	0.439	68.7	73.5	.129	71.9
Early enhancement that correspond with finding on other sequences	0.363	0.404	0.387	67.0	70.3	.307	69.2
≥15 mm	0.359	0.452	0.418	83.3	86.7	.181	85.6
T2 score ≥3	0.333	0.124	0.215	75.7	75.7	>.999	75.7
T2 score ≥4	0.497	0.550	0.529	75.7	77.7	.770	77.0
DWI score ≥3	0.613	0.479	0.534	83.0	81.3	.541	81.9
DWI score ≥4	0.699	0.574	0.617	85.3	78.7	.017	80.9
DCE positive	0.380	0.453	0.426	68.3	72.7	.176	71.2
PI-RADS assessment category ≥3	0.613	0.479	0.534	83.0	81.3	.541	81.9
PI-RADS assessment category ≥4	0.637	0.567	0.593	81.7	79.3	.409	80.1
TZ							
Circumscribed (vs obscured) margins	0.348	0.232	0.267	69.0	61.8	.035	64.2
Encapsulated	0.600	0.490	0.529	82.7	79.7	.283	80.7
Heterogeneous (vs homogeneous)	0.405	0.362	0.378	71.7	70.7	.755	71.0
Moderately hypointense	0.001	0.221	0.136	89.0	93.2	.034	91.8
Lenticular shape	0.036	0.531	0.472	88.0	81.7	.016	83.8
Definite extraprostatic extension or invasive behavior on T2-weighted imaging	0.348	0.303	0.318	85.7	79.5	.025	81.6
Focal (vs indistinct) shape on DWI and ADC map	0.360	0.365	0.370	80.7	87.7	.006	85.3
Markedly hyperintense on high-*b*-value DWI	0.612	0.381	0.465	80.7	70.8	.039	74.1
Markedly hypointense on ADC map	0.583	0.357	0.453	79.3	73.0	.002	75.1
≥15 mm	0.575	0.708	0.667	80.7	85.8	.046	84.1
T2 score ≥3	0.387	0.383	0.386	74.7	77.3	.374	76.4
T2 score ≥4	0.419	0.461	0.447	71.0	73.0	.527	72.3
DWI score ≥3	0.302	0.348	0.343	78.3	90.5	<.001	86.4
DWI score ≥4	0.518	0.356	0.418	76.0	70.2	.066	72.1
PI-RADS assessment category ≥3	0.387	0.383	0.386	74.7	77.3	.374	76.4
PI-RADS assessment category ≥4	0.426	0.550	0.509	71.3	77.5	.043	75.4
PZ and TZ combined							
PI-RADS assessment category ≥3	0.501	0.428	0.458	78.8	79.3	.806	79.2
PI-RADS assessment category ≥4	0.531	0.561	0.552	76.5	78.4	.357	77.8

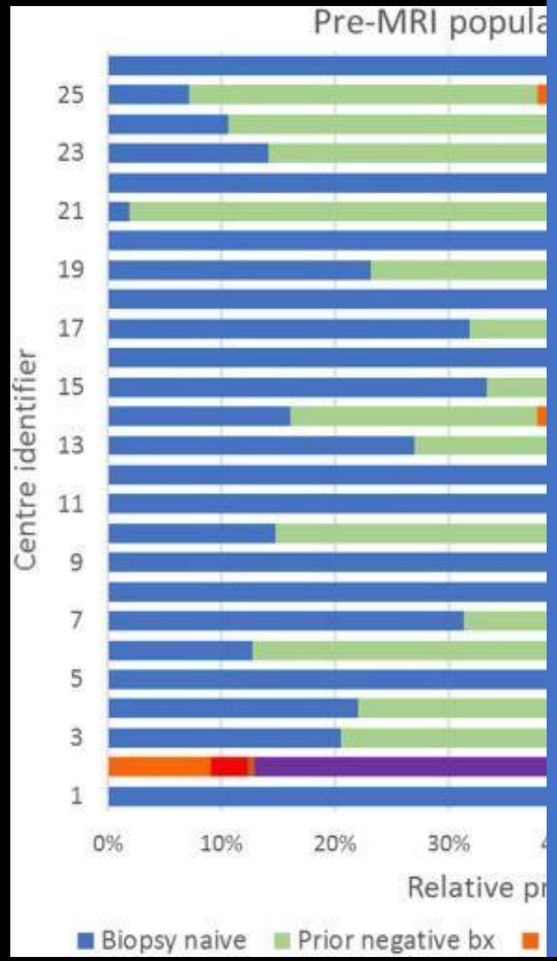
Moderate reproducibility

Agreement PZ > TZ

PI-RADS is not as objective as it may seem to be.





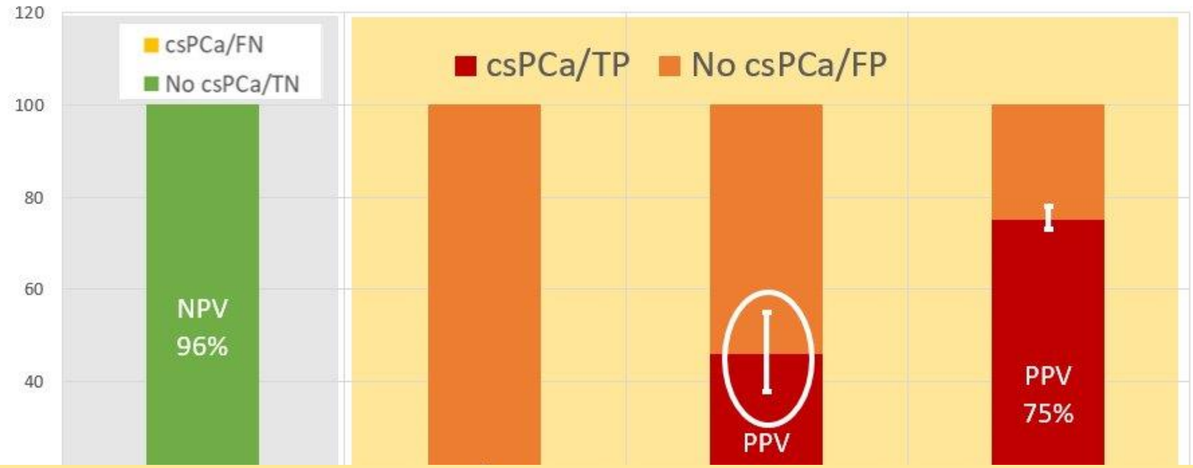


Likelihood of ISUP≥2 according to PI-RADS v2 lesion category

13 prospective studies
4265 mixed population
4641 patients/lesions
bp/mp studies

Park KJ, et al. Risk Stratification of Prostate Cancer According to PI-RADS Version 2 Categories: Meta-analysis for Prospective Studies. J Urol 2020 [Epub]

PI-RADS 5 lesions are large, PI-RADS 4 could measure only a few mm

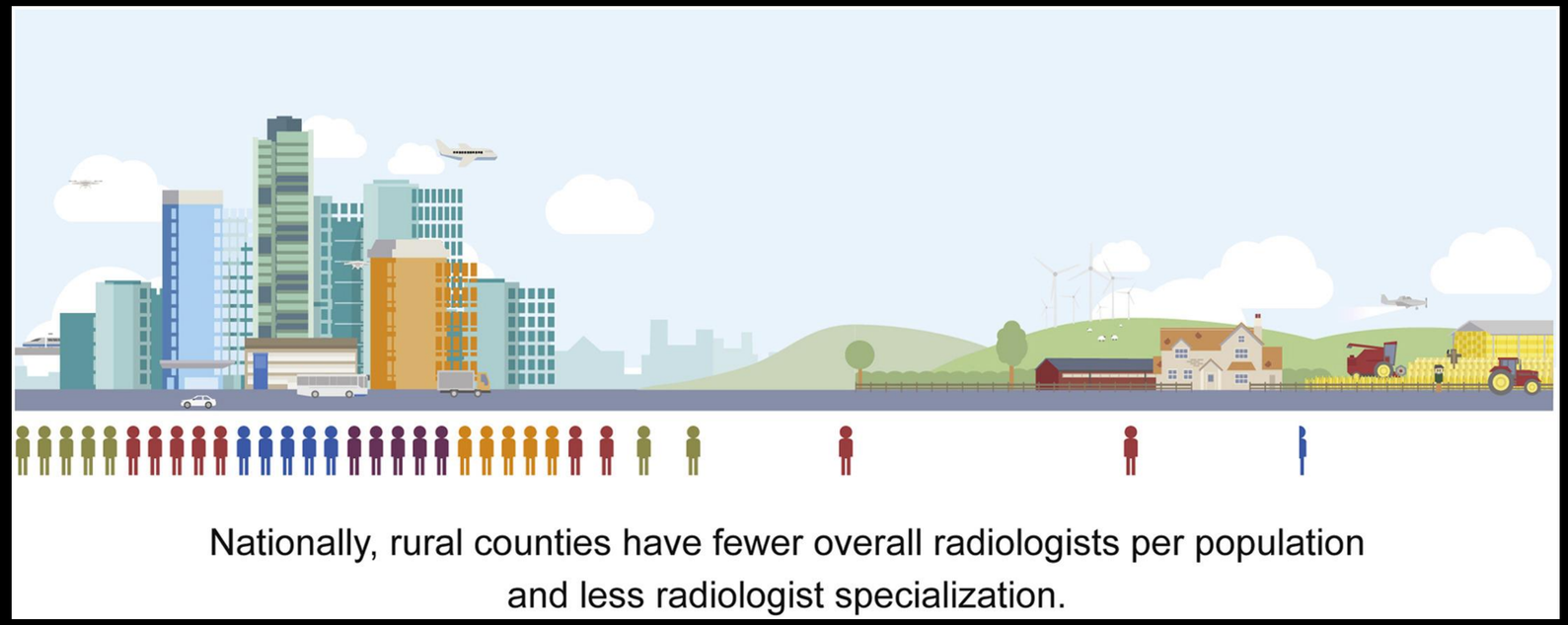


Adherence to technical standards
MR image quality
Reader expertise
Suspicion threshold for biopsy
Biopsy method and operator expertise
Histopathology definition & expertise
Teamwork

PI-RADS is …


NOT PERFECT...
but good & getting better.

mpMRI is not PI-RADS



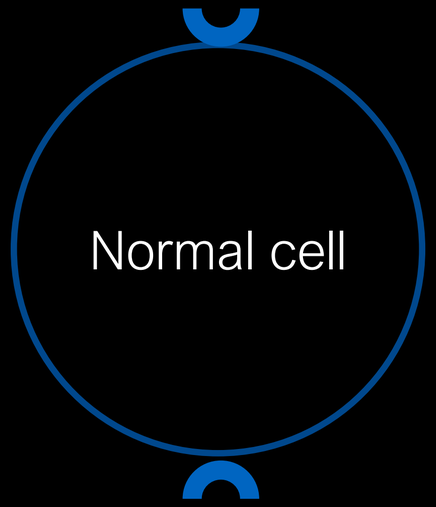
Rosenkrantz AB.. JACR 2018 15 (4):601-6.

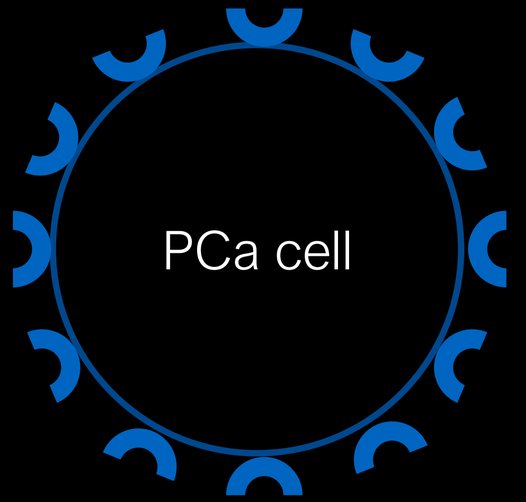
Molecular imaging

PSMA

PSMA imaging agents

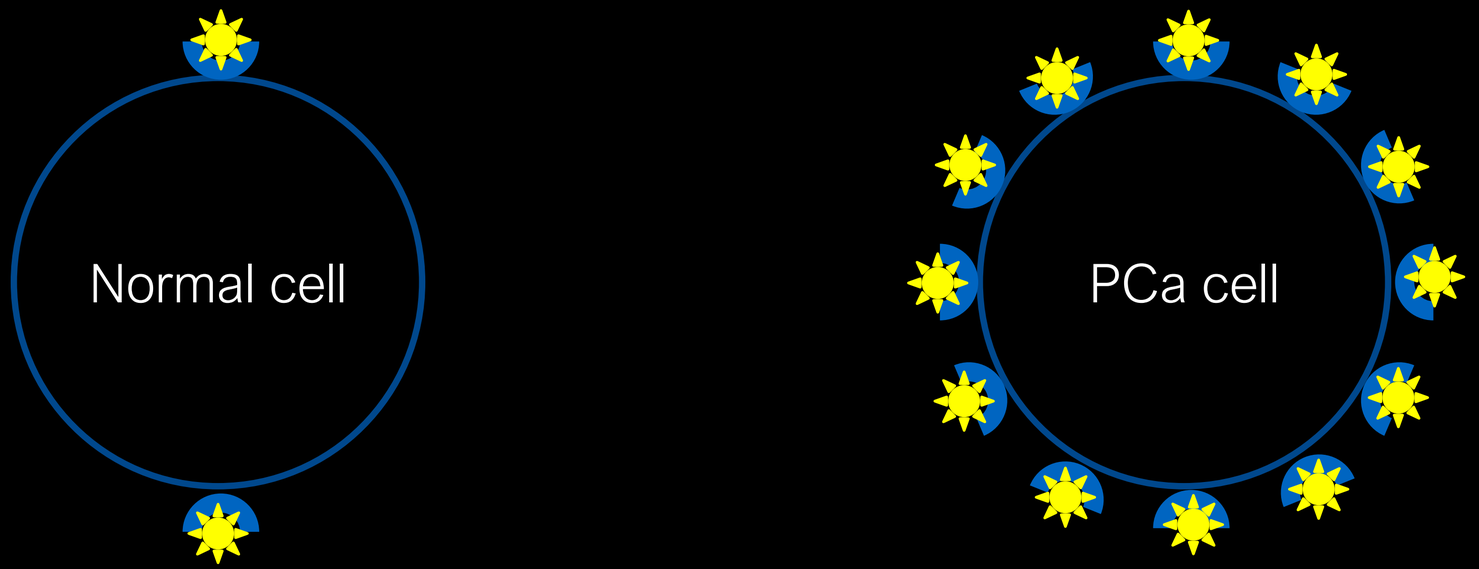
- The prostate-specific membrane antigen (PSMA) is a transmembrane protein that is overexpressed in most prostate cancers.



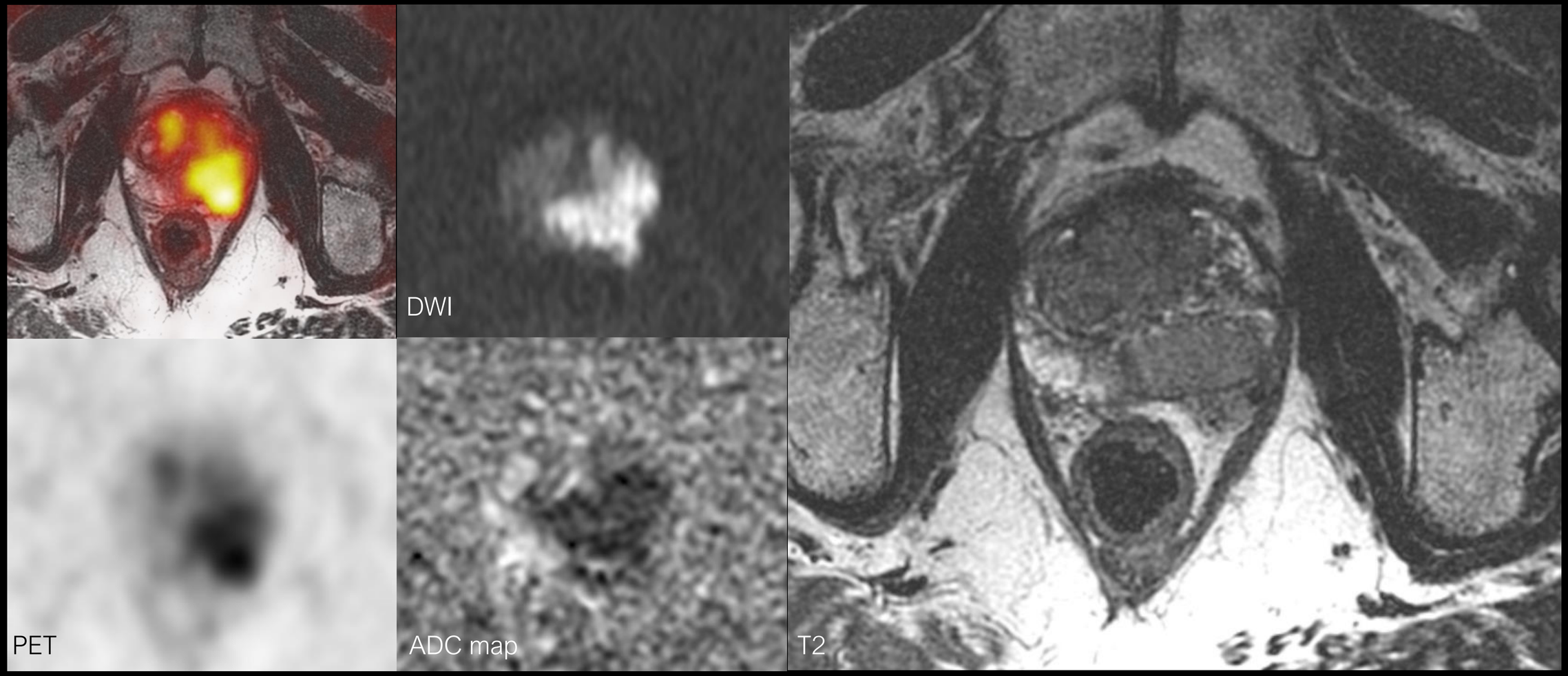


PSMA imaging agents

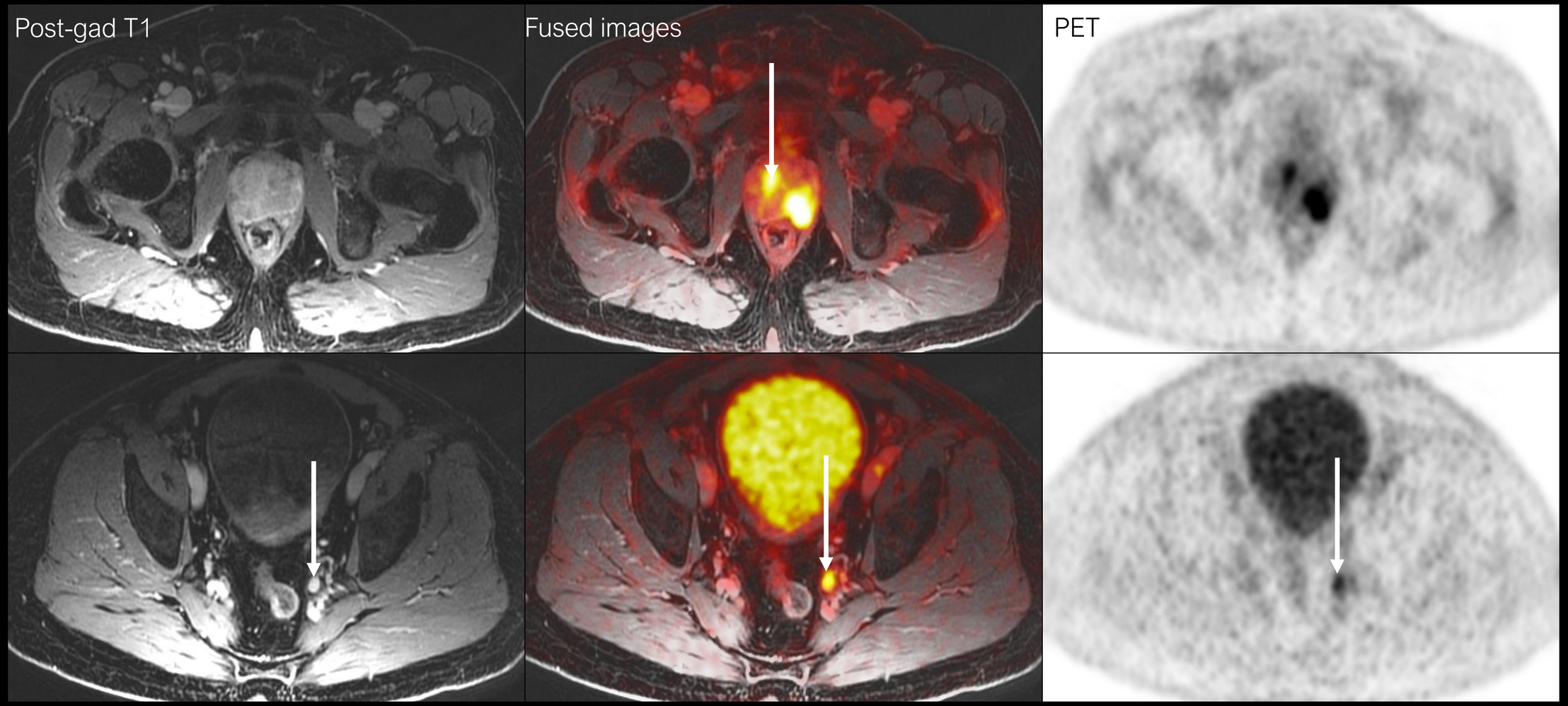
- Several radionuclides can be ligated to the same urea moiety of the PSMA protein and used for imaging. These include ^{68}Ga-PSMA-11, and indium (^{111}In) and fluorinated (^{18}F) agents.



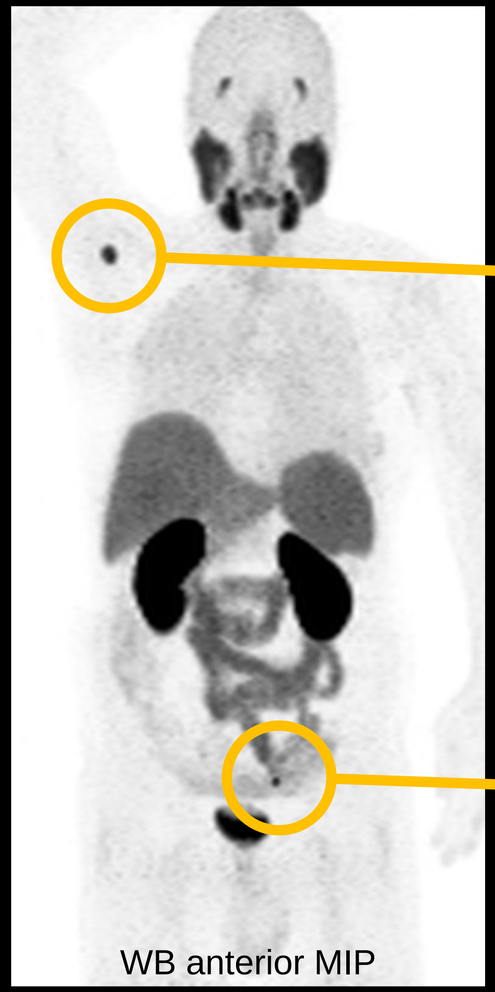
72 years old, Gleason 4+4



72 years old, Gleason 4+4

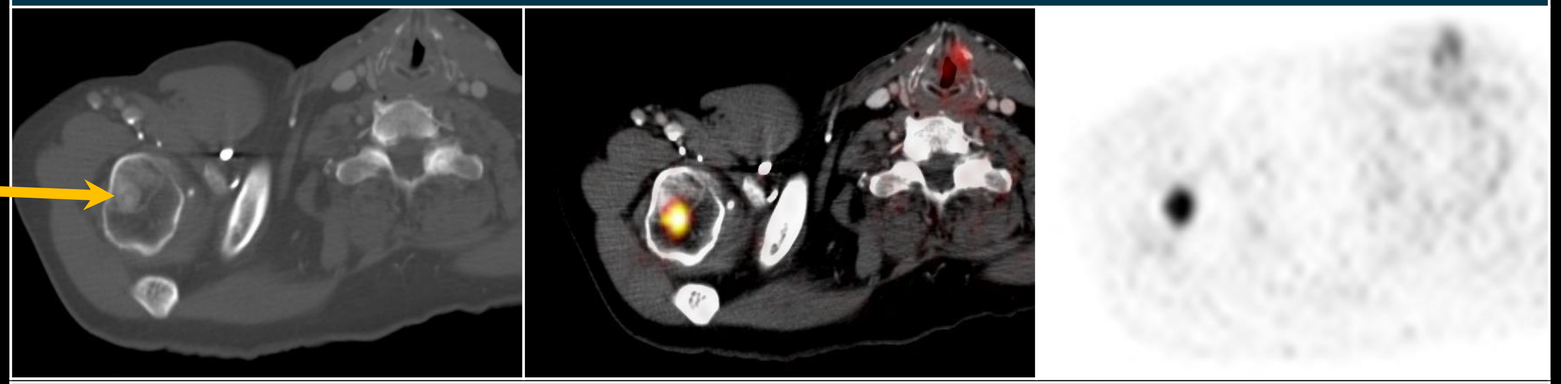


69 years old, S/P RP, PSA = 0.67 ng/ml

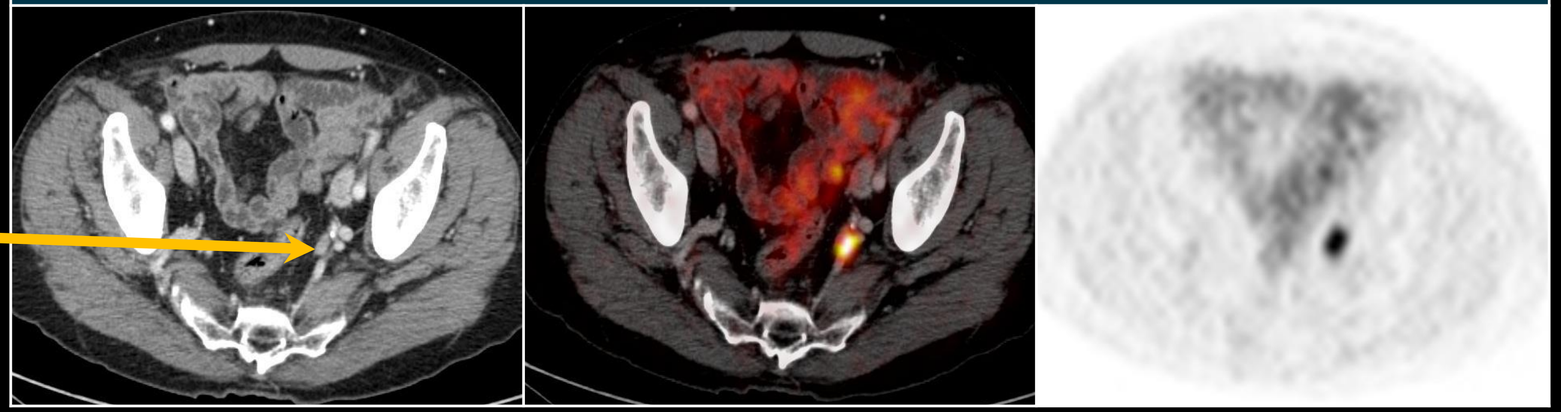


WB anterior MIP

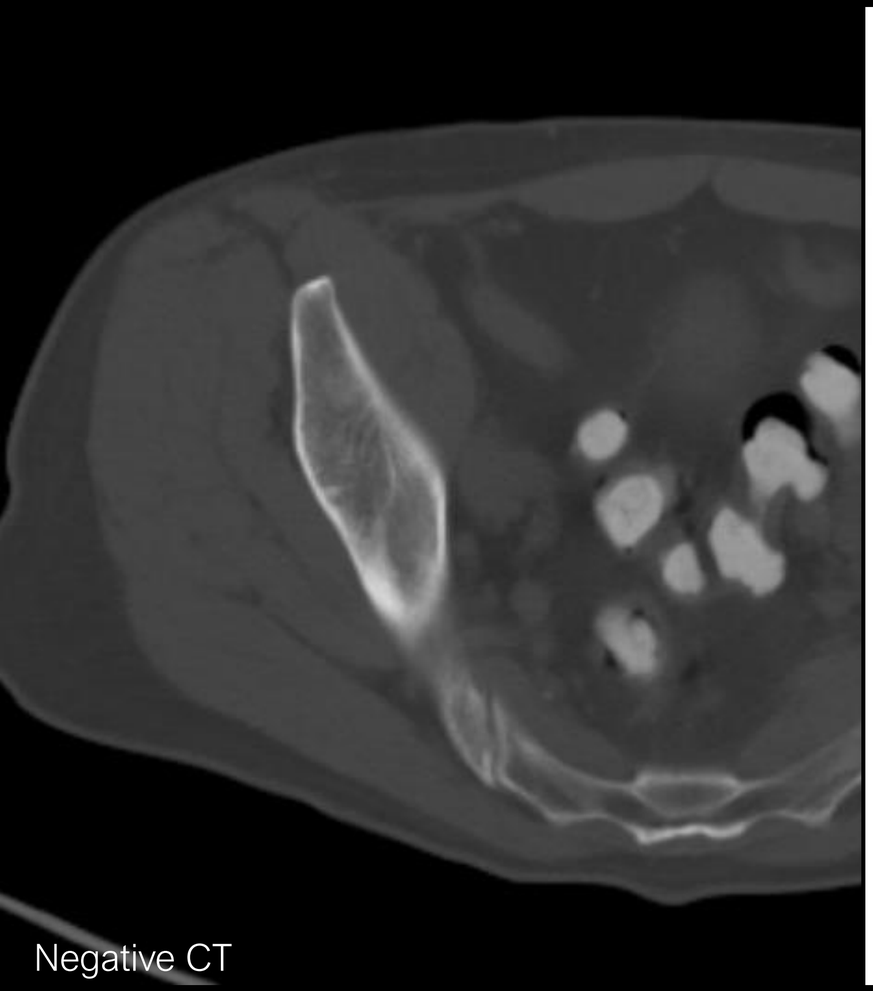
Disease site 1: right humerus



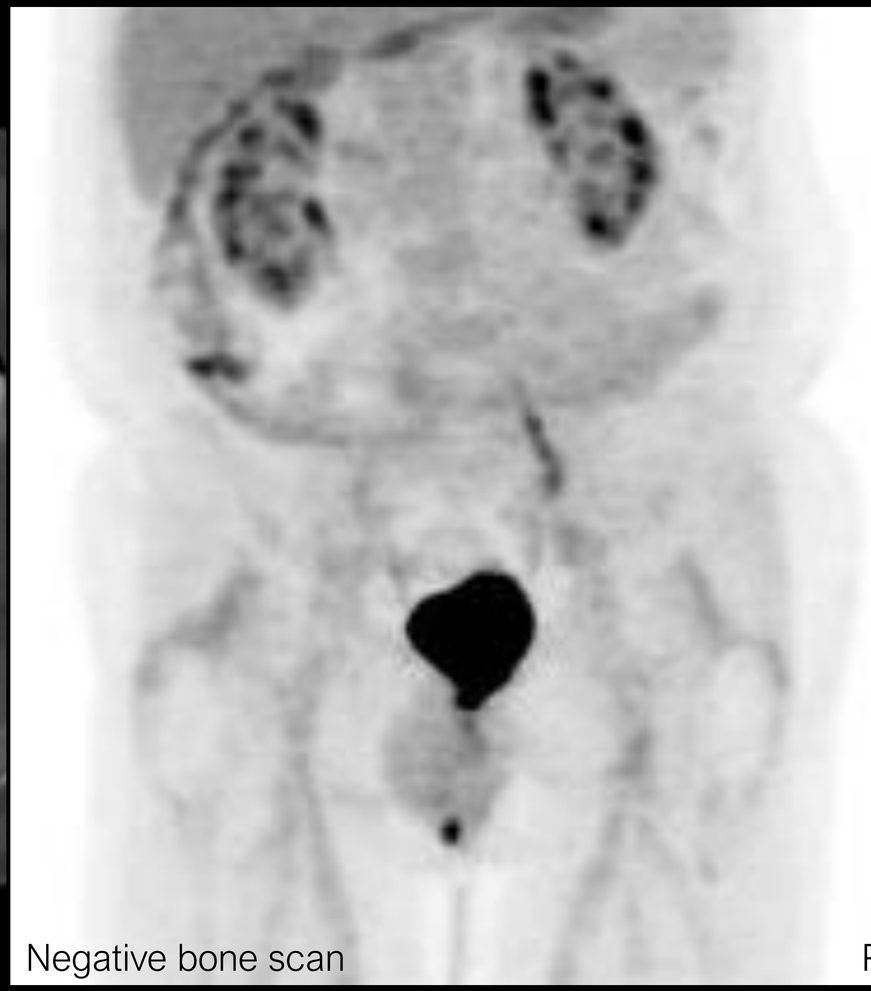
Disease site 2: left internal iliac node



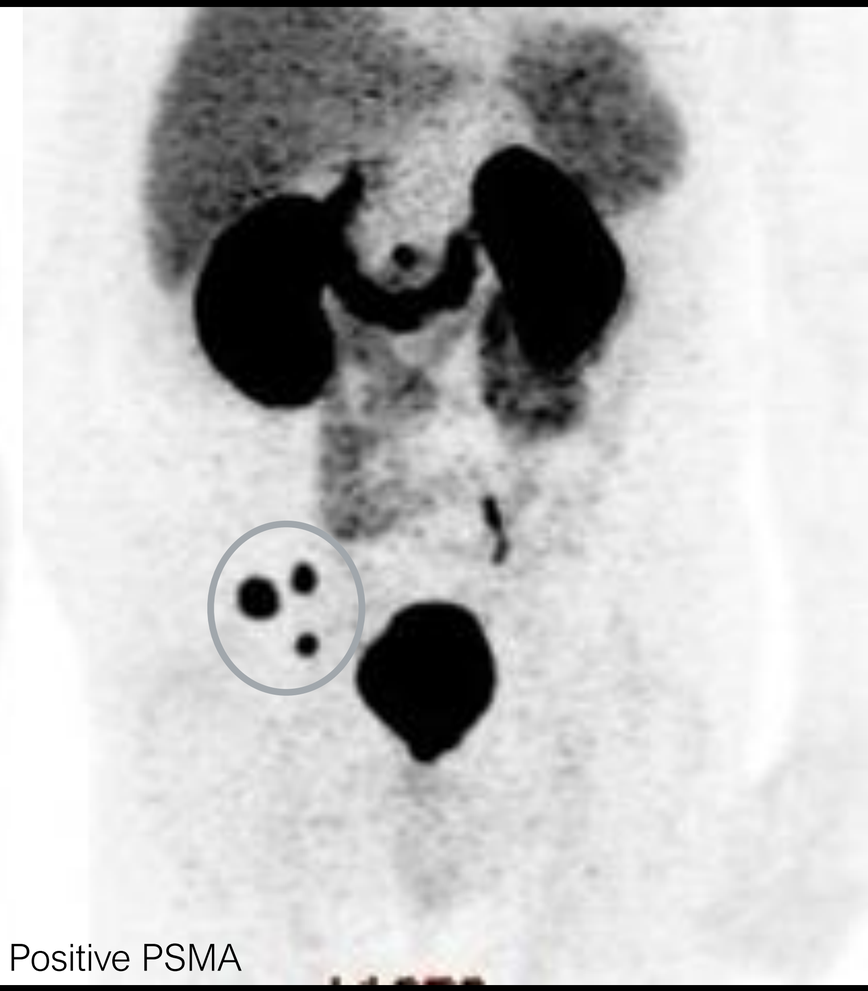
69 year old, S/P RP, PSA = 3.5 ng/ml



Negative CT



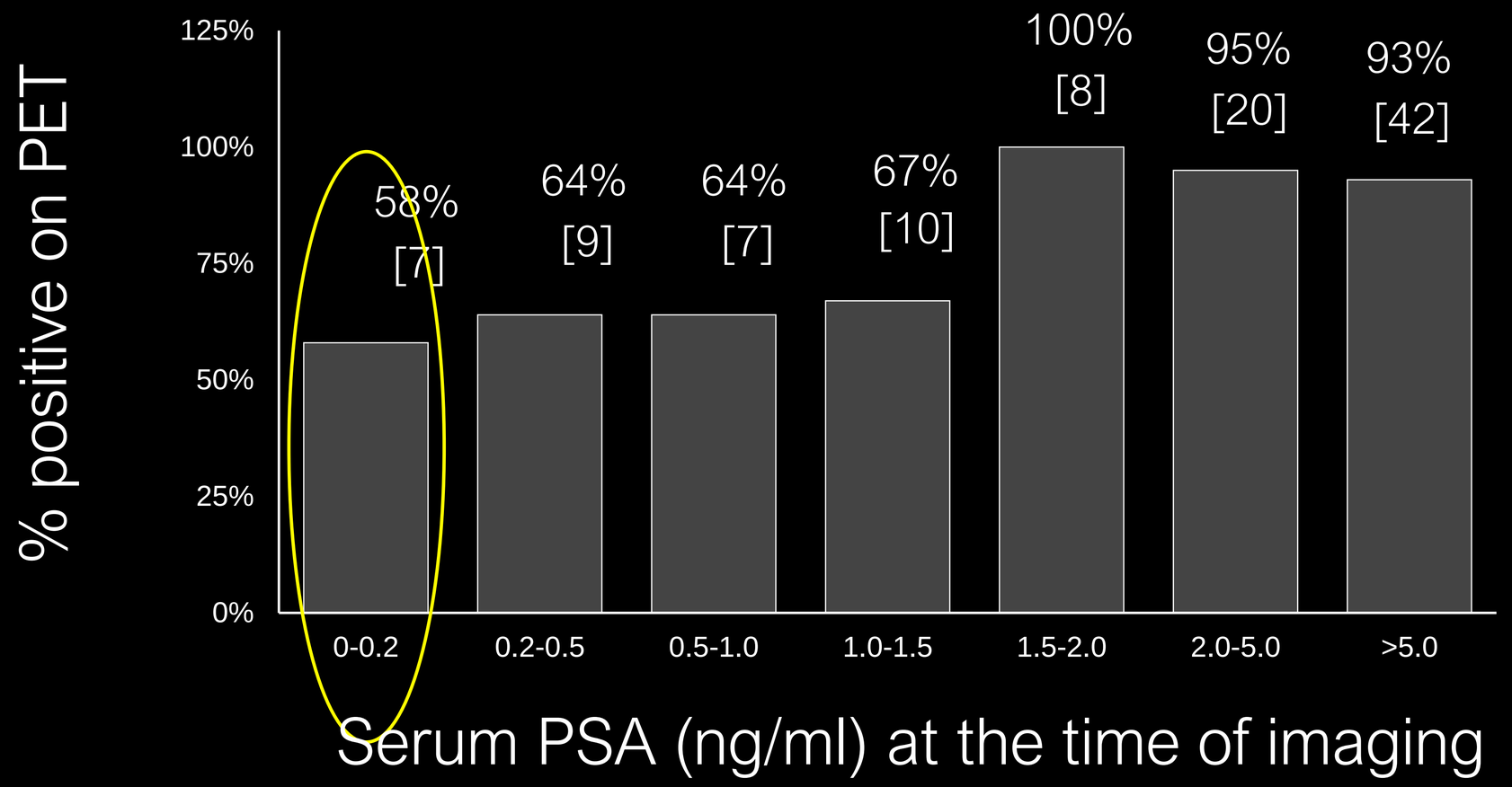
Negative bone scan



Positive PSMA

S/P RP

rate positive PSMA by serum PSA

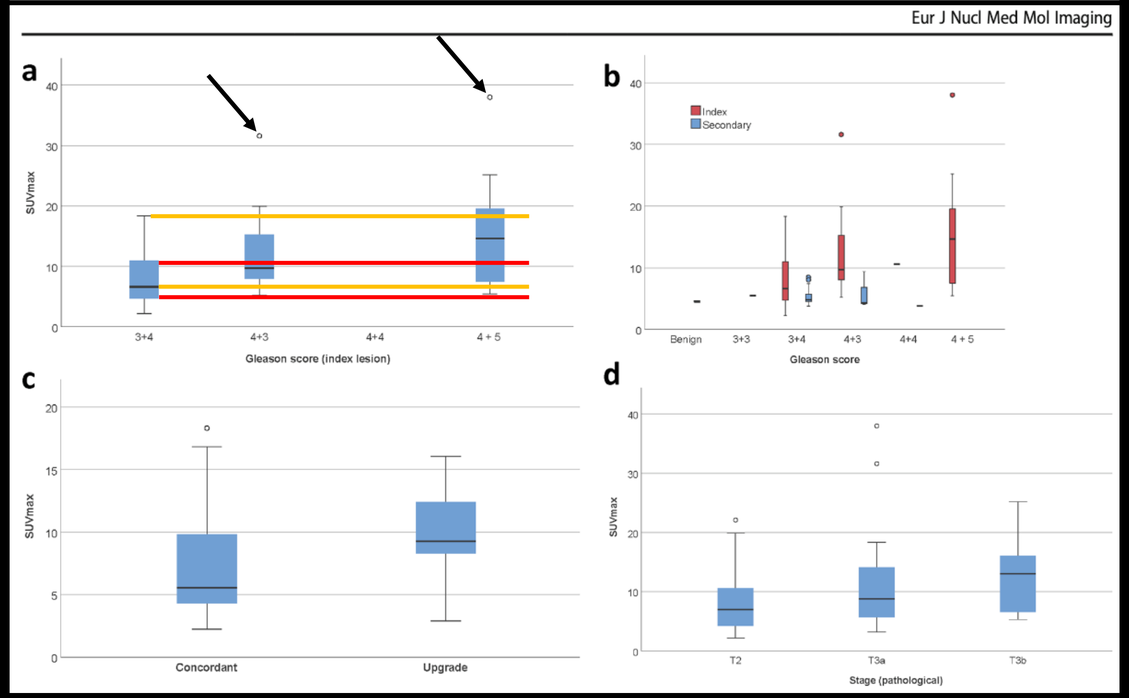


PSMA and active surveillance

^{68}Ga-PSMA PET/CT tumour intensity pre-operatively predicts adverse pathological outcomes and progression-free survival in localised prostate cancer

European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-020-04944-2

Matthew J. Roberts[1,2,3,4] · Andrew Morton[4] · Peter Donato[1,4] · Samuel Kyle[4,5] · David A. Pattison[4,5] · Paul Thomas[4,5] · Geoff Coughlin[1] · Rachel Esler[1] · Nigel Dunglison[1] · Robert A. Gardiner[1,2,6,7] · Suhail A. Doi[8] · Louise Emmett[9,10] · John Yaxley[1,4]



There is non-negligible overlap of SUV_{max}

Results may look better due to outliers

No ISUP grade group 1

PSMA and active surveillance

Original article

Nuclear Medicine Communications

Can SUVmax values of Ga-68-PSMA PET/CT scan predict the clinically significant prostate cancer?

Emre Demirci[a], Levent Kabasakal[b], Onur E. Şahin[b], Elife Akgün[b], Mehmet Hamza Gültekin[c], Tünkut Doğanca[d], Mustafa B. Tuna[e], Can Öbek[d], Mert Kılıç[f], Tarık Esen[g] and Ali R. Kural[h]

Fig. 2

Nuclear Medicine Communications 2019; 40:86-91

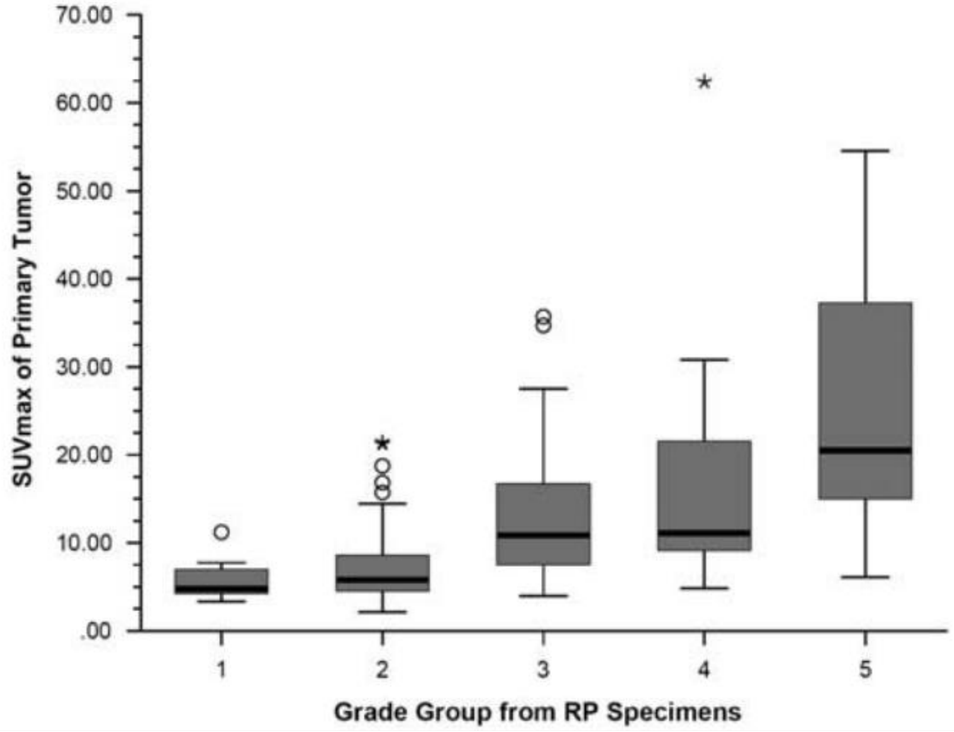
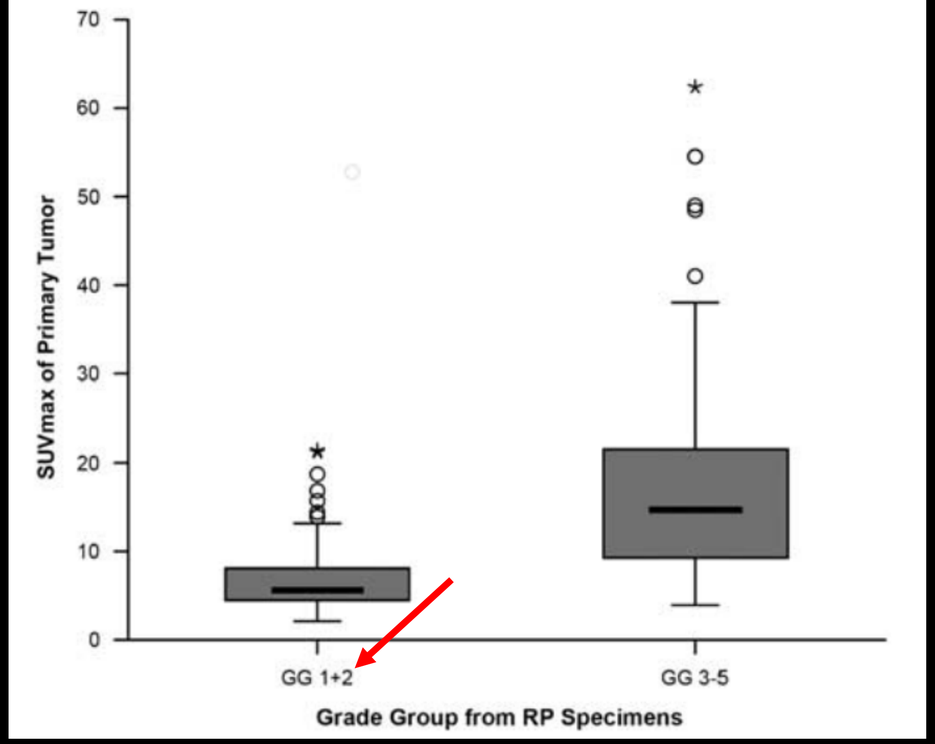


Fig. 3



RP, n = 141

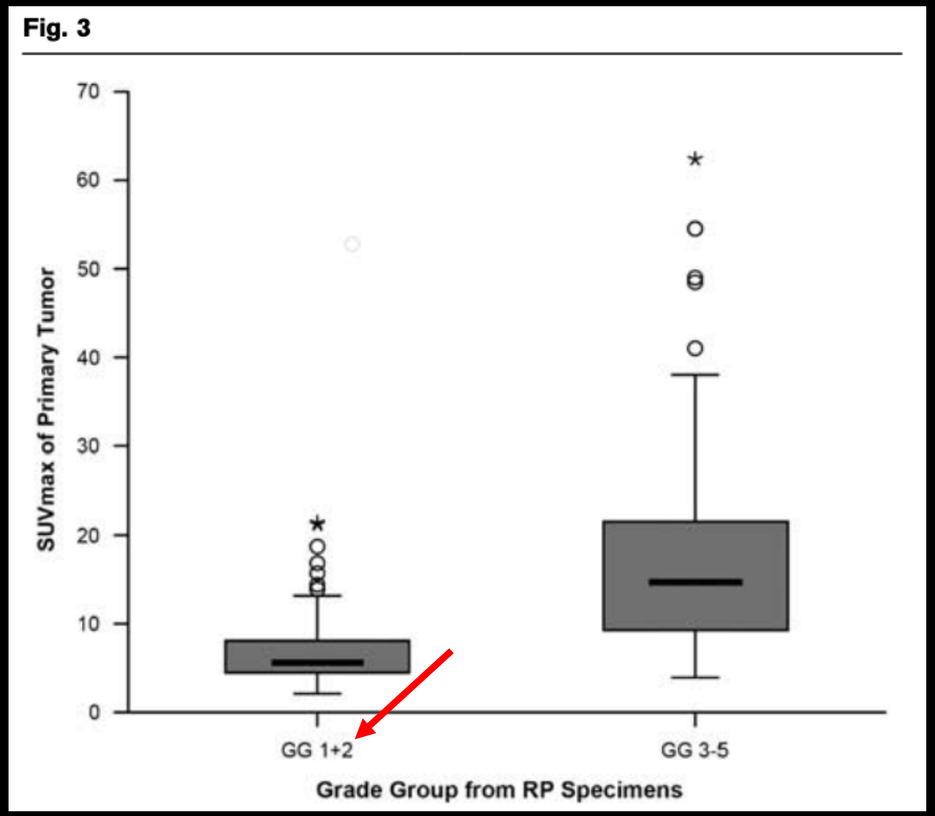
SUVmax positively correlates with GG

PSMA and active surveillance

GG2 cancers SUV_{max} overlap with higher GG

GG1 PCa may indeed have lower uptake

Small number of GG1 tumors (n=10)



RP, n = 141
SUVmax positively correlates with GG

PSMA and active surveillance

Data is too scarce and preliminary

PSMA is not yet FDA approved for clearly adequate indications

It should be seen as investigational in the setting of AS

Micro-Ultrasound

Disclaimer: I do not have any personal experience

Micro-ultrasound

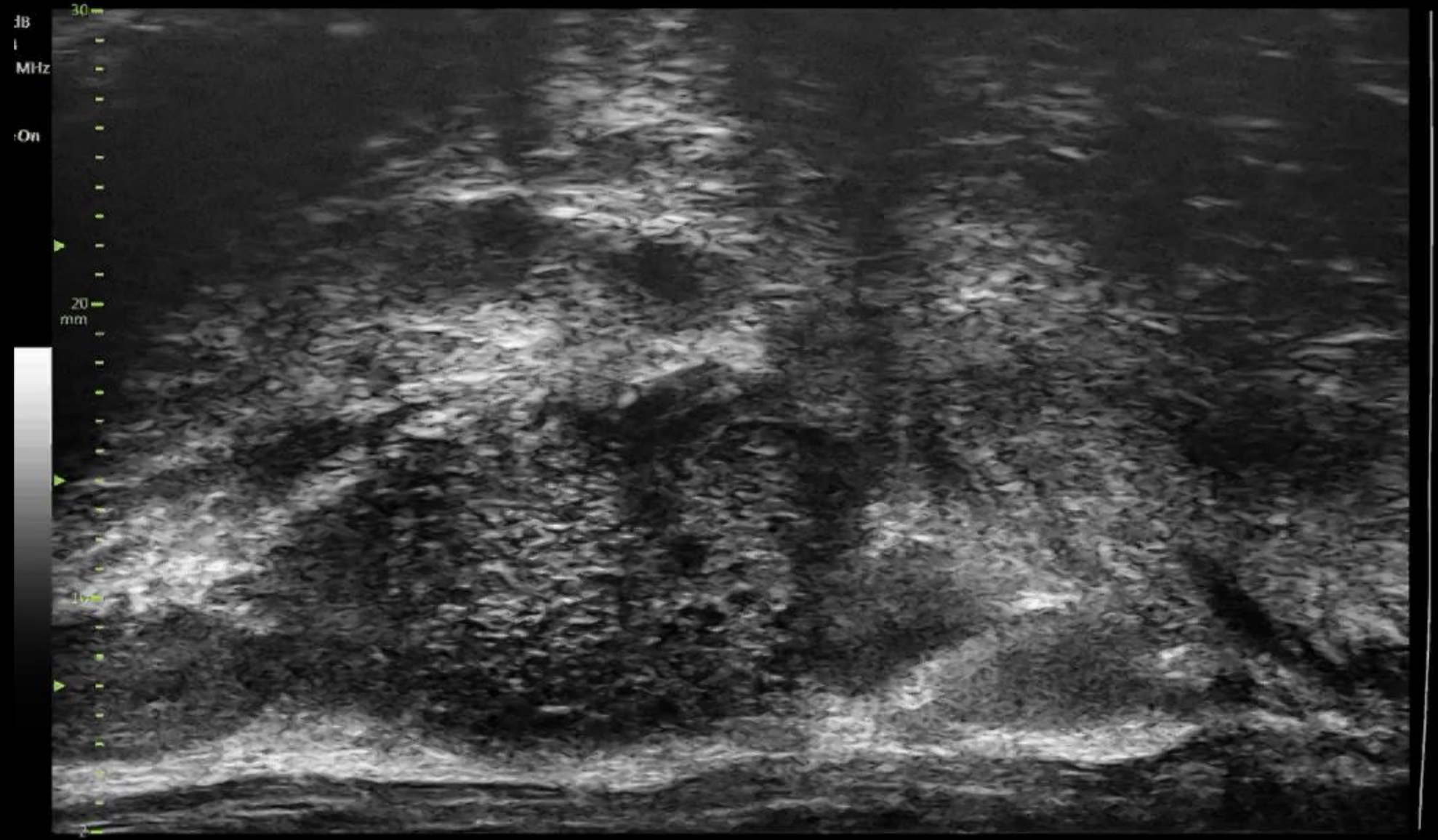
- Novel ultrasound-based system **operating at 29 MHz**
- Much higher than conventional 6-9 MHz systems

- **300% improvement in resolution (**down to 70 microns)

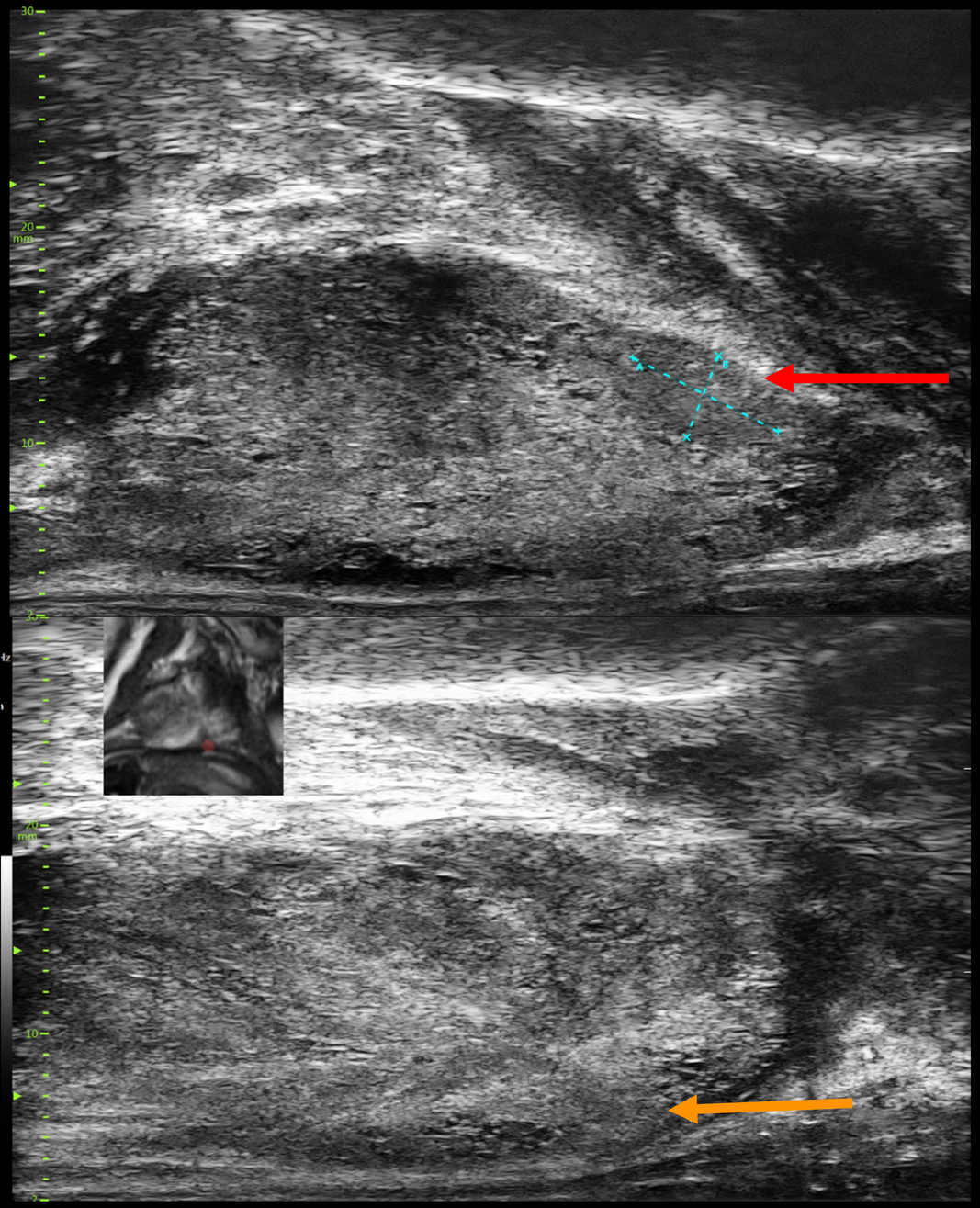
- Visualizes suspicious areas using **PRI-MUS™**

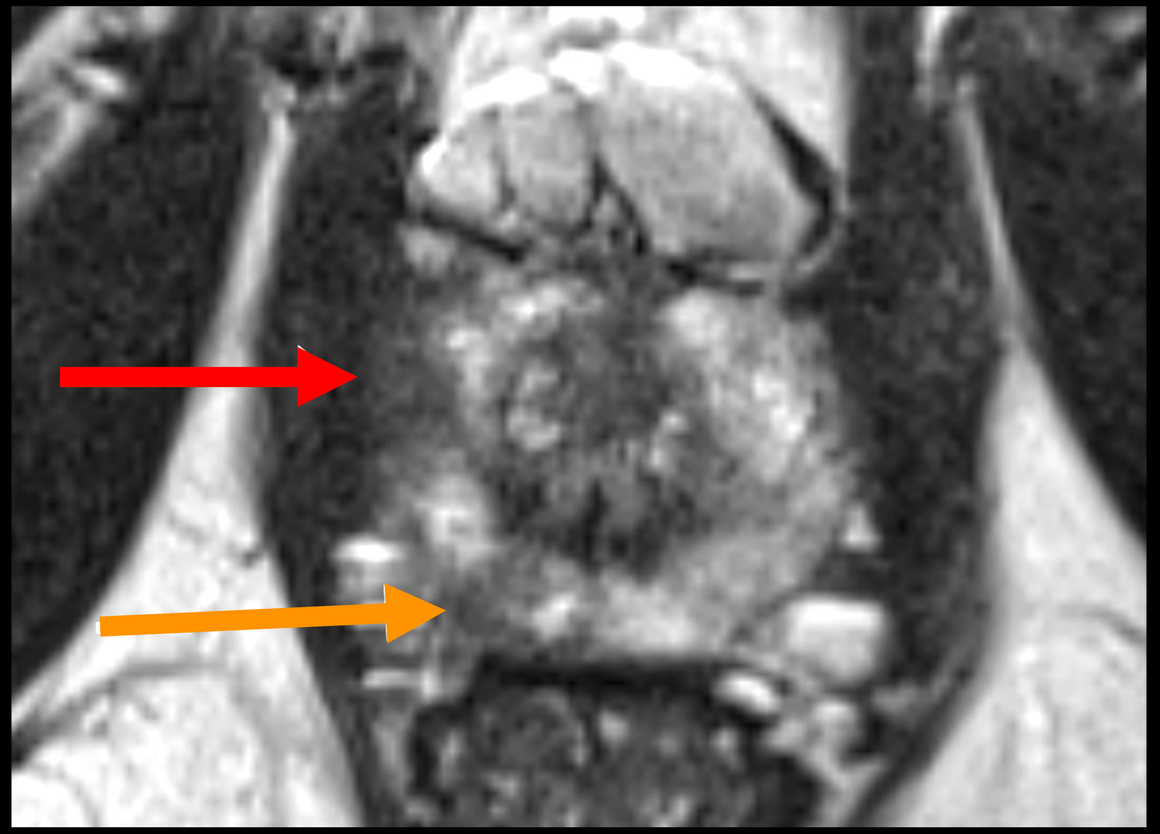
- **Consistent with traditional TRUS** set up and technique
- Technologically friendly for all ho perform traditional TRUS

Courtesy Dr. Sangeet Ghai, University of Toronto



Courtesy Dr. Sangeet Ghai, University of Toronto





Courtesy Dr. Sangeet Ghai, University of Toronto

Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: A multicenter, prospective analysis

Klotz, L., Lughezzani, G., Maffei, D., Sanchez, A., Pereira, J. G., Staerman, F., Cash, H., Luger, F., Lopez, L., Sanchez-Salas, R., Abouassally, R., Shore, N. D., & Eure, G. (2020). Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: A multicenter, prospective analysis. *Canadian Urological Association Journal*, *15*(1). https://doi.org/10.5489/cuaj.6712

1040 men, 11 institutions, 7 countries

Positive test = PI-RADS ≥ 3, PRIMUS ≥ 3
Outcome = GG ≥ 2 on targeted and/or systematic biopsy

µUS more sensitive than and as specific as MRI (PI-RADS)

Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: A multicenter, prospective analysis

Klotz, L., Lughezzani, G., Maffei, D., Sanchez, A., Pereira, J. G., Staerman, F., Cash, H., Luger, F., Lopez, L., Sanchez-Salas, R., Abouassally, R., Shore, N. D., & Eure, G. (2020). Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: A multicenter, prospective analysis. *Canadian Urological Association Journal*, *15*(1). https://doi.org/10.5489/cuaj.6712

Promising, but there are limitations.

Heterogeneity of protocol:

ity. There was substantial variation between sites. Micr

- µUS done after MRI (target identification)
- biopsy of borderline lesions (i.e. scores 3), or not
- TRUS/MRI fusion targeting, or not (plus other examples)

Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: A multicenter, prospective analysis

Klotz, L., Lughezzani, G., Maffei, D., Sanchez, A., Pereira, J. G., Staerman, F., Cash, H., Luger, F., Lopez, L., Sanchez-Salas, R., Abouassally, R., Shore, N. D., & Eure, G. (2020). Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: A multicenter, prospective analysis. *Canadian Urological Association Journal*, *15*(1). https://doi.org/10.5489/cuaj.6712

Table 2. Performance metrics comparing mpMRI and micro-ultrasound

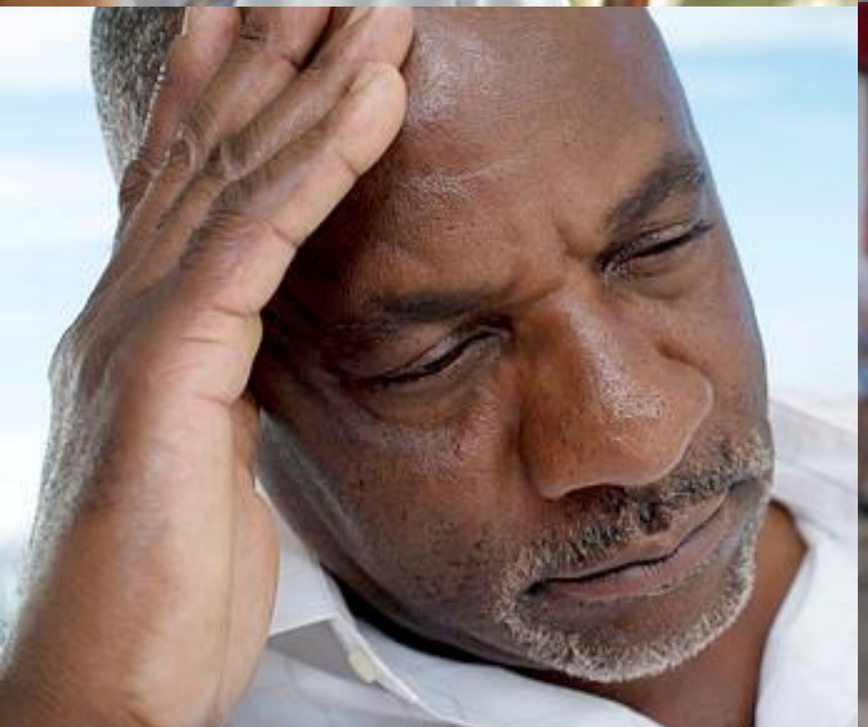
A. For detection of GG ≥2 PCa (39% of cases)

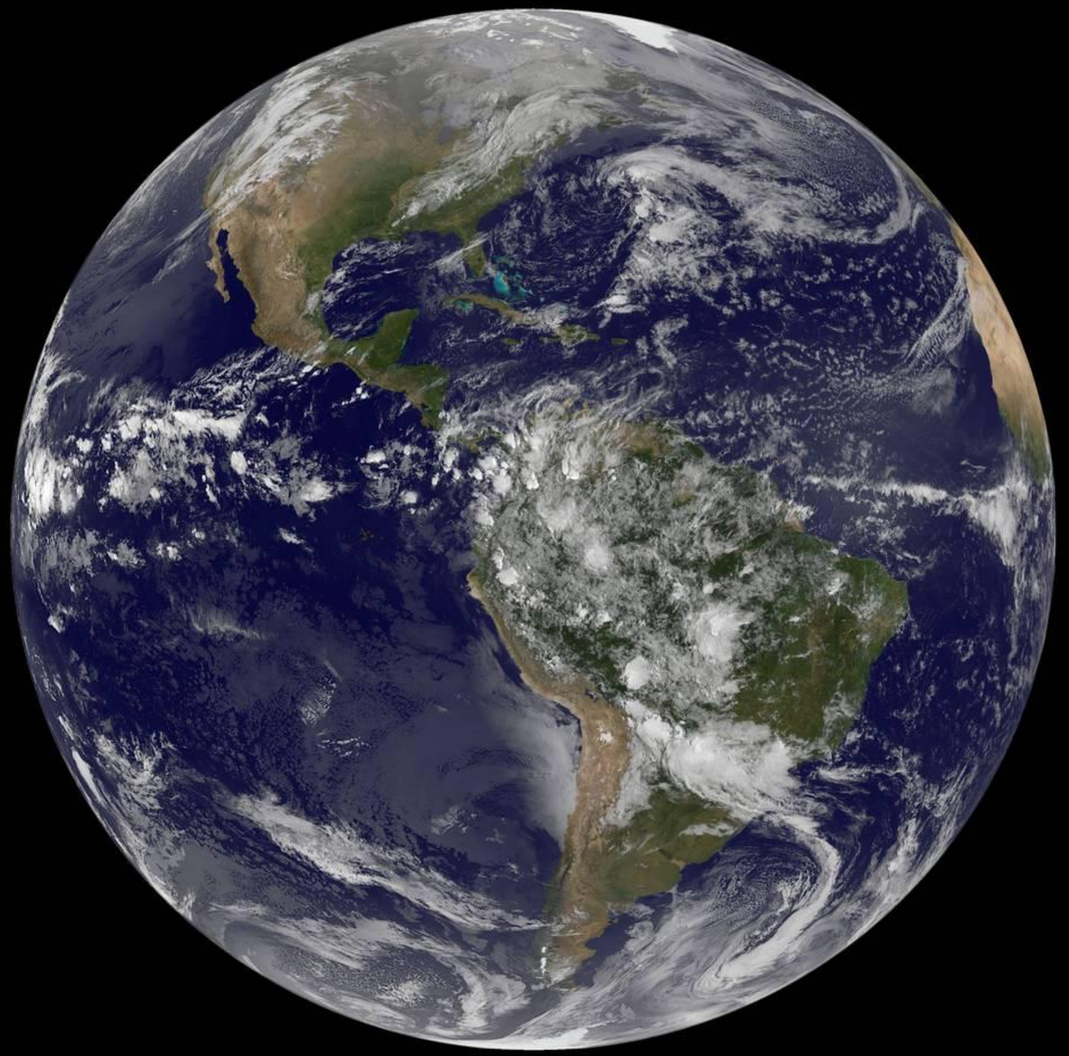
Modality	Sensitivity	Specificity	PPV	NPV
mpMRI	90% (371/411)	22% (136/629)	43% (371/864)	77% (136/176)
Micro-ultrasound	94% (386/411)	22% (138/629)	44% (386/877)	85% (138/163)
p (non-inferiority)	<0.001	<0.001	<0.001	<0.001
p-value (superior)	0.03	0.45	0.32	0.04

Value of Micro-Ultrasound

TBD





Summary

- mpMRI of the prostate is not perfect …

  but it is a marked improvement compared to what we had before

  and it is an excellent addition to the AS toolbox!

THANK YOU!

acwestph@uw.edu

Twitter @acw_rad