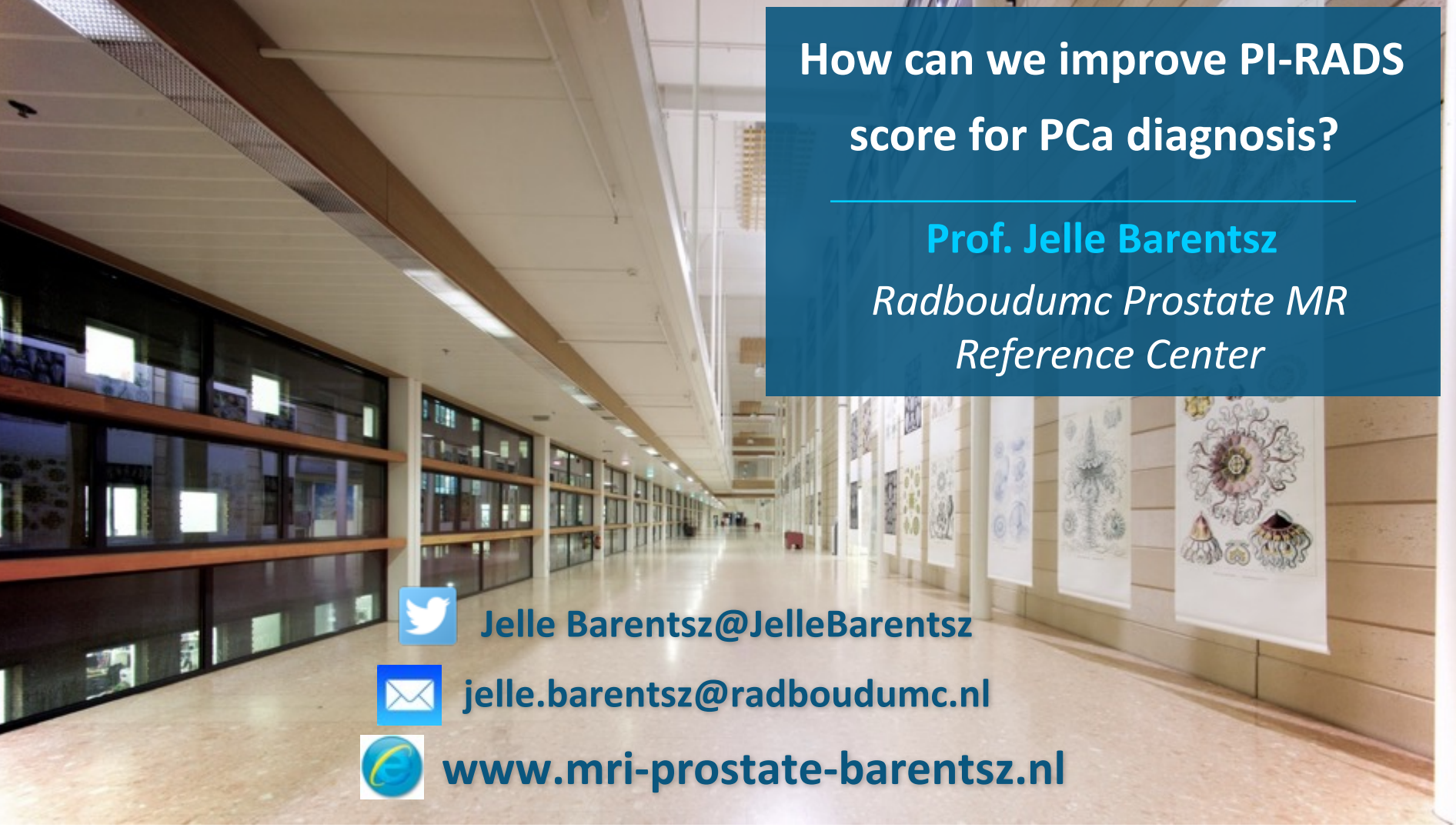


How can we improve PI-RADS score for PCa diagnosis?

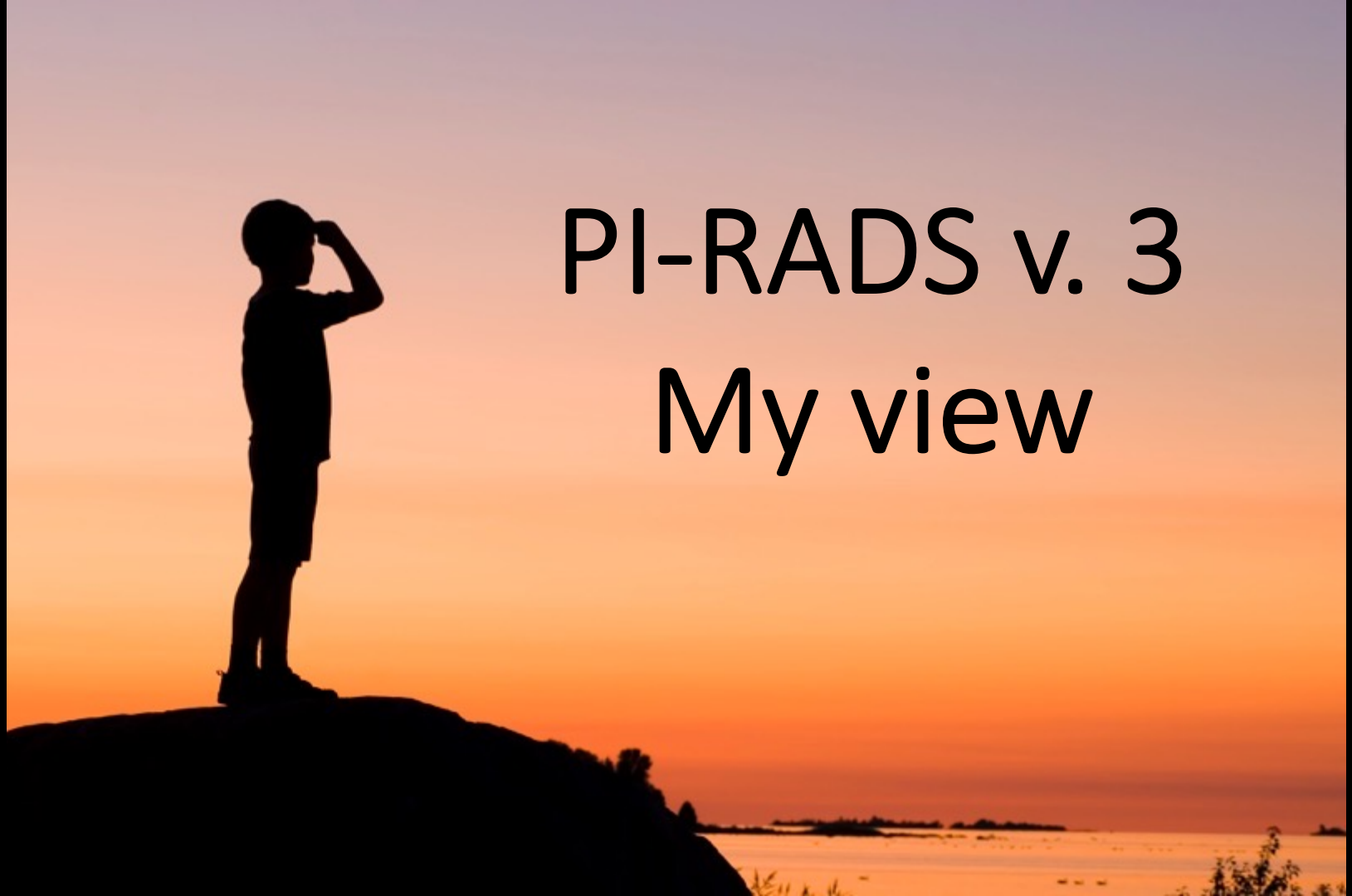
Prof. Jelle Barentsz

Radboudumc Prostate MR Reference Center

Jelle Barentsz@JelleBarentsz

jelle.barentsz@radboudumc.nl

www.mri-prostate-barentsz.nl


PI-RADS v. 3
My view

DEFINITION S-PCa

Definition

What is sPCa?

Table 6 – Definition of clinically significant disease

Study (year)	Clinically significant disease
[25] (2014) [a]	UCL1 / UCL2 / Gleason 3 + 4 or higher / Gleason 4 + 3 or higher / CCL_{max} ≥6 mm / CCL_{max} ≥4 mm
[26] (2014)	Epstein criteria / Epstein criteria or ADC <850 $\mu m^2/s$
[27] (2013)	Epstein criteria / UCL1 / UCL2 / Gleason score ≥7 / Gleason score ≥8
[28] (2014) [a]	UCL2
[22] (2013) [a]	UCL1 / UCL2
[29] (2013) [a]	UCL2
[30] (2012)	PSA >10 ng/ml, PSA density >0.15, clinical stage ≥T2b, Gleason 4 or 5, total CCL ≥10 mm
[31] (2013)	Gleason ≥7 / Gleason ≥8
[32] (2011) [a]	CCLI ≥3 mm and/or Gleason ≥7 / CCLI ≥5 mm and/or Gleason ≥7
[33] (2014)*	Gleason 7 with >5% Gleason 4 + either ≥30% of cores positive or Or Gleason 6–7 with ≤5% Gleason 4 + either ≥30% of cores positive or CCL_{max} >8 mm
[34] (2014)	Gleason ≥7
[35] (2014)	Epstein criteria

ADC = apparent diffusion coefficient; CCL = cancer core length; CCL_{max} = maximum CCL; Epstein criteria = Gleason score > 6, PSA >10 ng/ml, >3 biopsy cores positive, or at least one biopsy core with >50% involvement; UCL1 = University College London definition 1: Gleason ≥4 + 3 and/or CCL_{max} ≥6 mm and/or total CCL ≥6 mm; UCL2 = UCL definition 2: Gleason ≥3 + 4 and/or CCL_{max} ≥4 mm and/or total CCL ≥6 mm.

* Definition 4 was used.

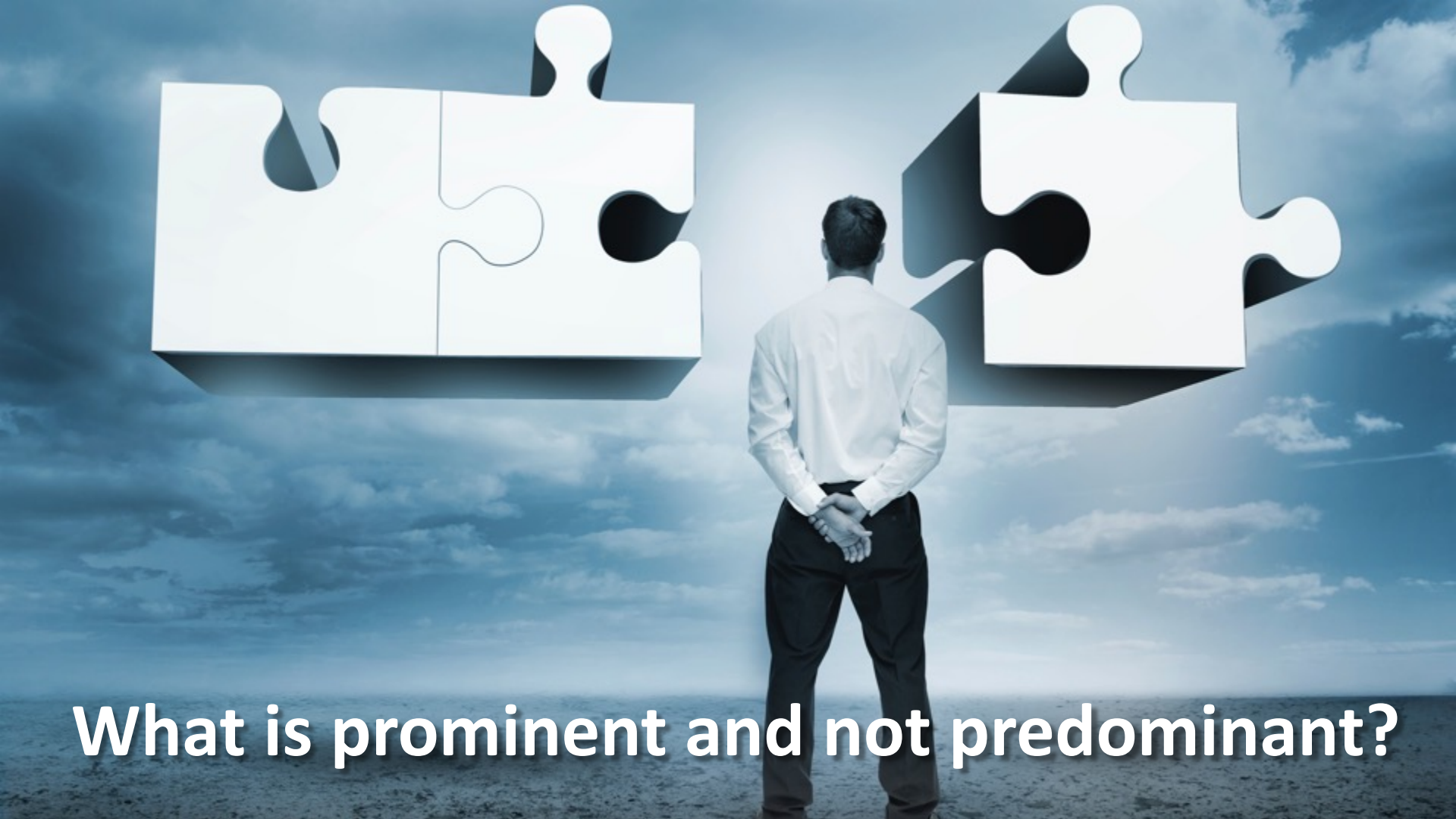
[a] Publications from the same centre.

Futterer, Eur Urol 2015

PI-RADS v2: MRI-Clinically Significant PCa

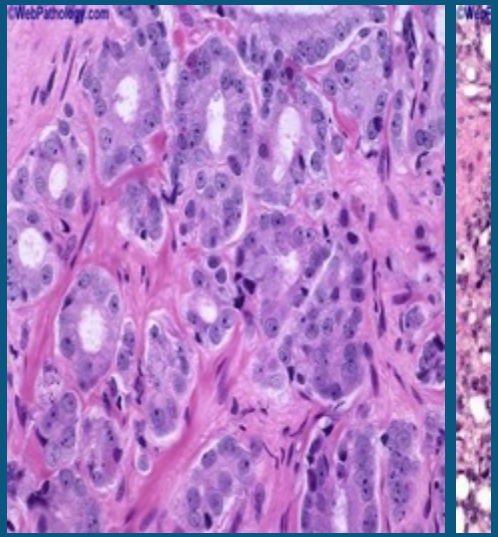
- **Gleason score ≥ 7 (including 3+4 with prominent but not predominant Gleason 4 component), or**
- Volume ≥ 0.5cc, or
- Extraprostatic extension (EPE)

Wolters T, et al. J Urol 2011;185:121-5


What is prominent and not predominant?

PI-RADS v2: MRI-Clinically Significant PCa

- Grade ≥2 (GS 3+4)



PI-RADS v2: MRI-Clinically Significant PCa

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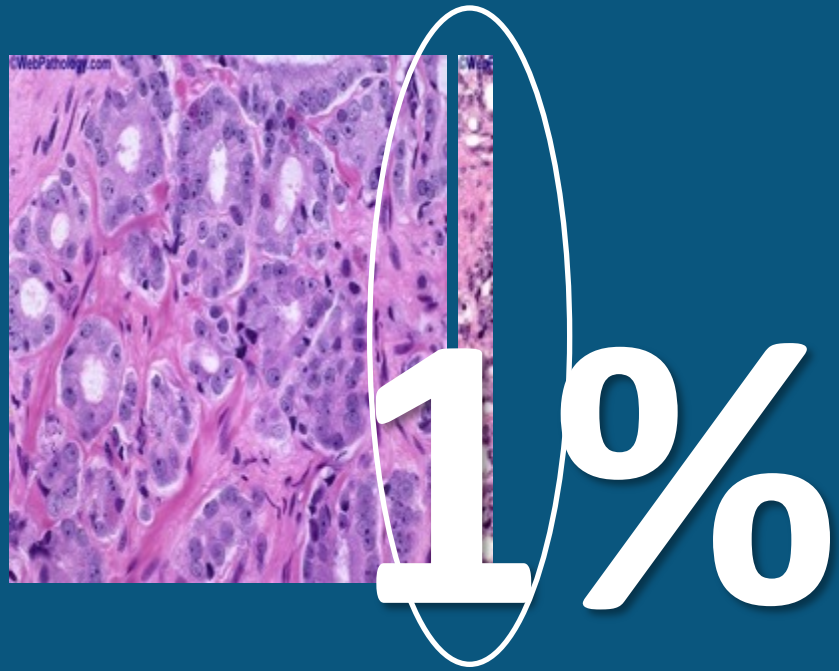

PI-RADS v2: MRI-Clinically Significant PCa

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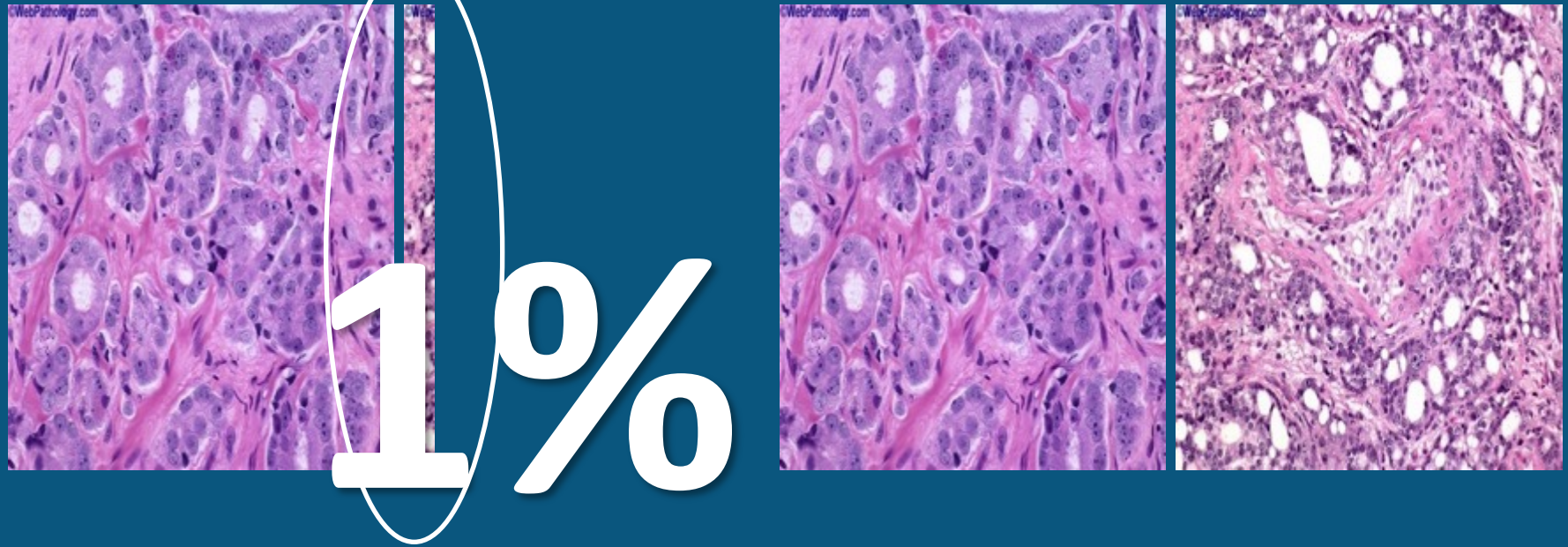
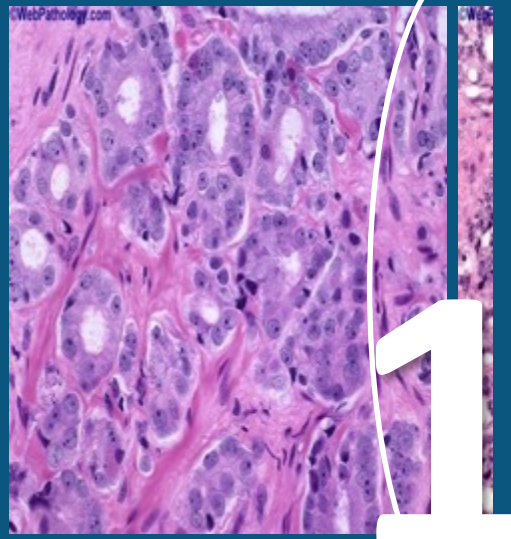
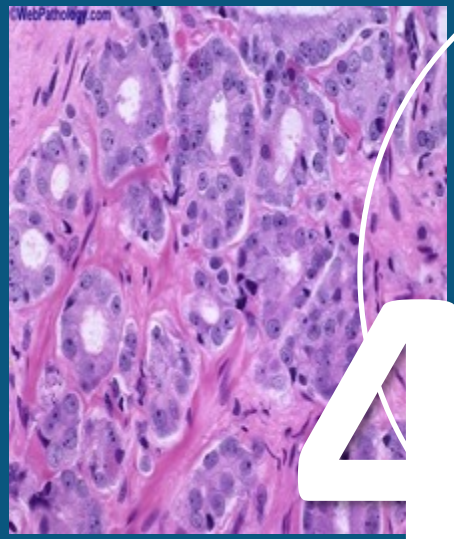


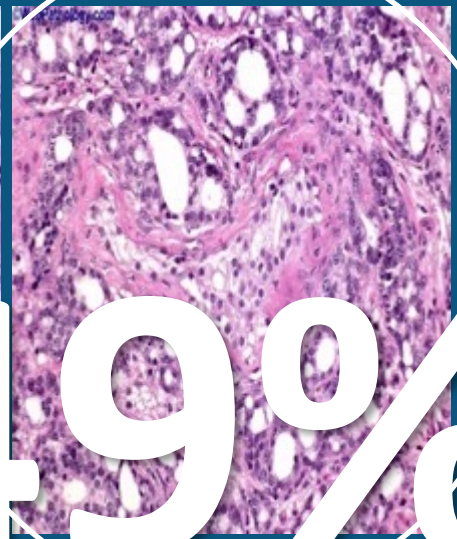
PI-RADS v2: MRI-Clinically Significant PCa

- Grade ≥2 (GS 3+4)



1%

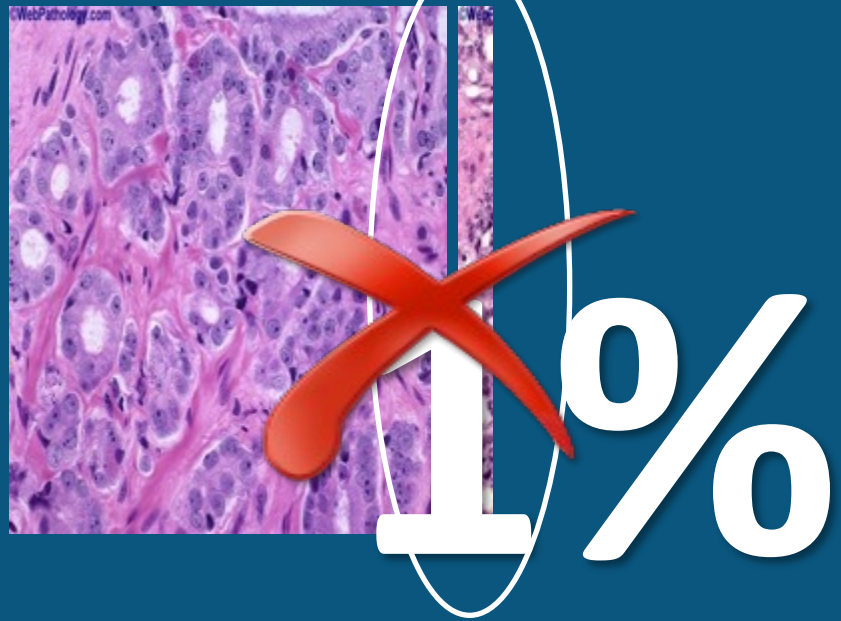


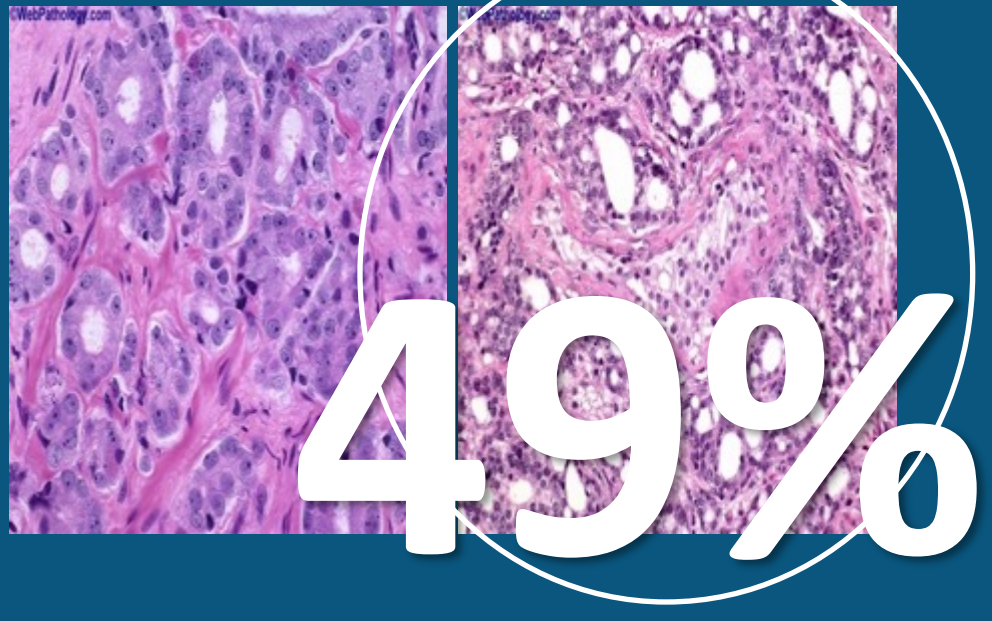


49%

PI-RADS v2: MRI-Clinically Significant PCa

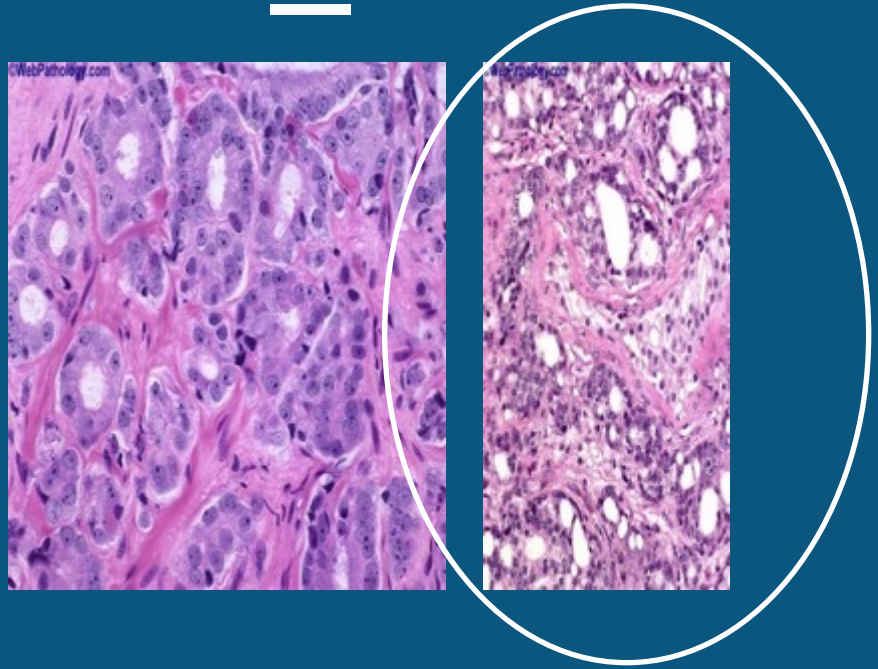
- Grade ≥2 (GS 3+4)





PI-RADS v2: MRI-Clinically Significant PCa

- Grade ≥2: GS 3+4 (>25%)



>25%

PI-RADS v2: MRI-Clinically Significant PCa

- Gleason score ≥ 7, or
- **Volume ≥ 0.5cc**, or
- Extraprostatic extension (EPE)

Wolters T, et al. J Urol 2011;185:121-5

SIZE

DOES IT MATTER?

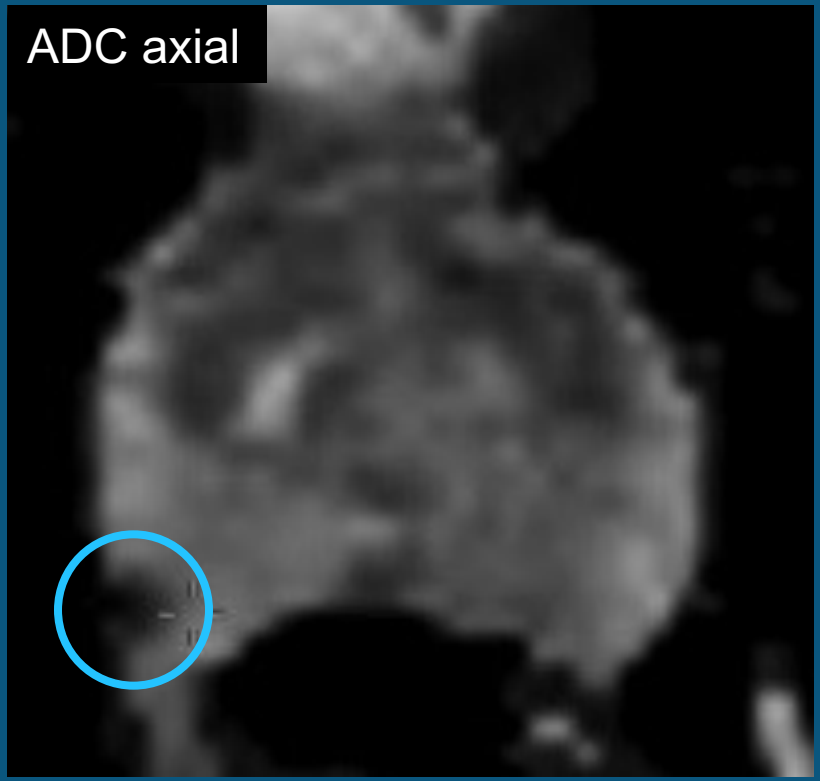
PIRADS v2: T2W: TZ + PZ

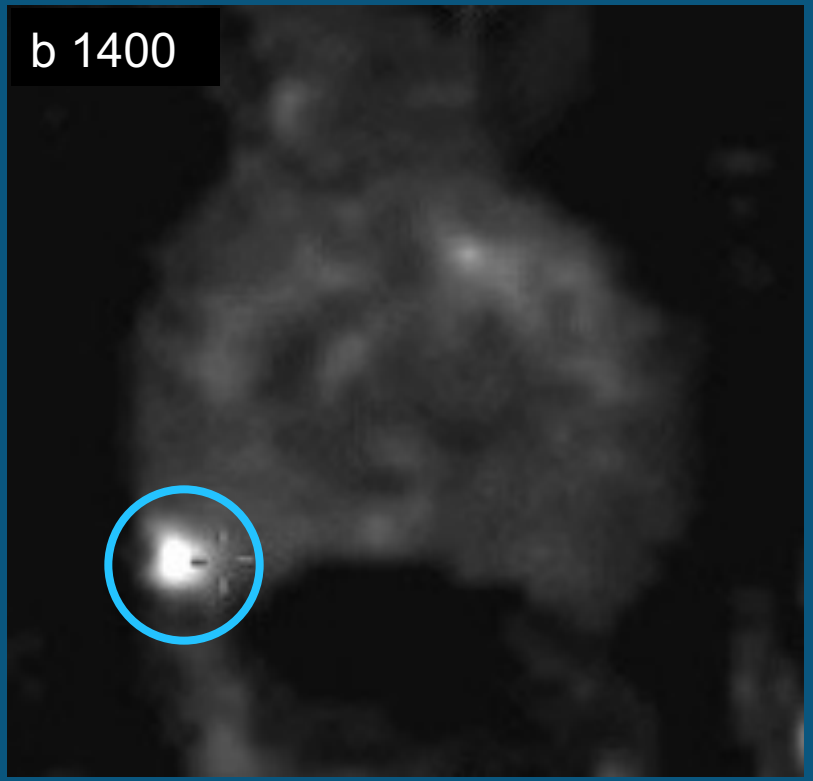
4 Non-circumscribed, homogenous moderate hypointense, and <1.5 cm in greatest dimension

5 Same as 4 but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

Size: 1.5 cm, 1.0 cm, 0.5 cm……

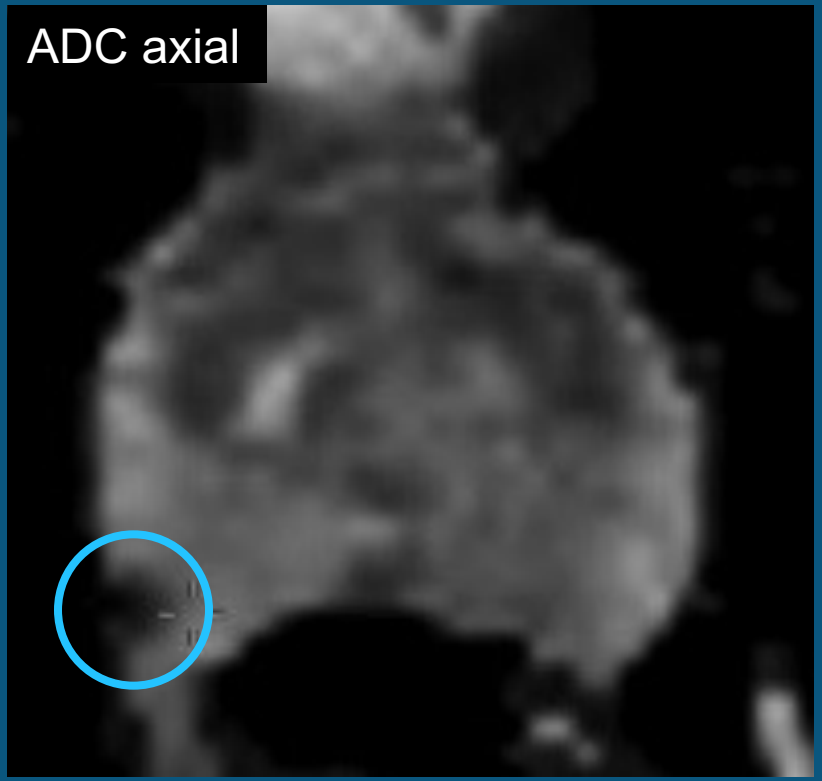
GG 5

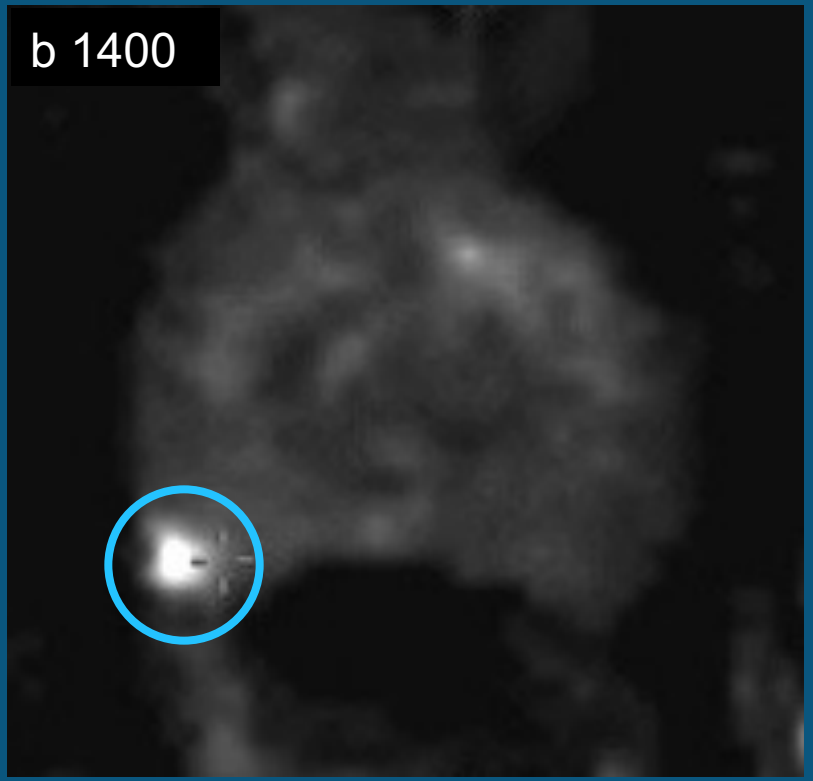


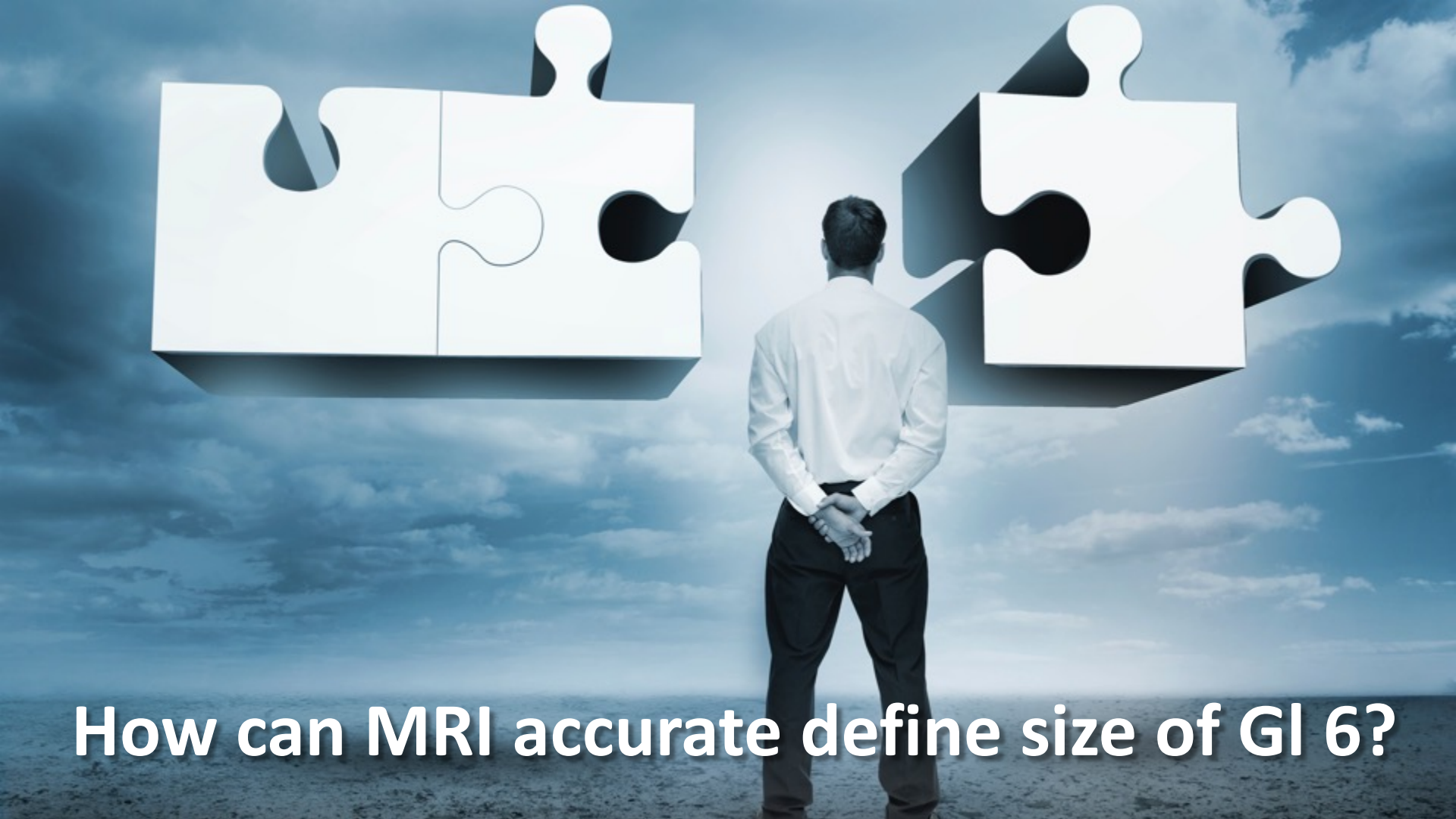


PIRADS 4

4 Focal markedly hypontense on ADC and markedly hyperintense on high b-value DWI; **<1.5cm on axial**

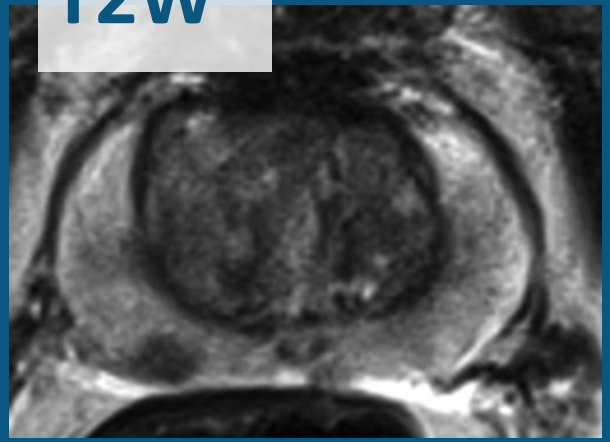




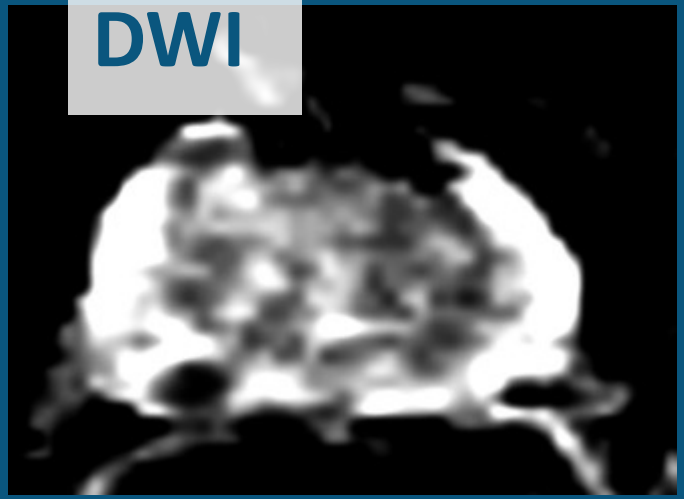

How can MRI accurate define size of GI 6?

62y, PSA 12 ng/ml, 4 negative TRUS biopsies

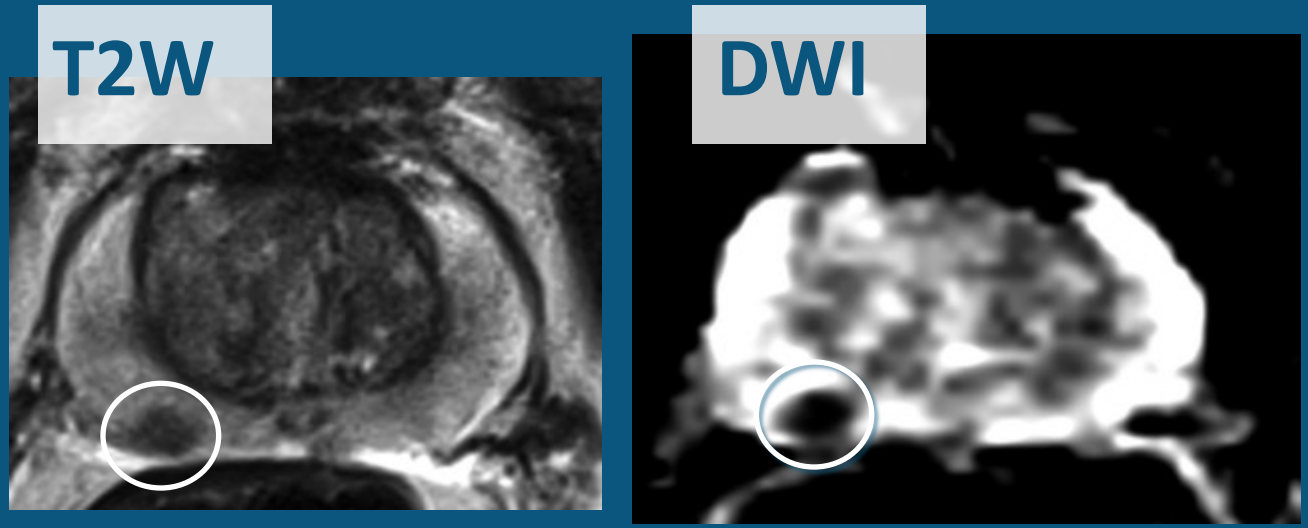
T2W



DWI



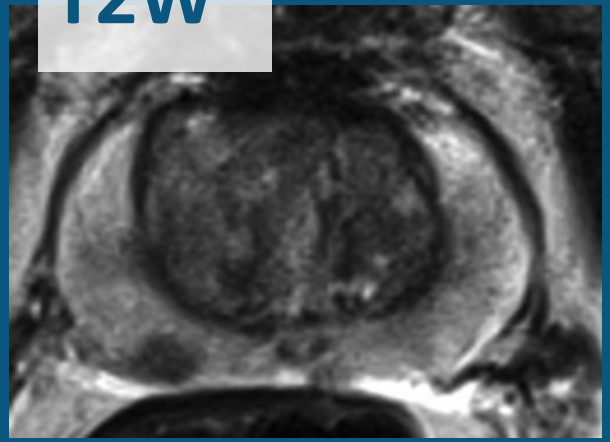
62 yr. PSA 12 ng/ml, 4 negative TRUS biopsies



MR-GB: Gl 4+3

62y, PSA 12 ng/ml, 4 negative TRUS biopsies

T2W



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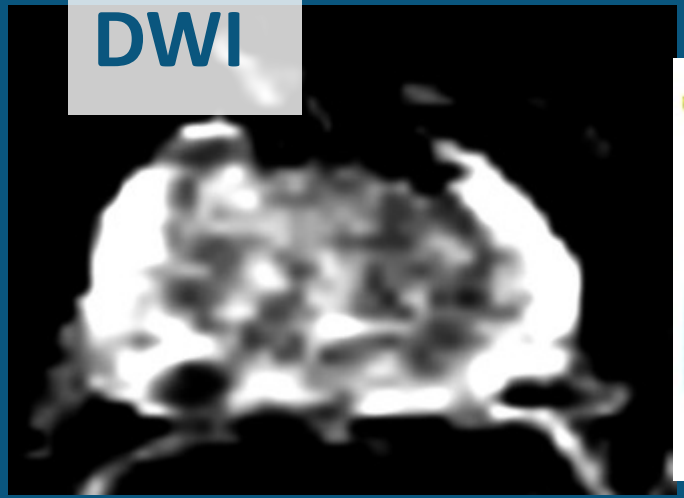
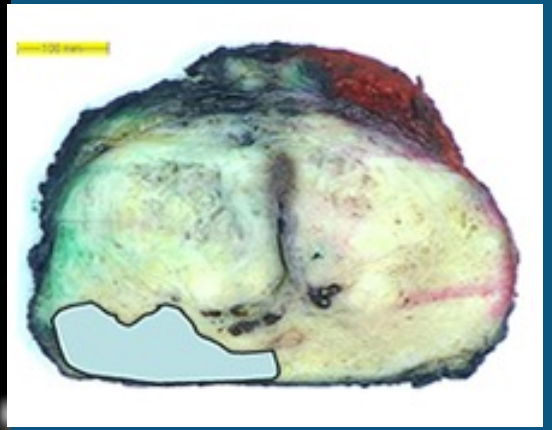


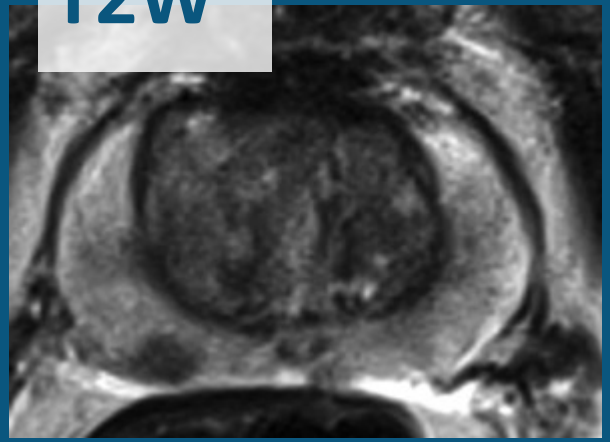


MR-GB: Gl 4+3

Px: lager tumor

EXPLANATION?

T2W



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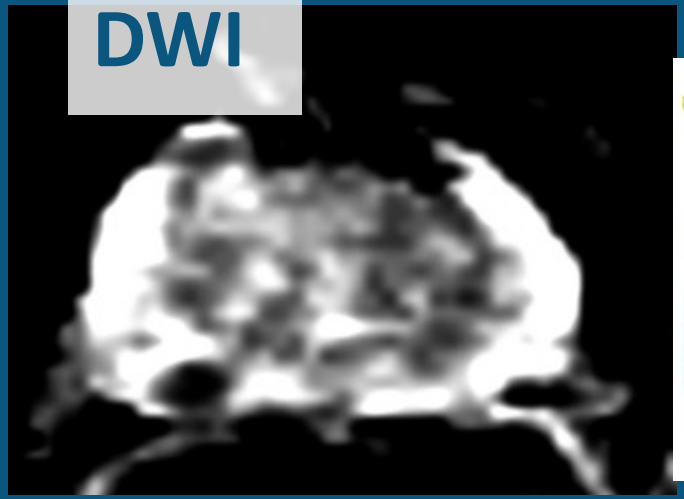
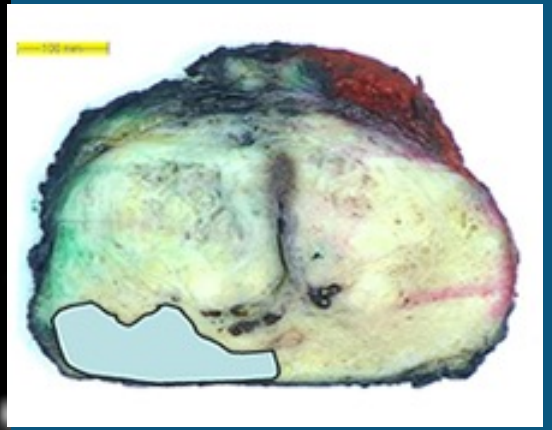


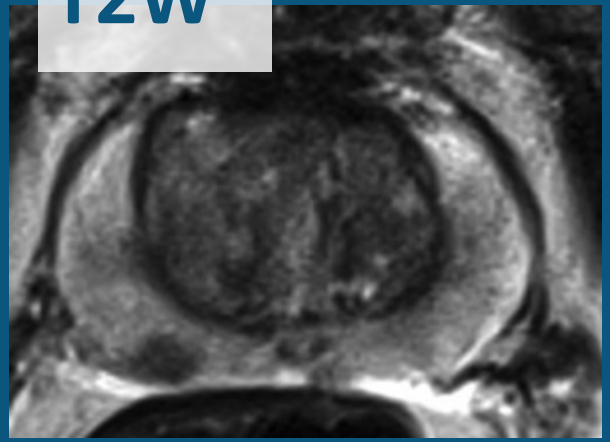


MR-GB: Gl 4+3

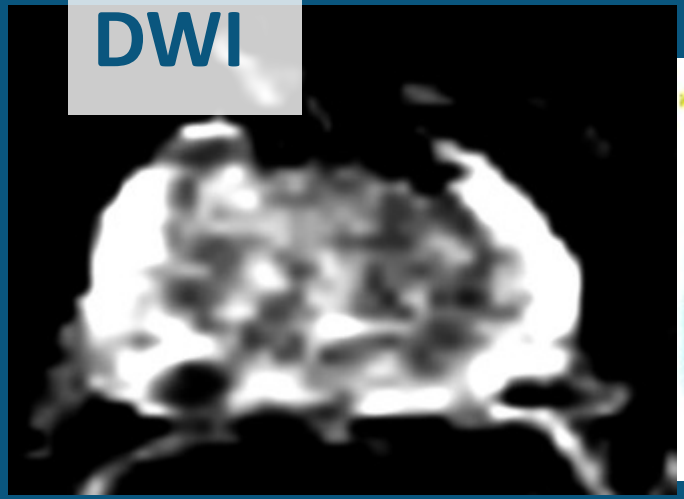
Px: lager tumor

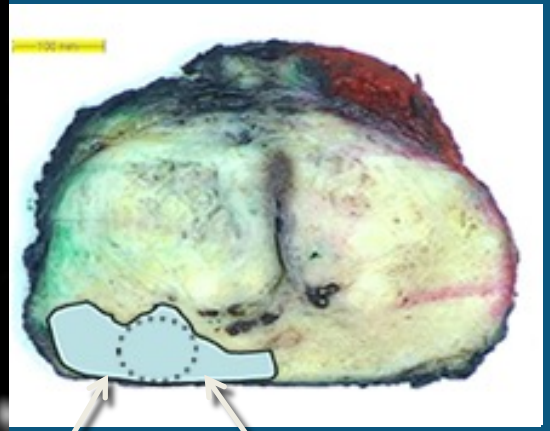
MRGB and Prostatectomy GI 4+3

T2W



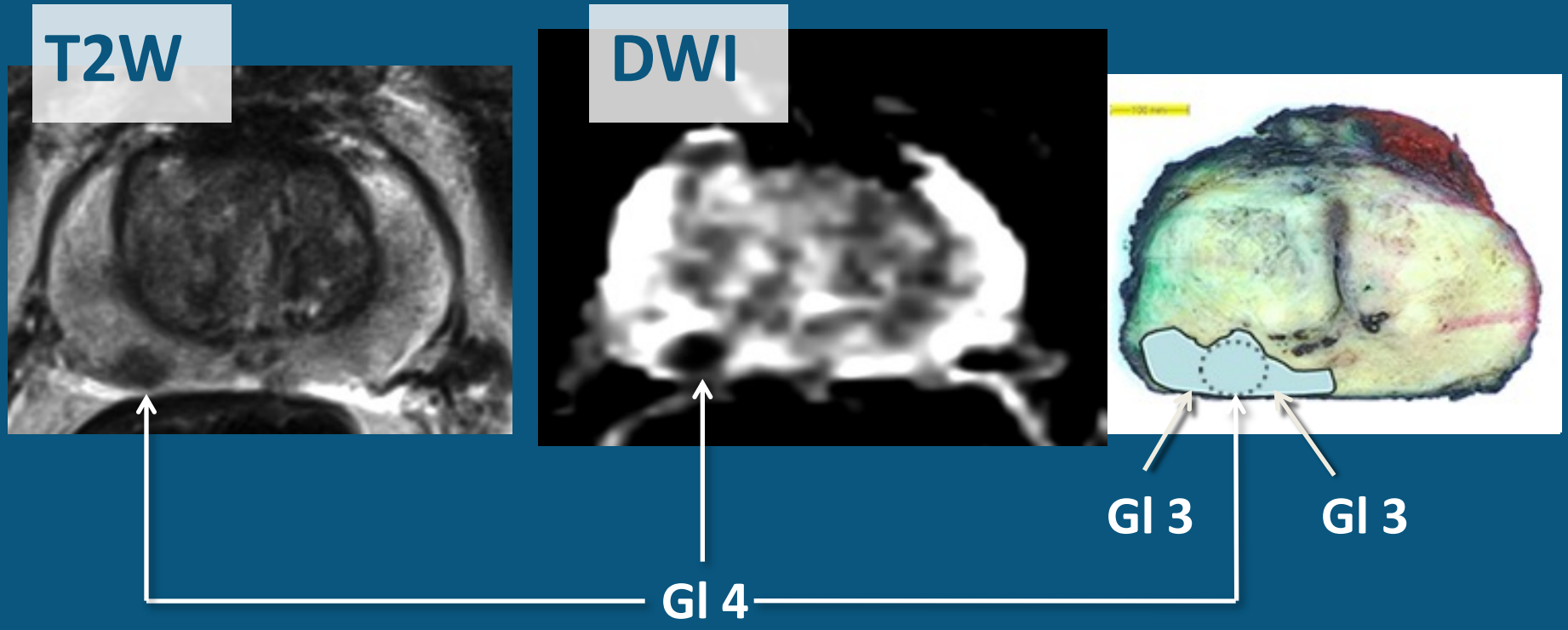
DWI





GI 3 GI 3

MRGB and Prostatectomy GI 4+3



CLINICAL RISK

PI-RADS v2

Should not take into account clinical scenarios?

High suspicion:

- PSAD >0.15
- Free/Total PSA ratio <25%
- Hereditary (incl. BRCA positive)
- Positive DRE

PI-RADS 3 and PSAD

Table 5 – – Summary of clinical consequences when applying PSAD cutoff levels to predict csPCa in patients with PI-RADS 3

	PSAD cutoff (ng/ml/ml)	≥0.1	≥0.11	≥0.12	≥0.13	≥0.14	≥0.15
PI-RADS 3	Patients with PI-RADS 3 who avoid biopsy (%)	19	21	26	32	37	42
	csPCa missed in patients below the cutoff (95% CI)	0% (0–12)	0% (0–11)	0% (0–9)	4% (1–13)	3% (1–12)	6% (2–15)
	csPCa detection above the cutoff	20% (14–29)	21% (15–29)	22% (16–31)	23% (16–31)	24% (17–34)	24% (17–34)

PSAD cutoff (ng/ml/ml)	≥0.16	≥0.17	≥0.18	≥0.19	≥0.2
Patients with PI-RADS 3 who avoid biopsy (%)	42	45	49	53	56
csPCa missed in patients below the cutoff (95% CI)	8% (3–17)	8% (3–17)	9% (5–18)	9% (4–17)	11% (6–20)
csPCa detection above the cutoff	23% (16–33)	23% (16–33)	24% (16–34)	26% (17–37)	24% (15–35)

PSAD cutoff (ng/ml/ml)	≥0.21	≥0.22	≥0.23	≥0.24	≥0.25
Patients with PI-RADS 3 who avoid biopsy (%)	60	64	68	70	71
csPCa missed in patients below the cutoff (95% CI)	11% (6–18)	11% (6–19)	14% (9–22)	15% (9–23)	15% (10–23)
csPCa detection above the cutoff	26% (17–38)	27% (17–40)	22% (13–35)	21% (12–35)	20% (11–34)

csPCa = clinically significant prostate cancer; PSAD = prostate-specific antigen density; PI-RADS = Prostate Imaging Reporting and Data System.

Venderink Eur Urol 2017

PI-RADS 3 and PSAD

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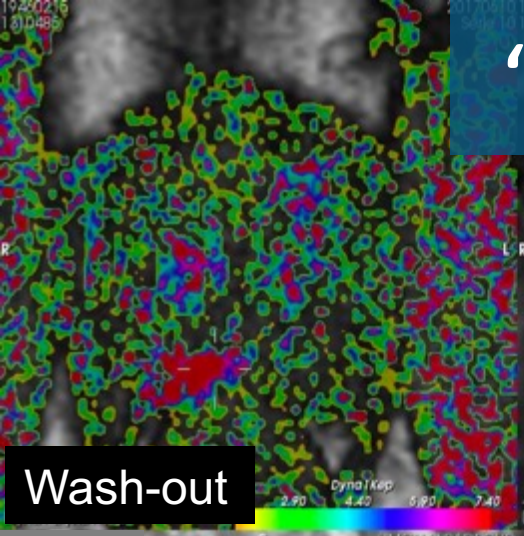
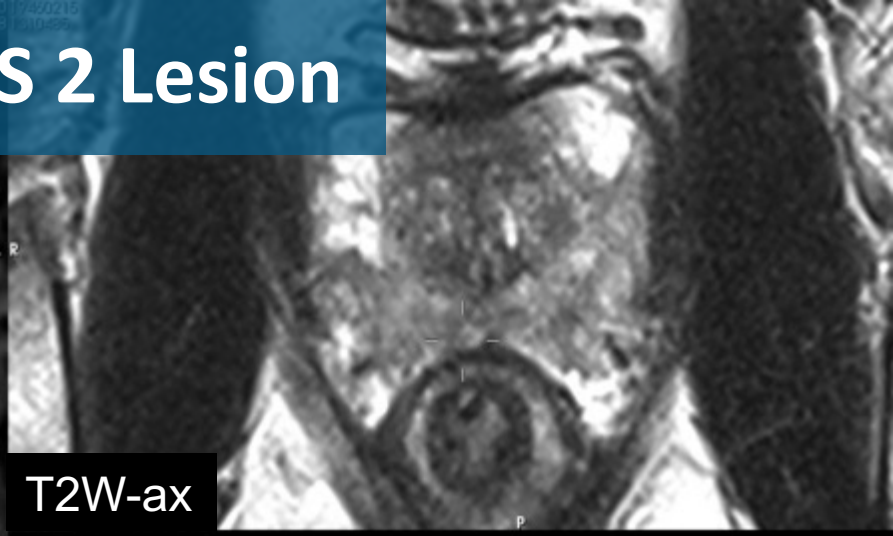
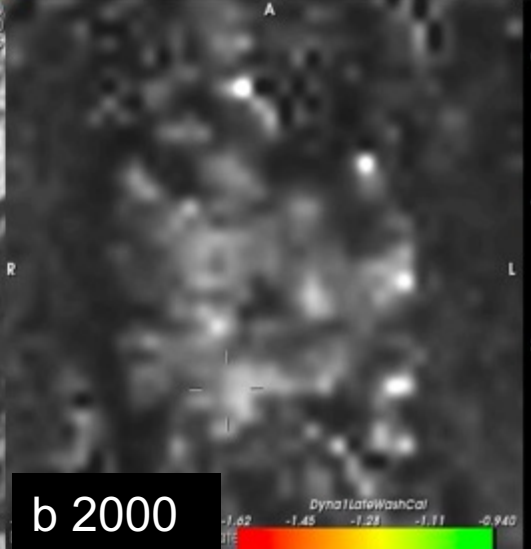
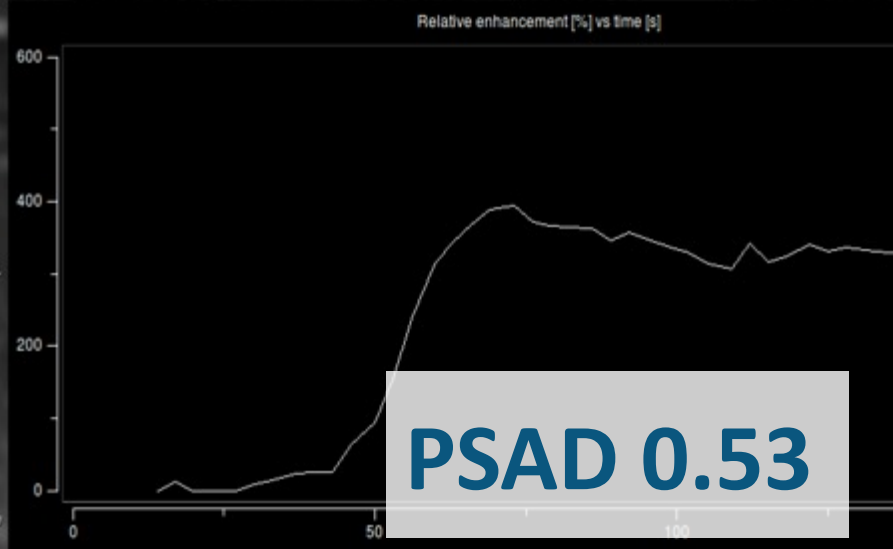
Venderink Eur Urol 2017

“Dirty” PI-RADS 2 Lesion



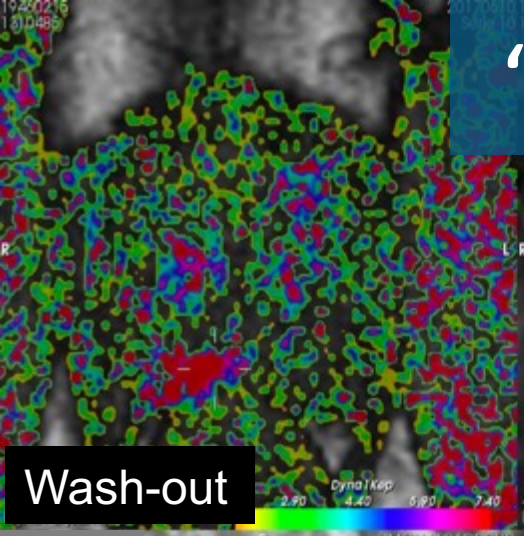


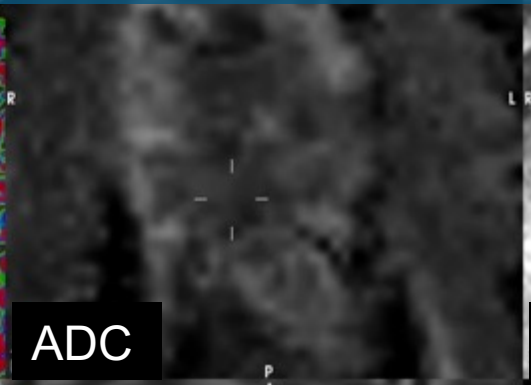


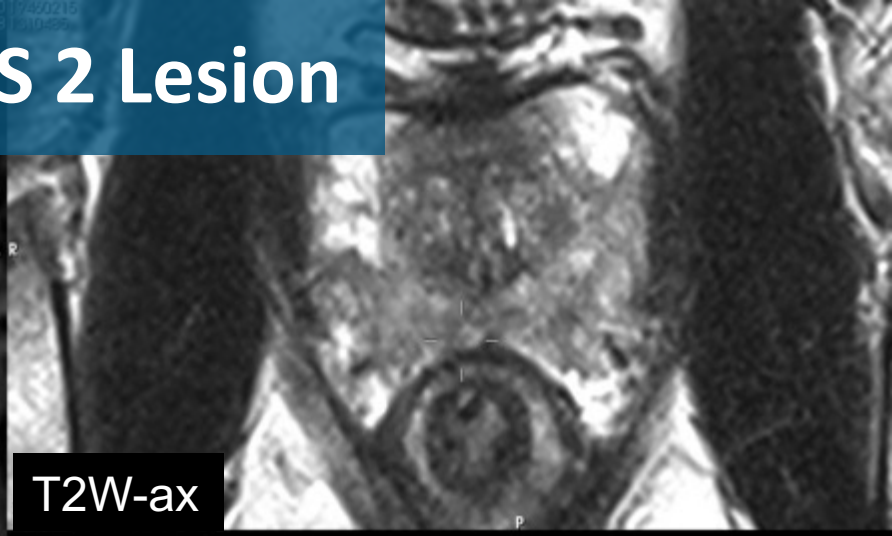


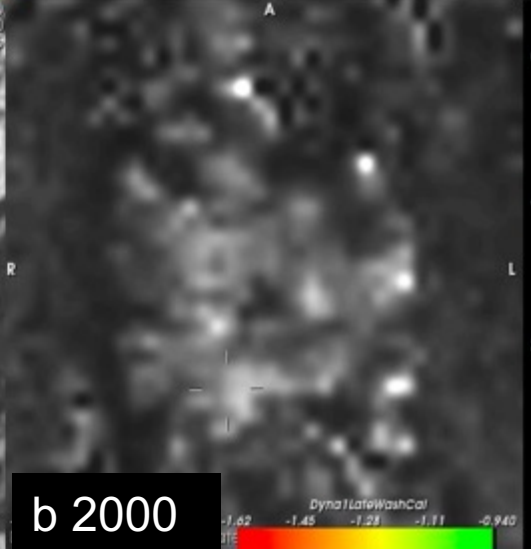
PSAD 0.53

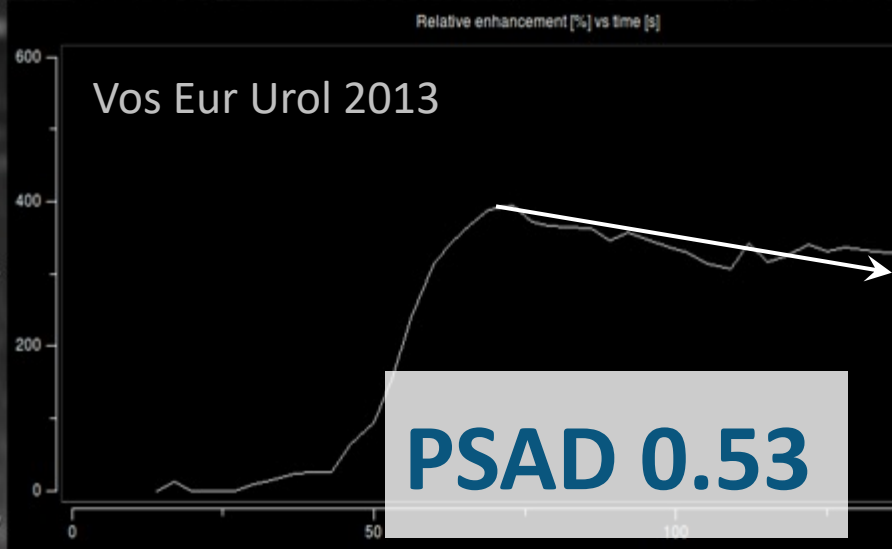
“Dirty” PI-RADS 2 Lesion











PI-RADS v2

Does not take into account clinical scenarios

Biopsy naïve:

- High specificity reading

PI-RADS v2

Does not take into account clinical scenarios

Biopsy naïve:

- High specificity reading

Post negative TRUS-Bx

- High sensitivity reading

PI-RADS v3:
What do I recommend?

1	Very low	no biopsy, no follow-up
2	Low	no biopsy, repeat MRI if PSA ↑
3	Intermediate	PSAD < 0.12: f.u.; PSAD >0.15: MR-biopsy (20%)
4	High	MR-guided biopsy (40-80%)
5	Very high	MR-guided biopsy (70-95%)

PI-RADS v3

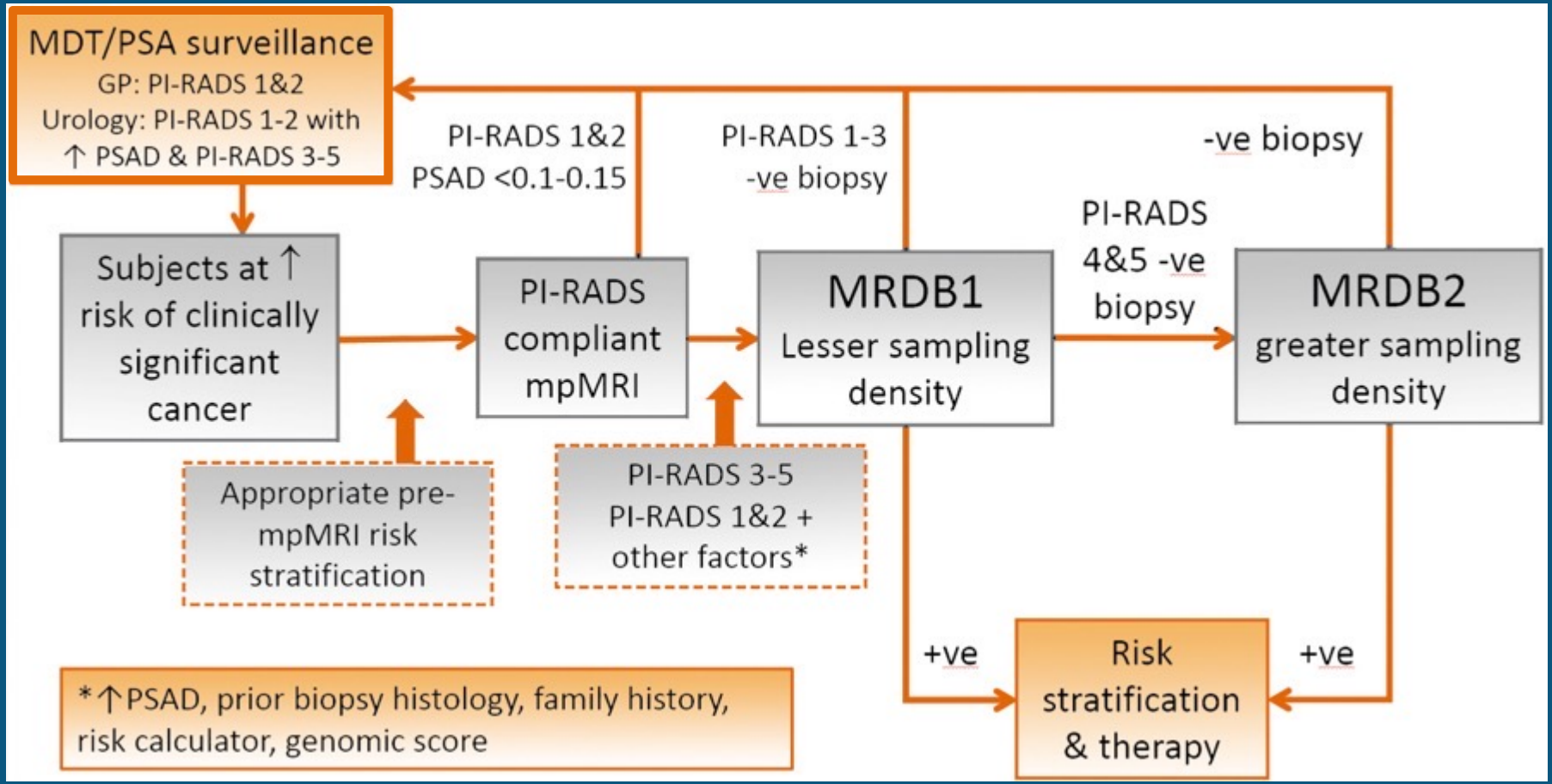
Also take into account clinical risk!

High suspicion:

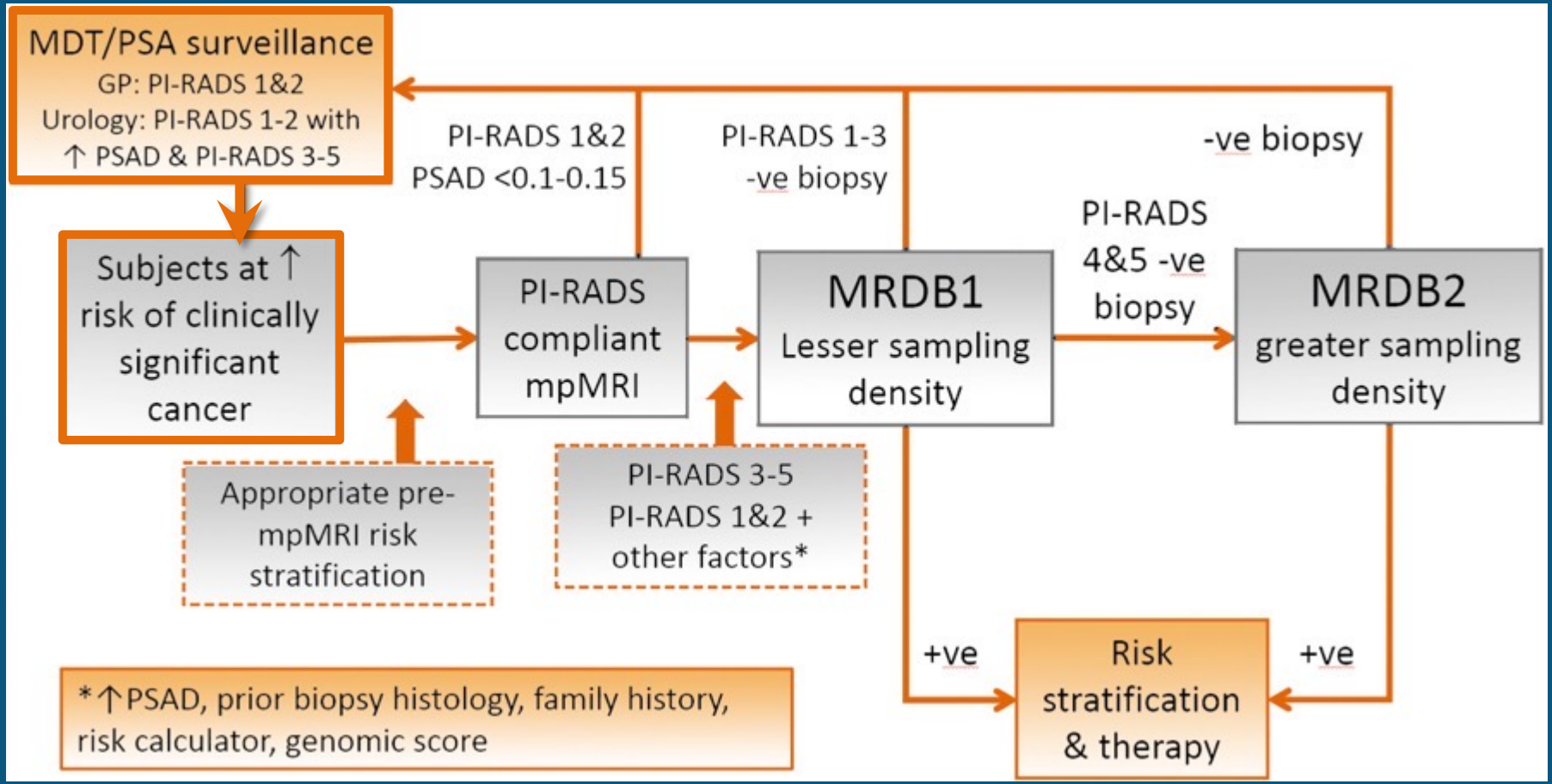
1. Venderink, Eur Urol 2017

- **PSAD >0.12[1]**
- **Free/Total PSA ratio <25%**
- **Hereditary (incl. BRCA positive)**
- **Positive DRE**

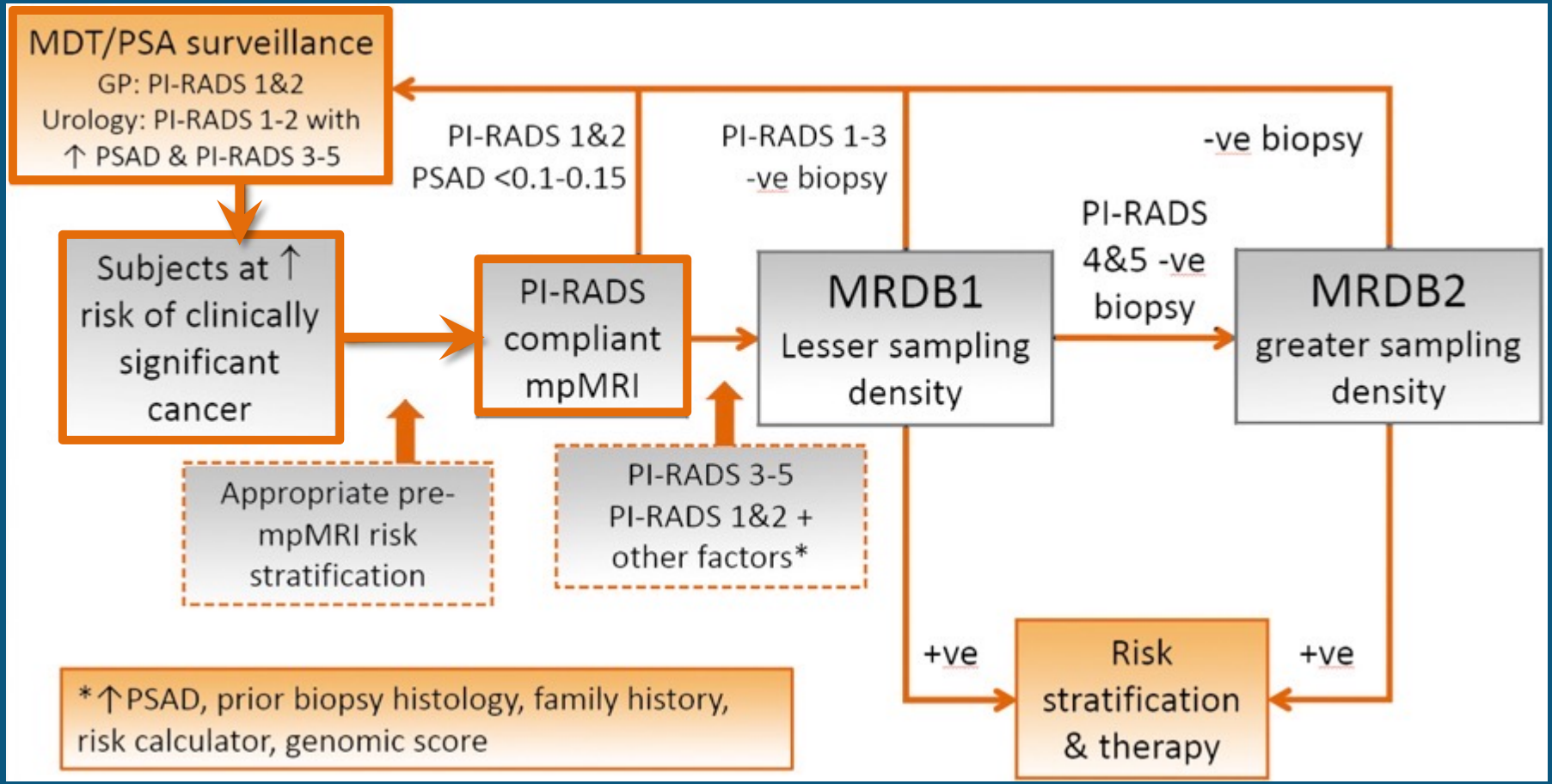
VALUE OF PATHWAYS



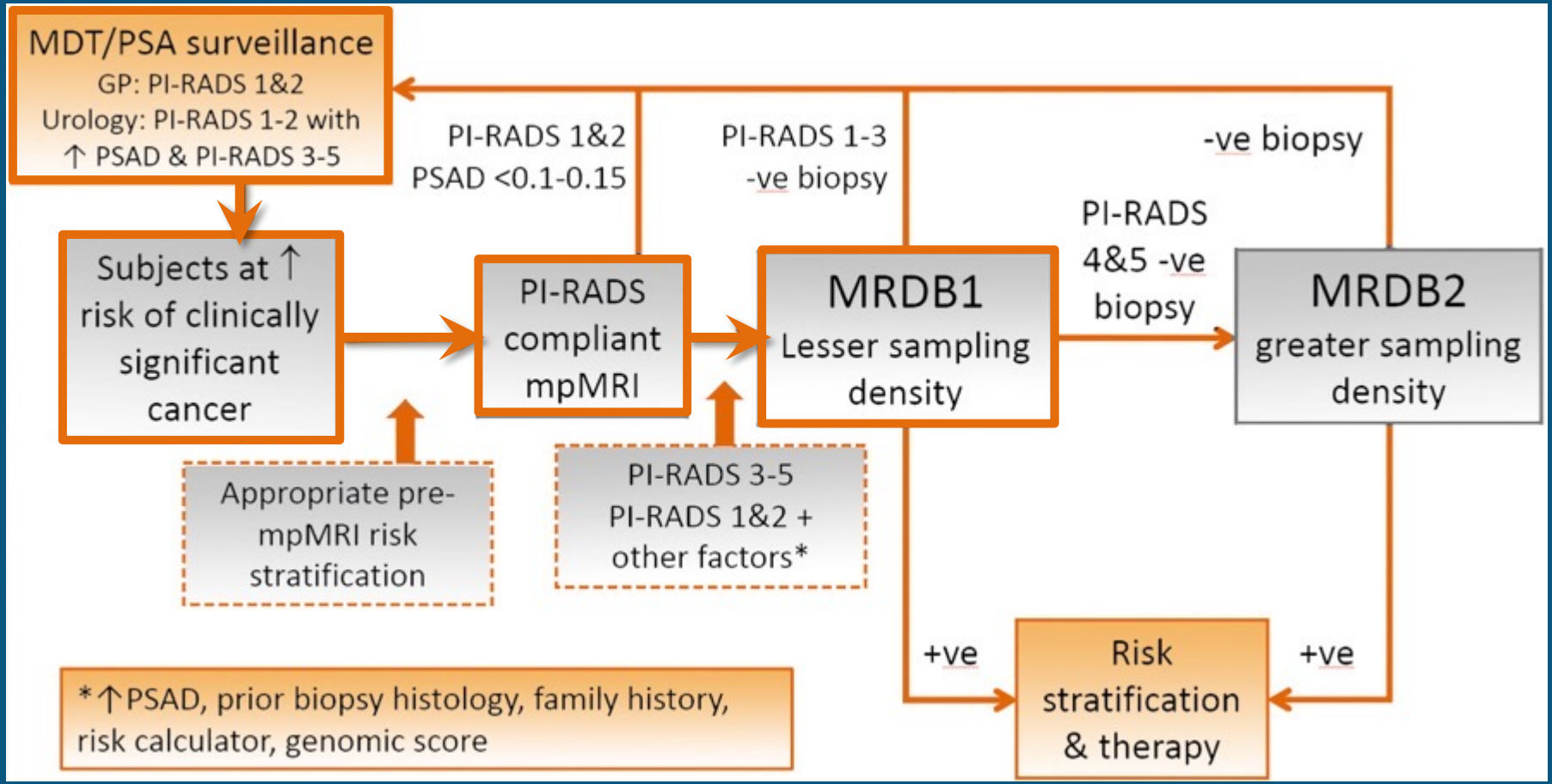
Padhani Eur Urol 2018



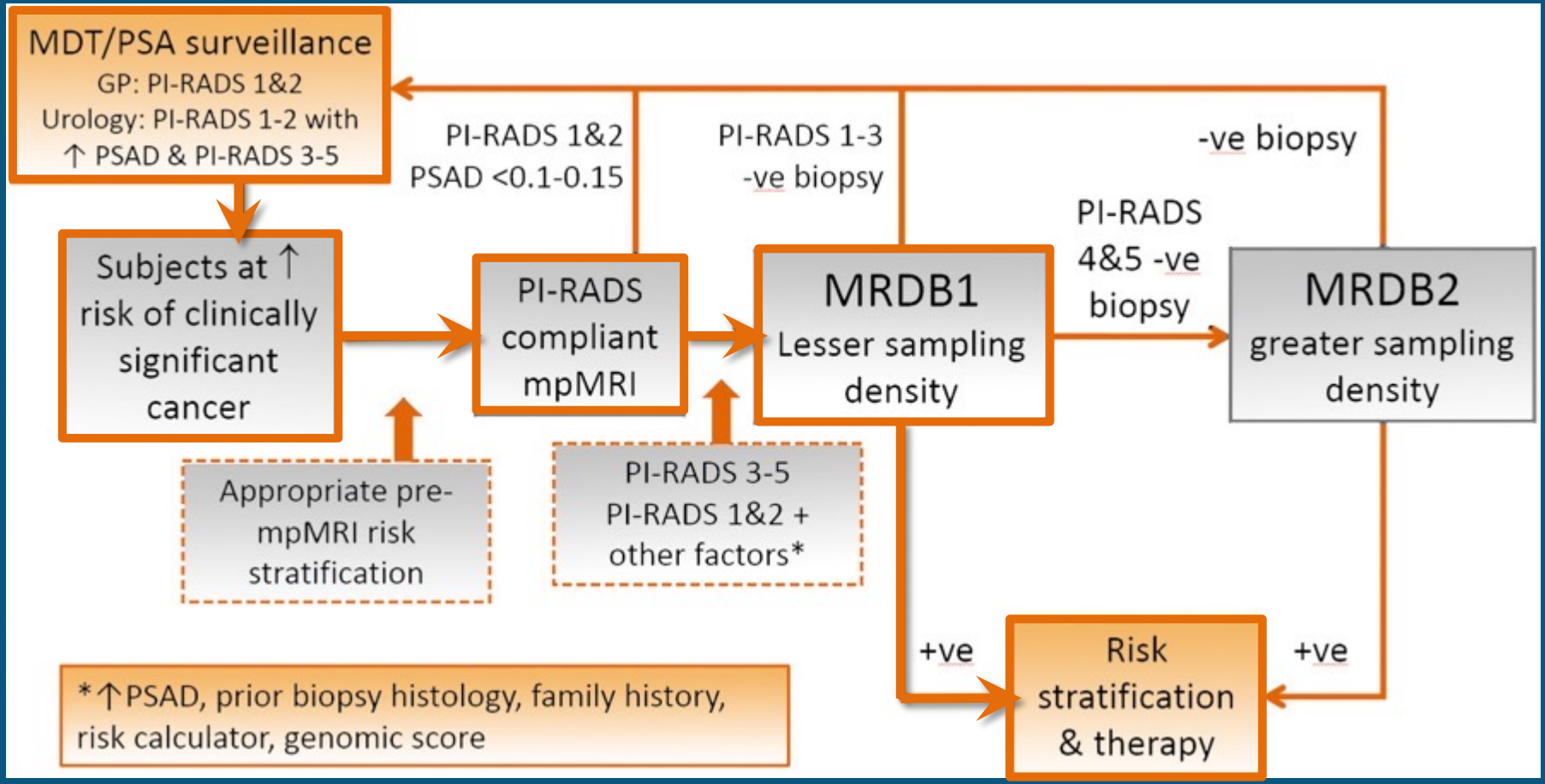
Padhani Eur Urol 2018



Padhani Eur Urol 2018



Padhani Eur Urol 2018



Padhani Eur Urol 2018

HOW DOMINANT

IS DOMINANT?

PI-RADS v2

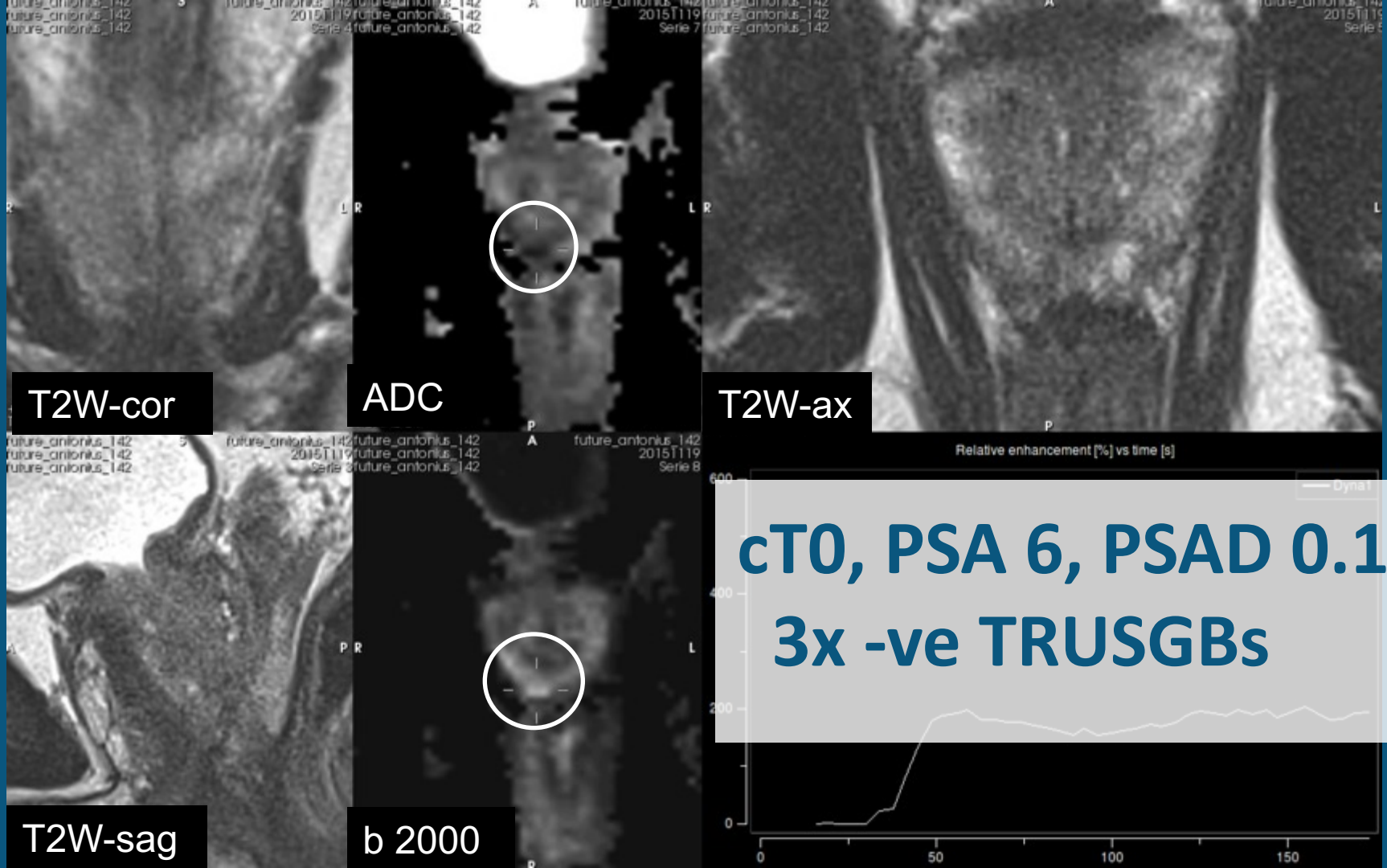
- **Different weighting for PZ and TZ**
  - DWI dominates in PZ
  - T2W dominates in TZ
  - DCE plays minor role

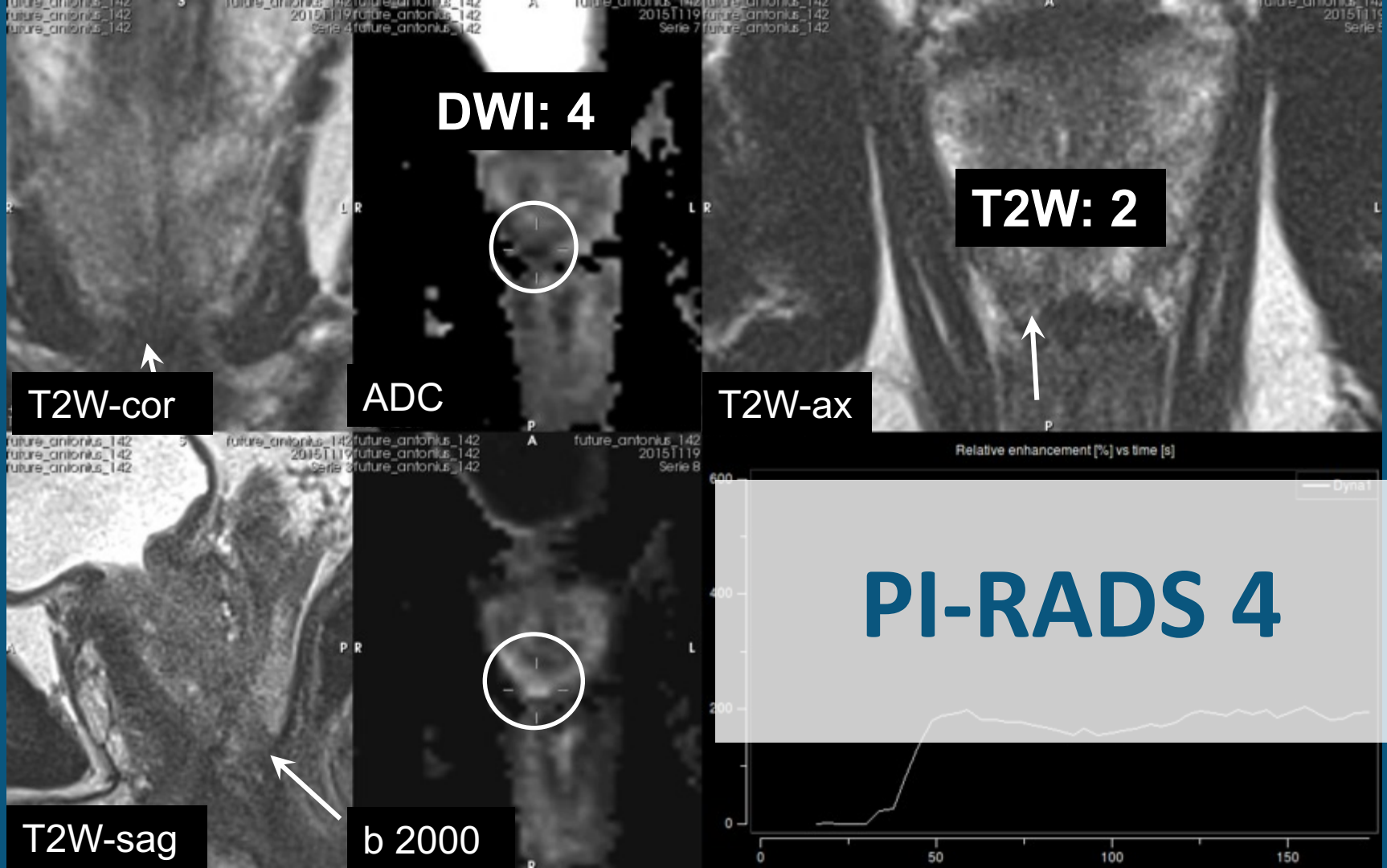
PI-RADS v3

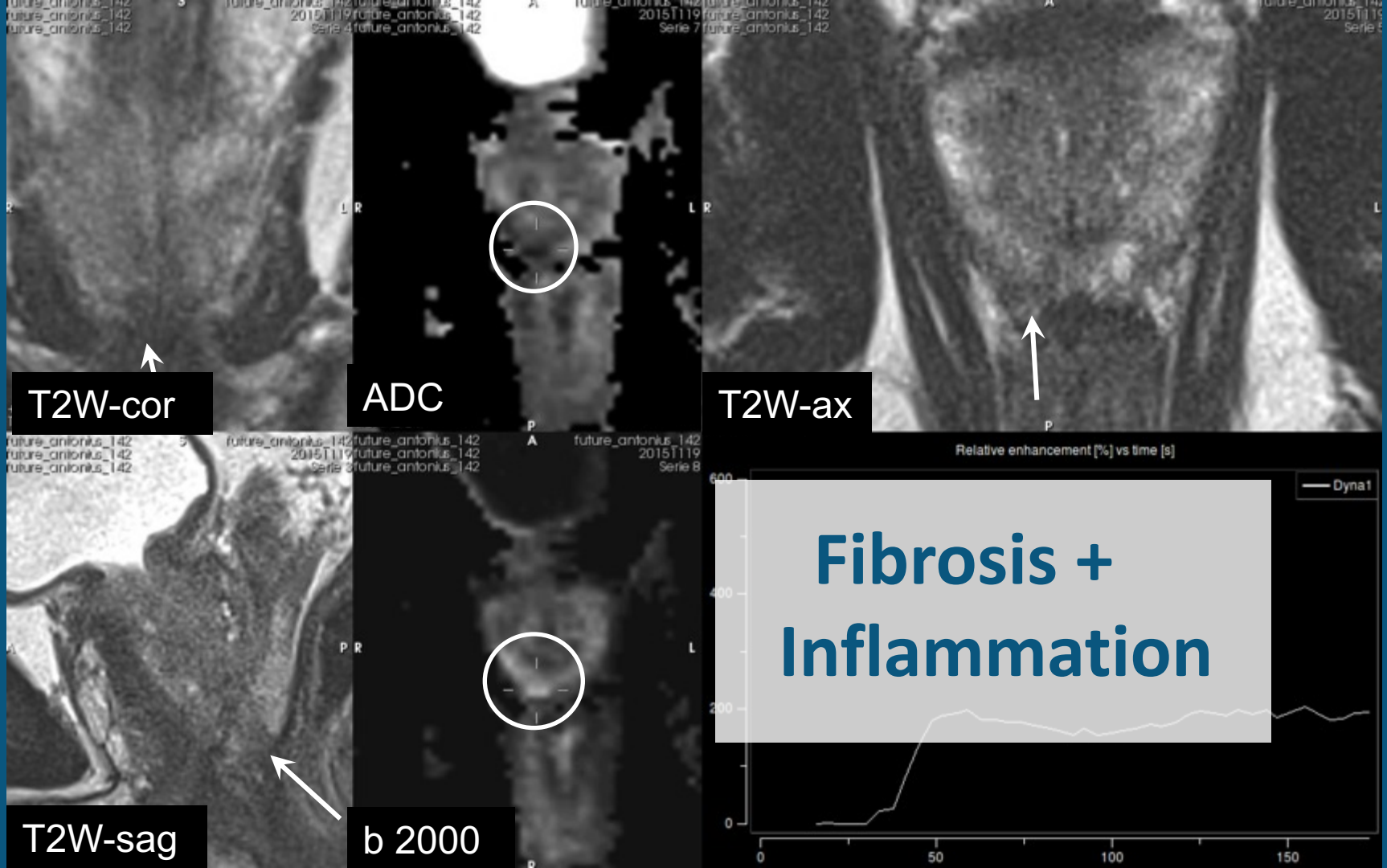
- **Different weighting for PZ and TZ**
  - **DWI dominates in PZ,**

but not 100%

Use common sense


T2W-cor
ADC
T2W-ax
T2W-sag
b 2000
Relative enhancement [%] vs time [s]
cT0, PSA 6, PSAD 0.11
3x -ve TRUSGBs


DWI: 4
T2W: 2
T2W-cor
ADC
T2W-ax
Relative enhancement [%] vs time [s]
PI-RADS 4
T2W-sag
b 2000
0
50
100
150


T2W-cor
ADC
T2W-ax
T2W-sag
b 2000
Relative enhancement [%] vs time [s]
Dyna1
Fibrosis +
Inflammation

PI-RADS v2

- **Different weighting for PZ and TZ**
  - DWI dominates in PZ
  - T2W dominates in TZ
  - DCE plays minor role

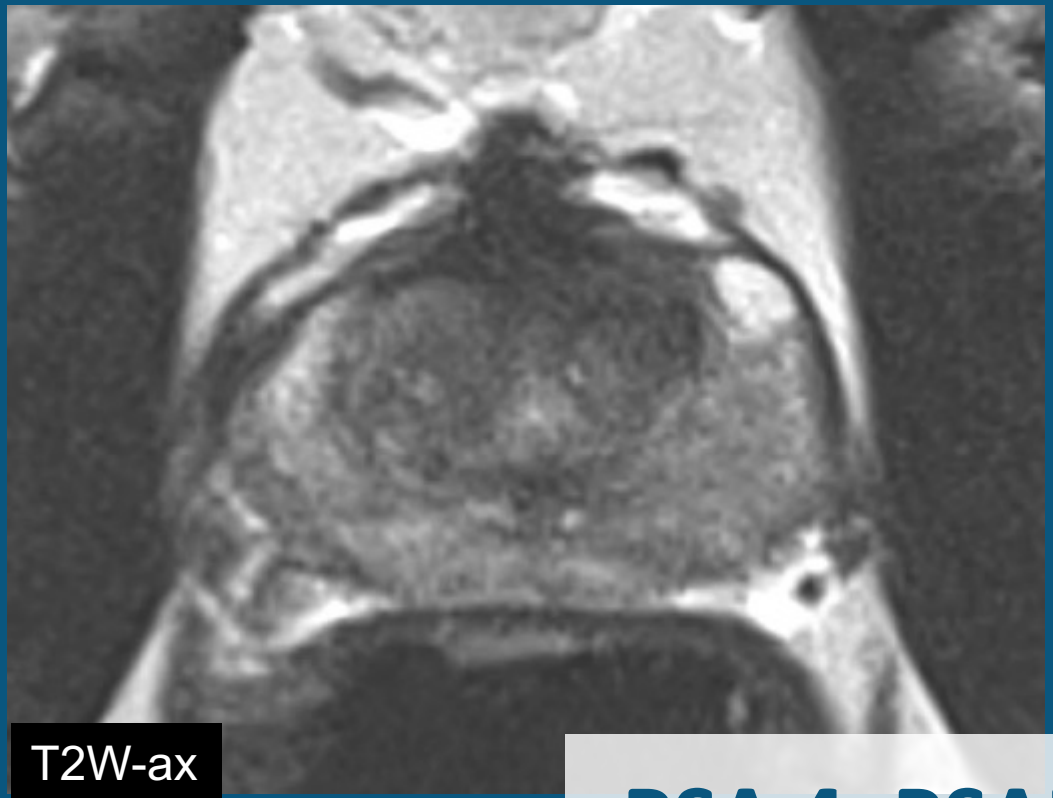
PI-RADS v3

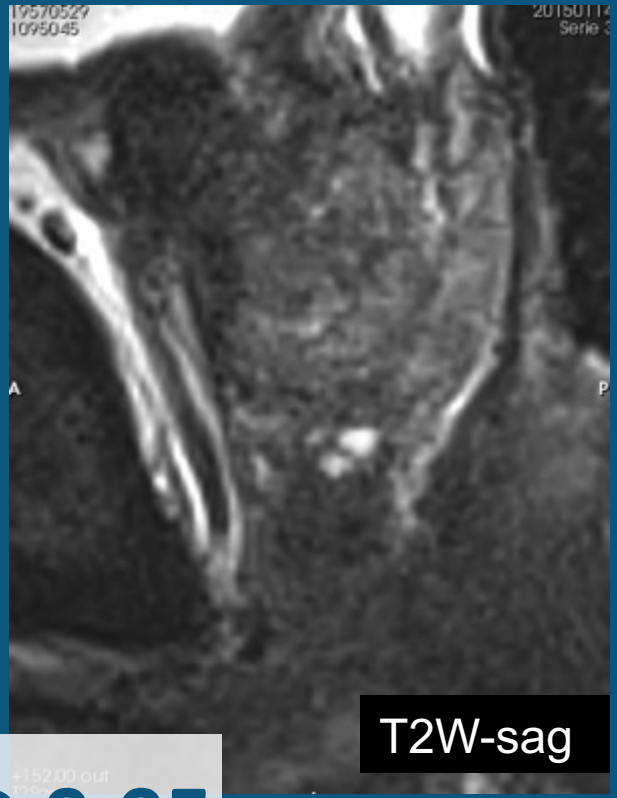
- **Different weighting for PZ and TZ**
  - **T2W dominates in TZ,**

but not 100%

Use common sense

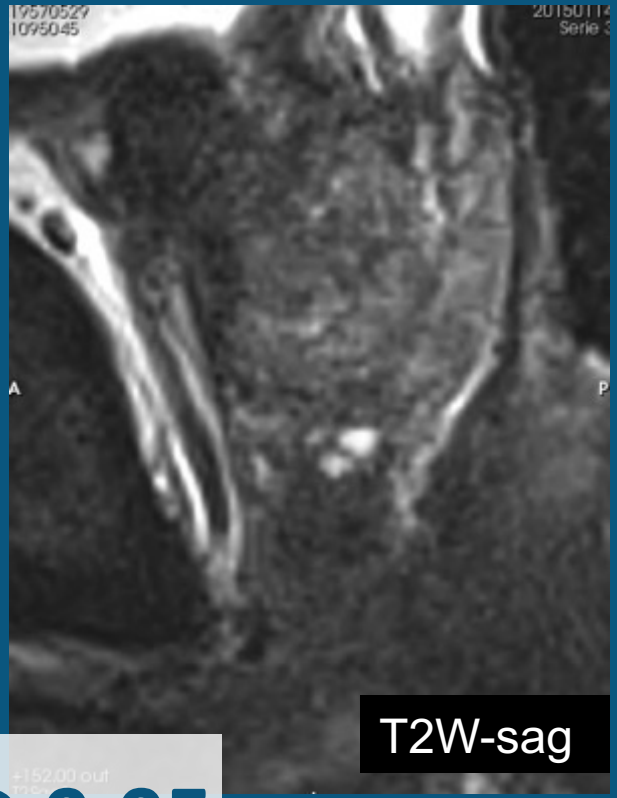
PI-RADS v3: value of DWI in TZ





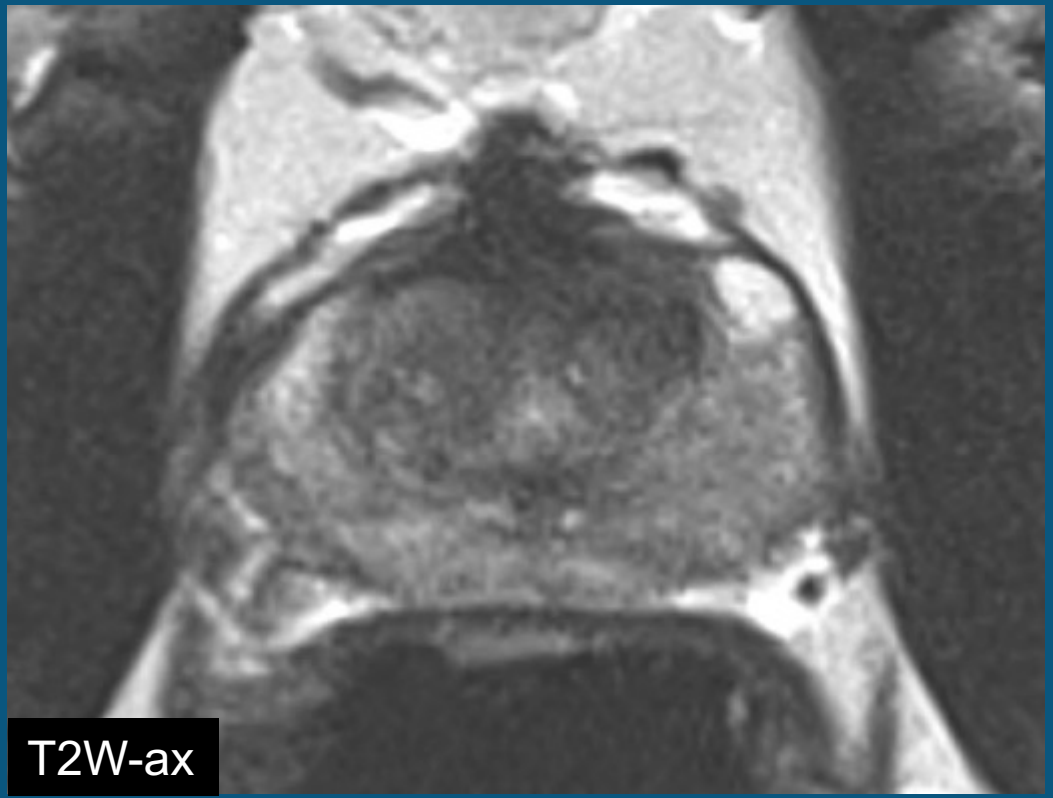
PSA 4, PSAD 0.05

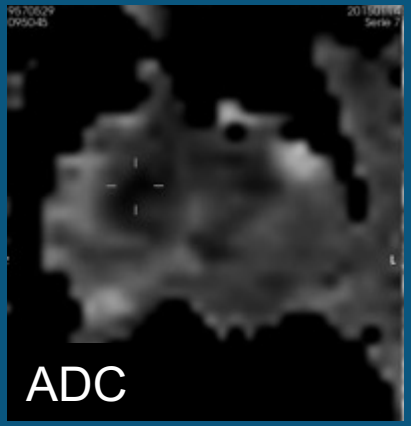
PI-RADS v3: value of DWI in TZ

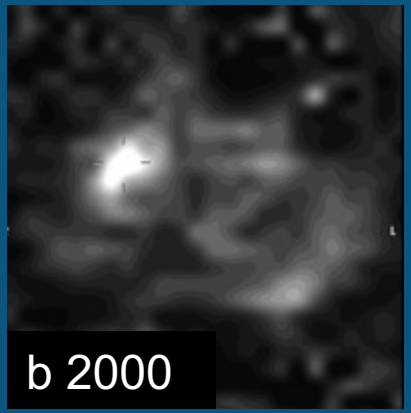


PSA 4, PSAD 0.05

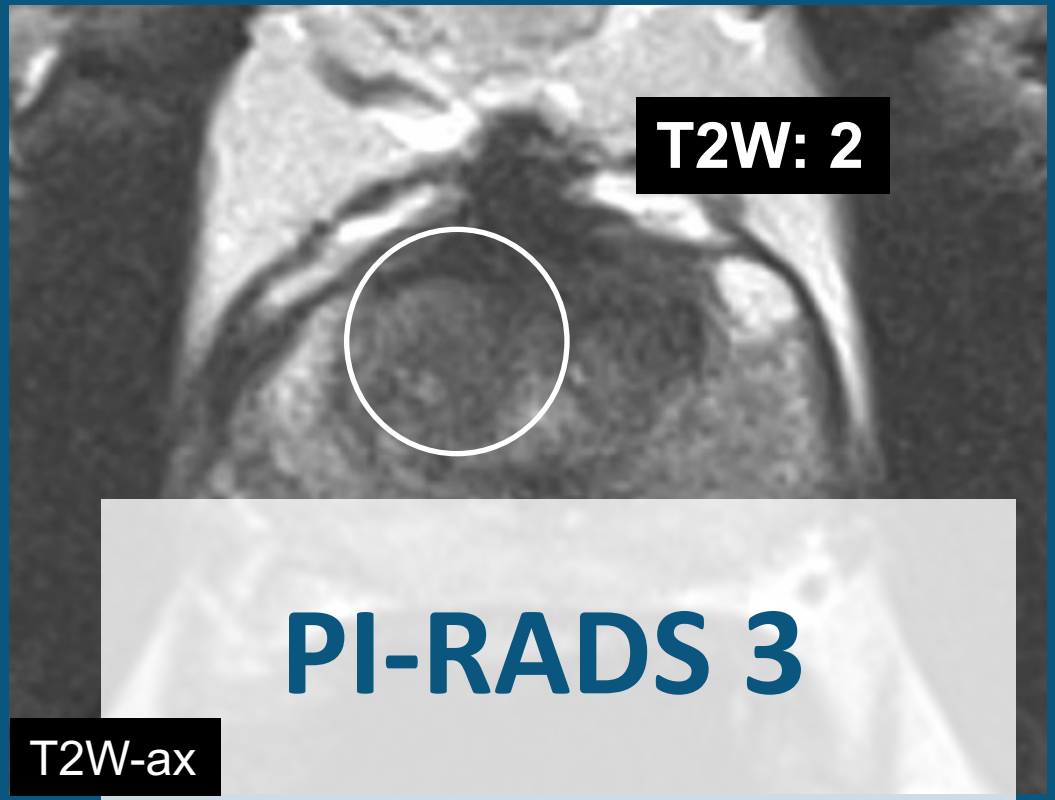
PI-RADS v3: value of DWI in TZ

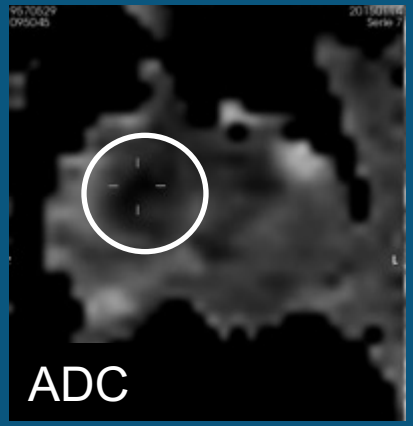




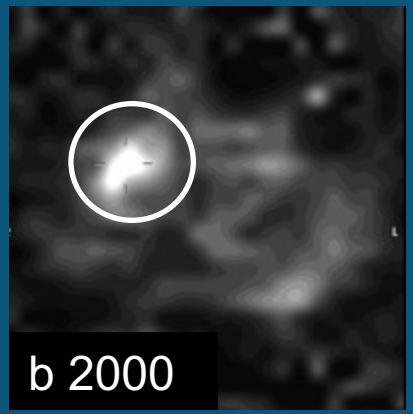


PI-RADS v3: value of DWI in TZ

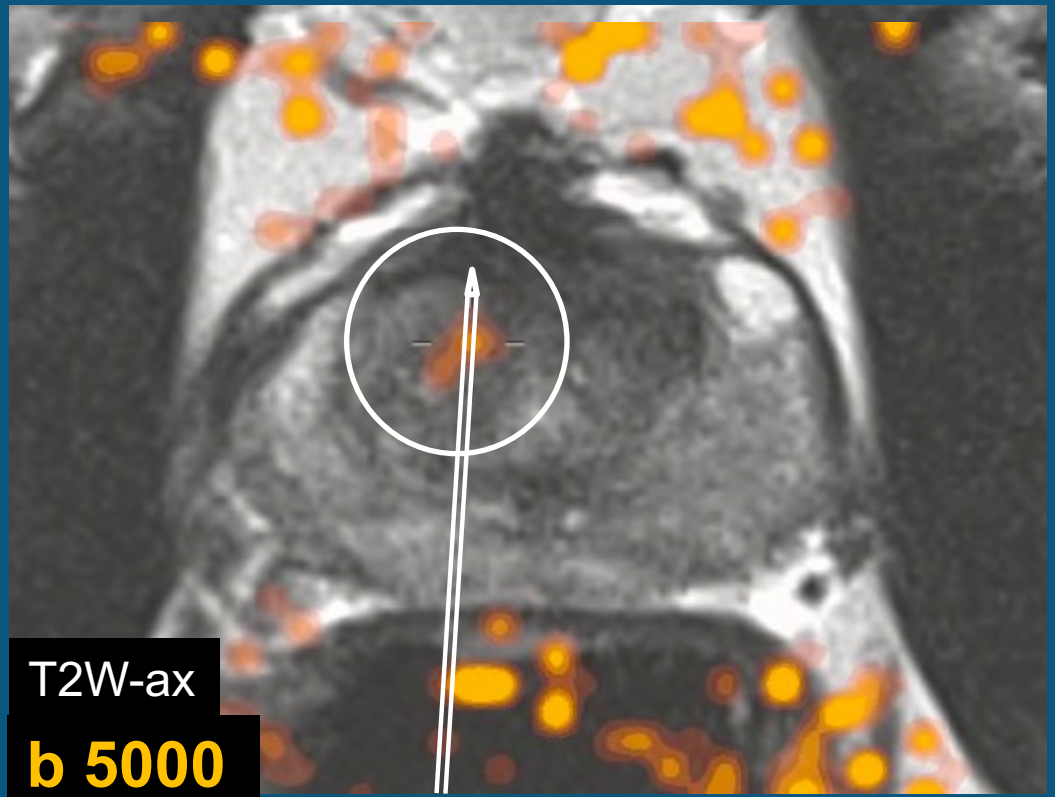


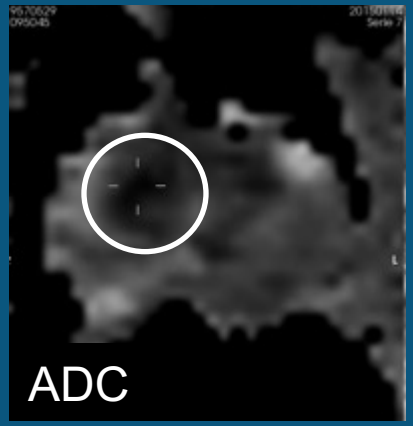


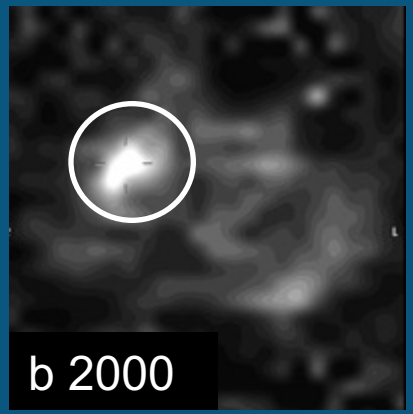
DWI: 4



PI-RADS v3: MR-GB: Gl 3+5

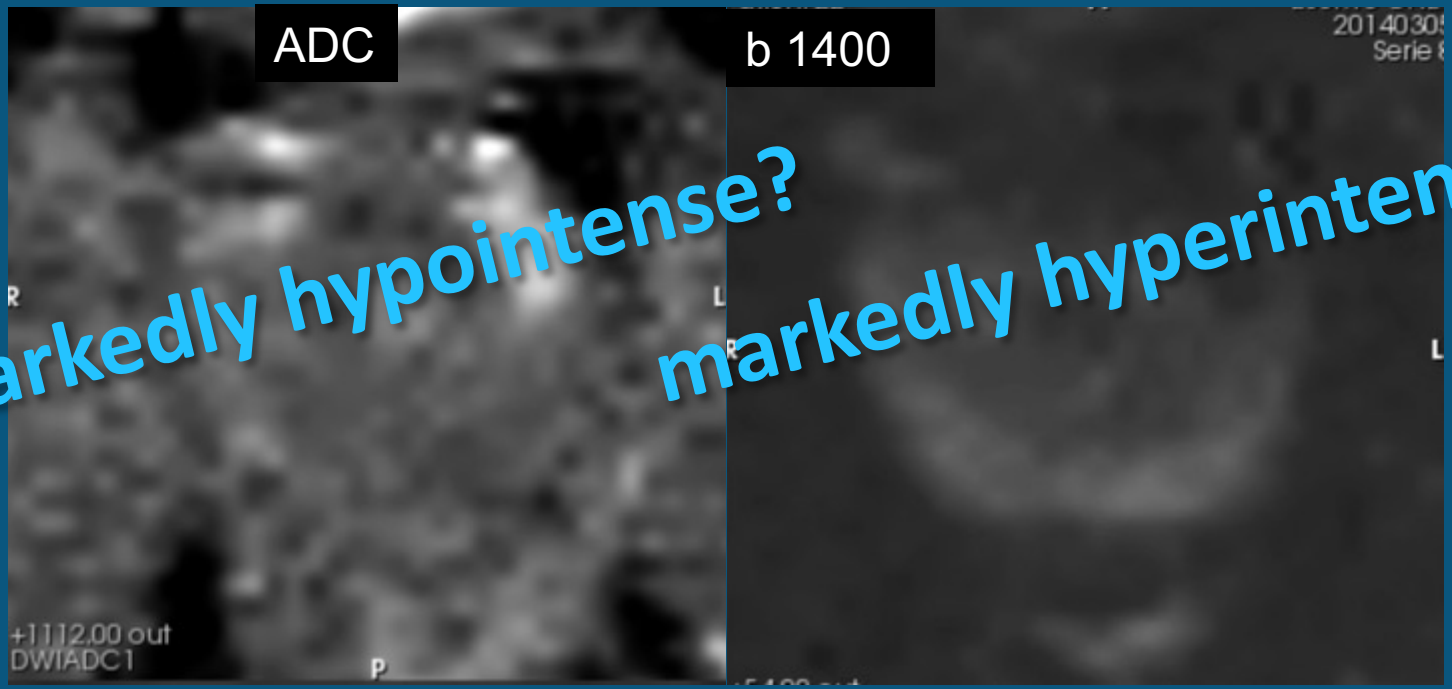




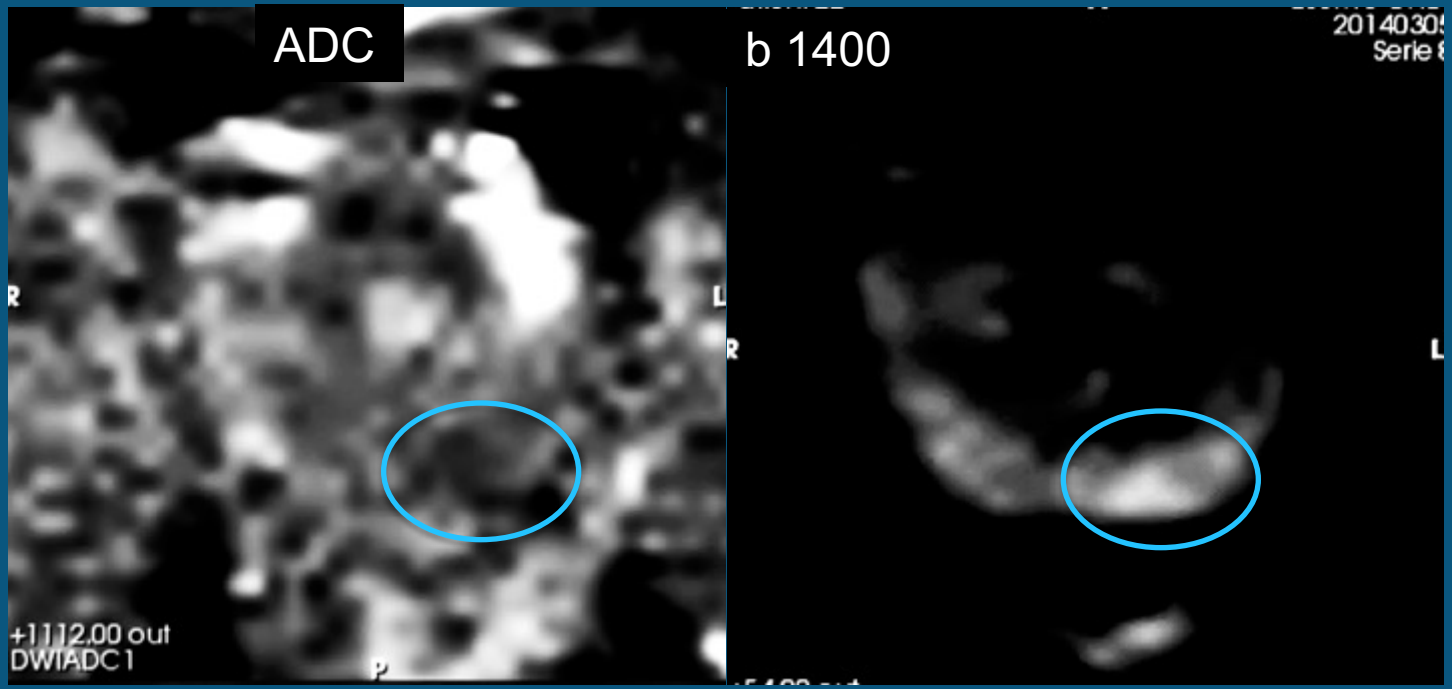


QUANTIFICATION

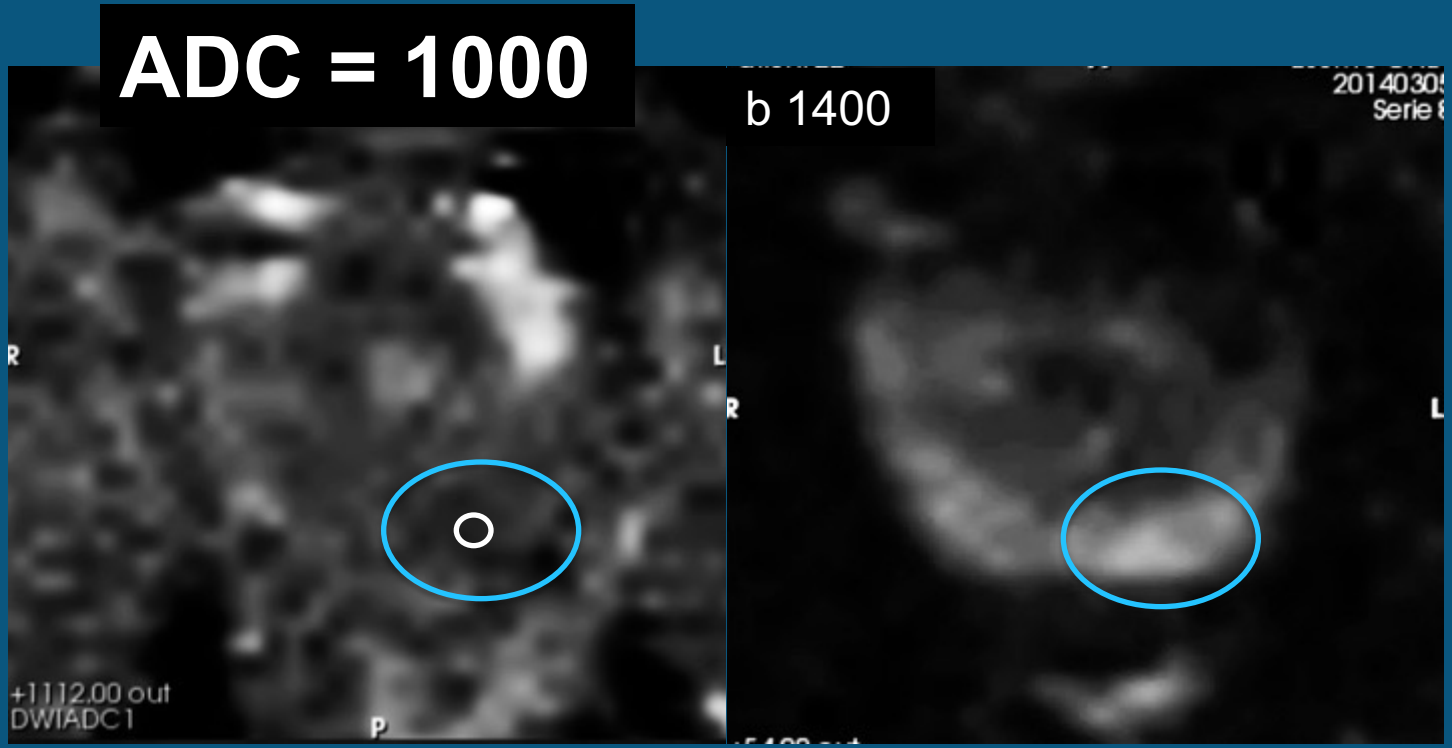
PI-RADS score for DWI?



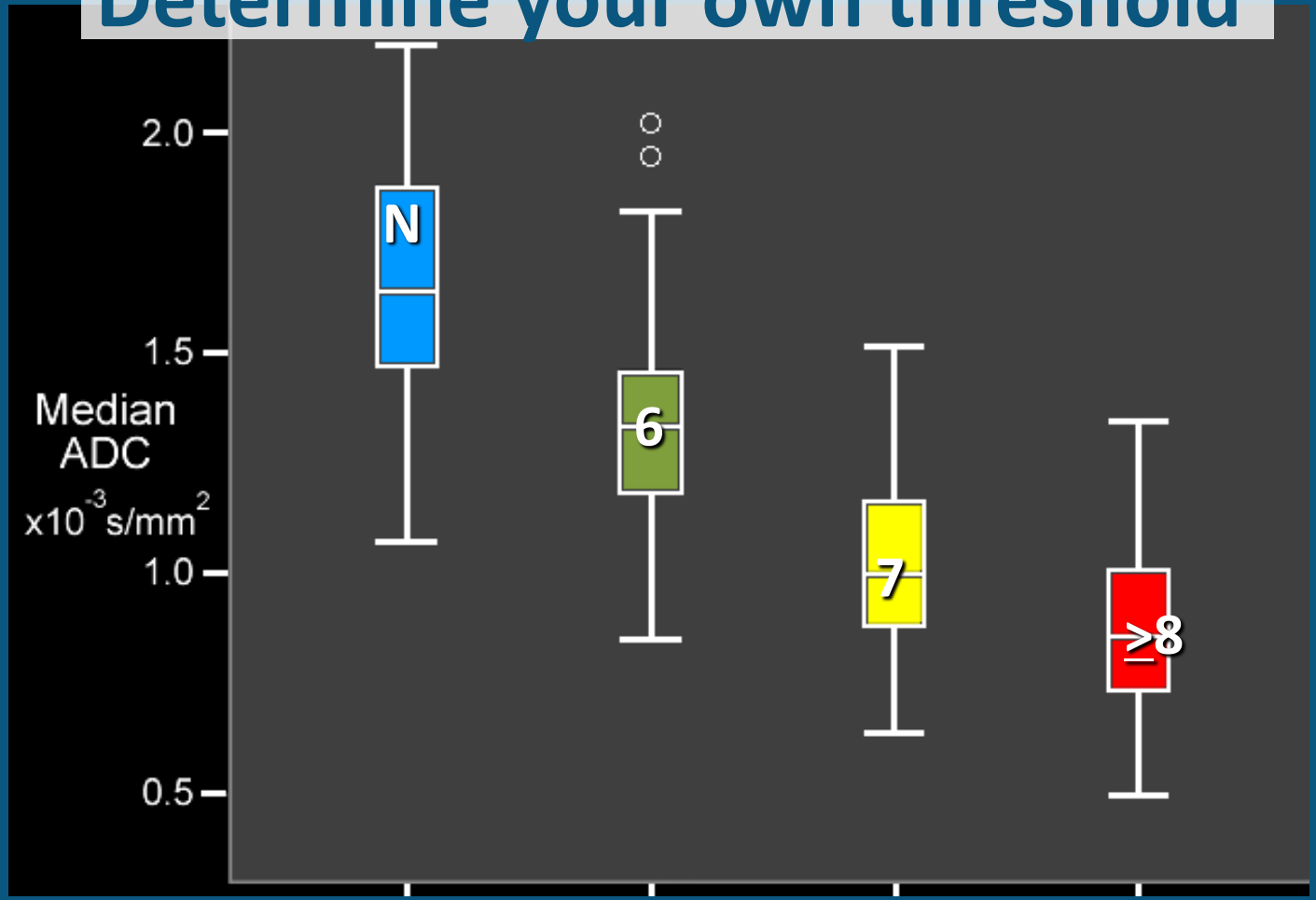
PI-RADS score for DWI?



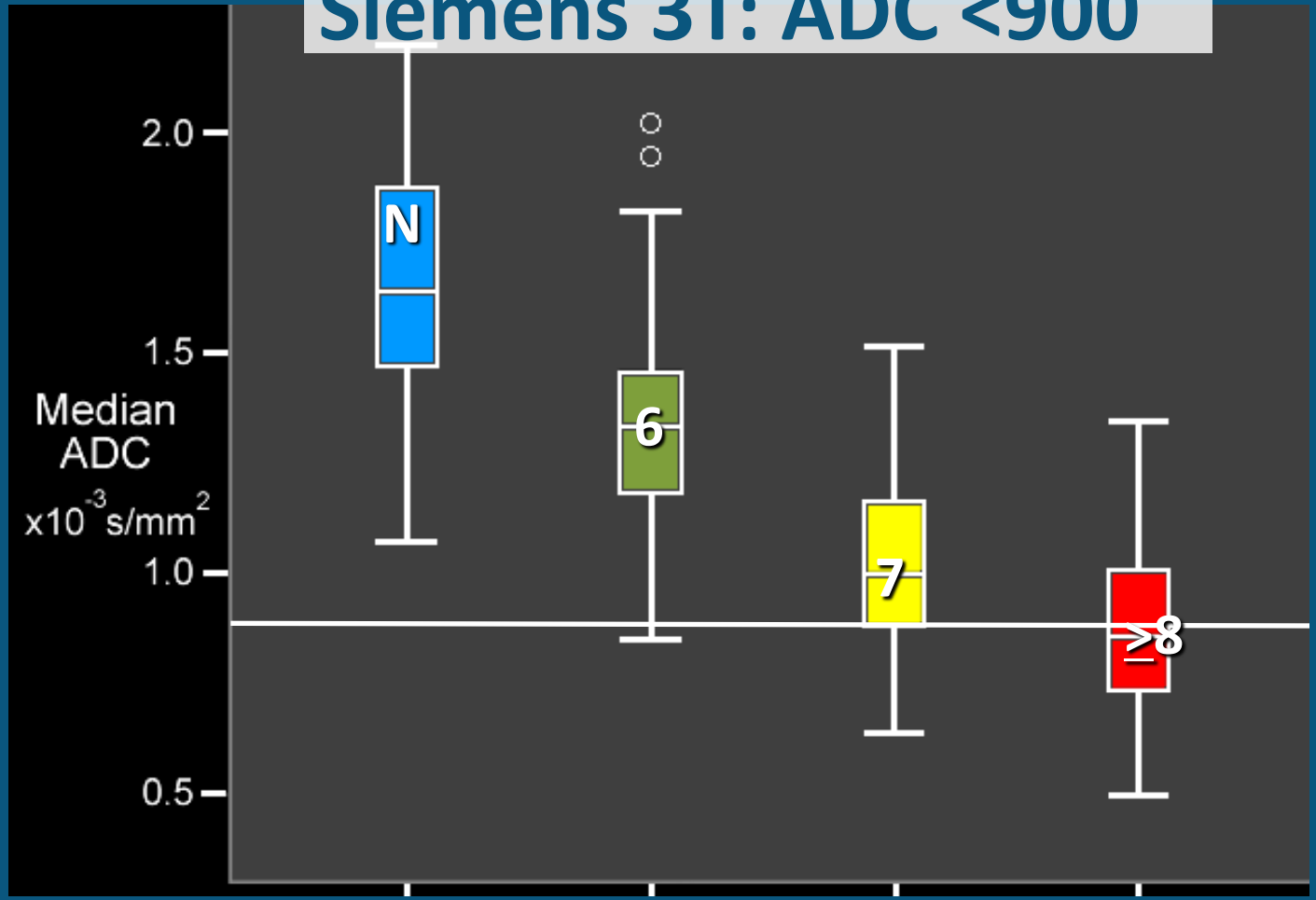
PI-RADS score for DWI?



Determine your own threshold

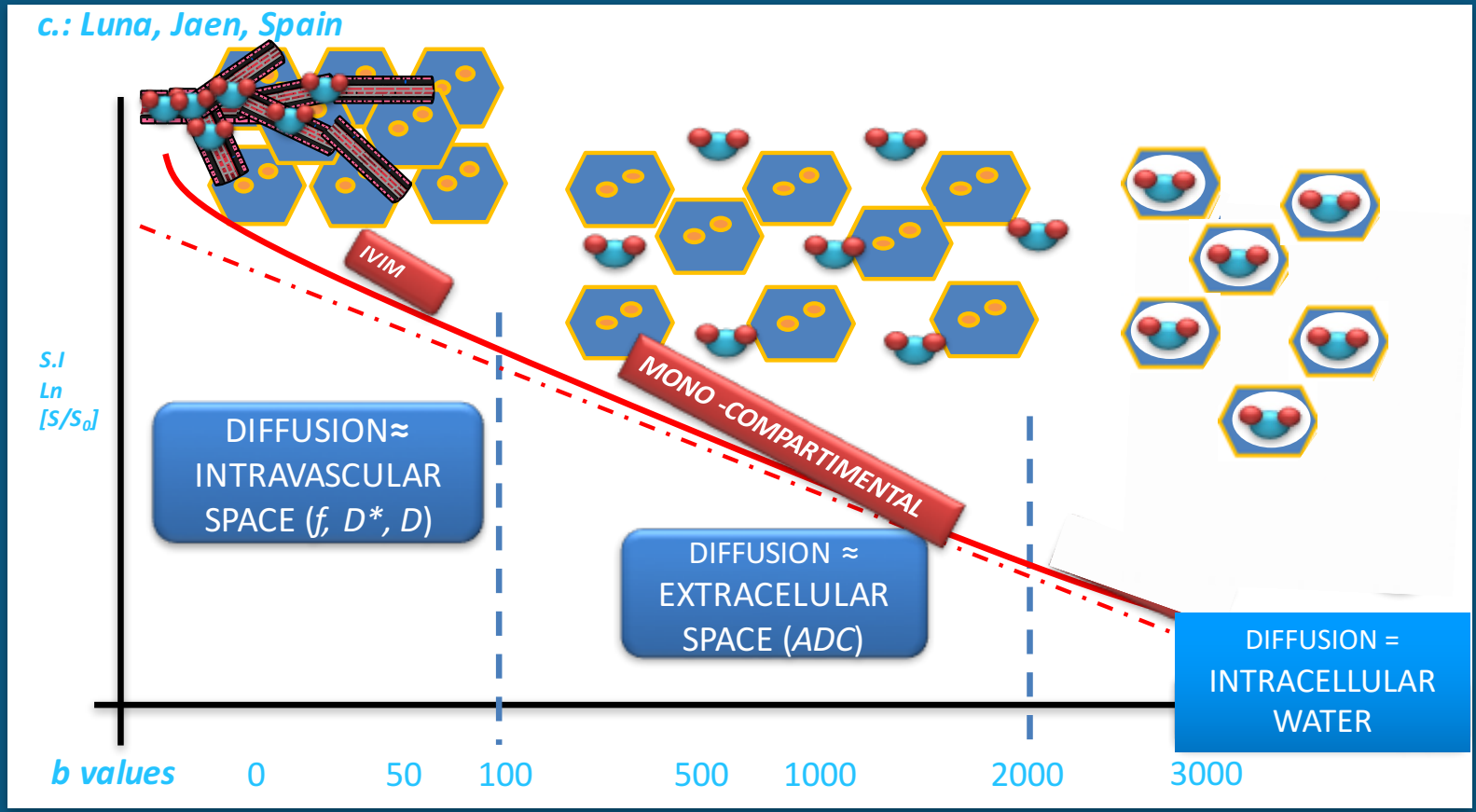


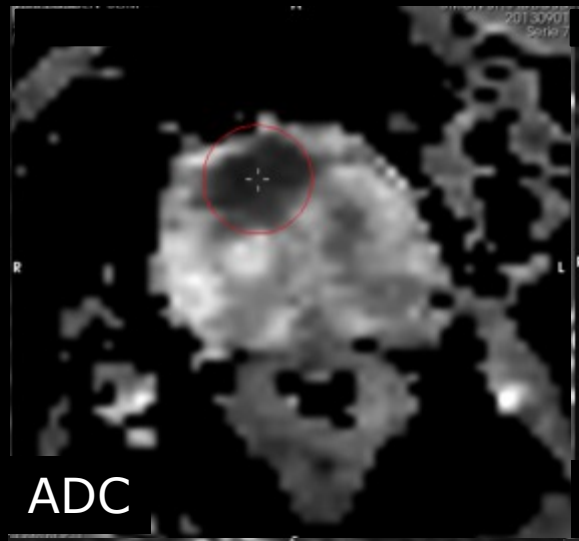
Siemens 3T: ADC <900

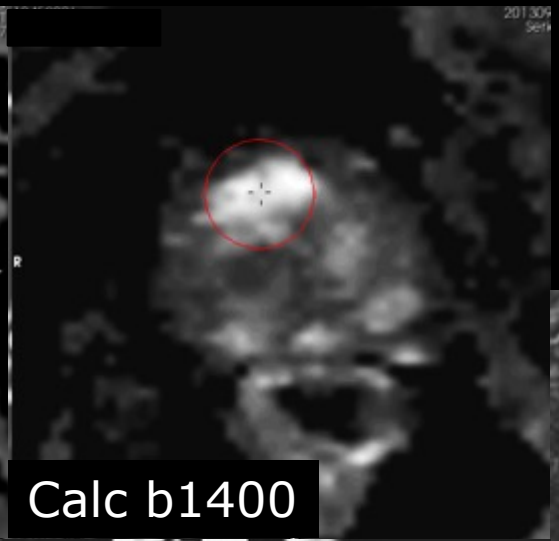


HIGH B-VALUE IN TZ

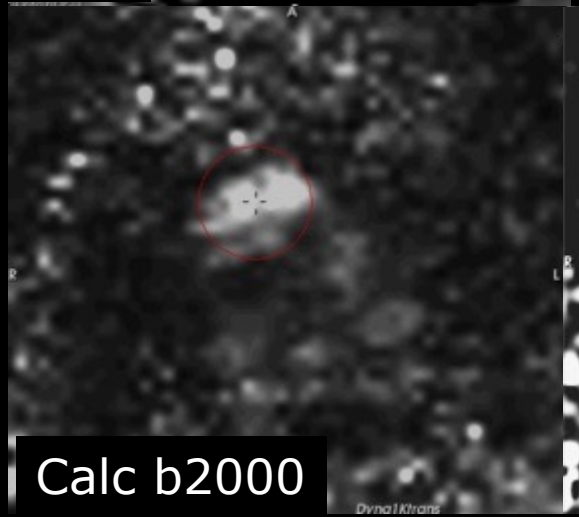
PI-RADS 3: higher b-values?

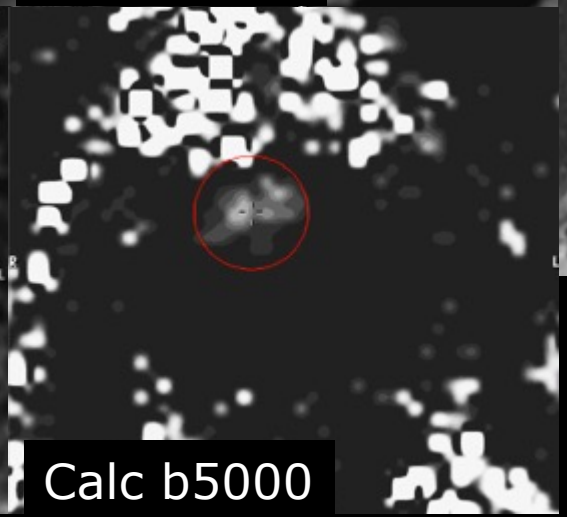



ADC

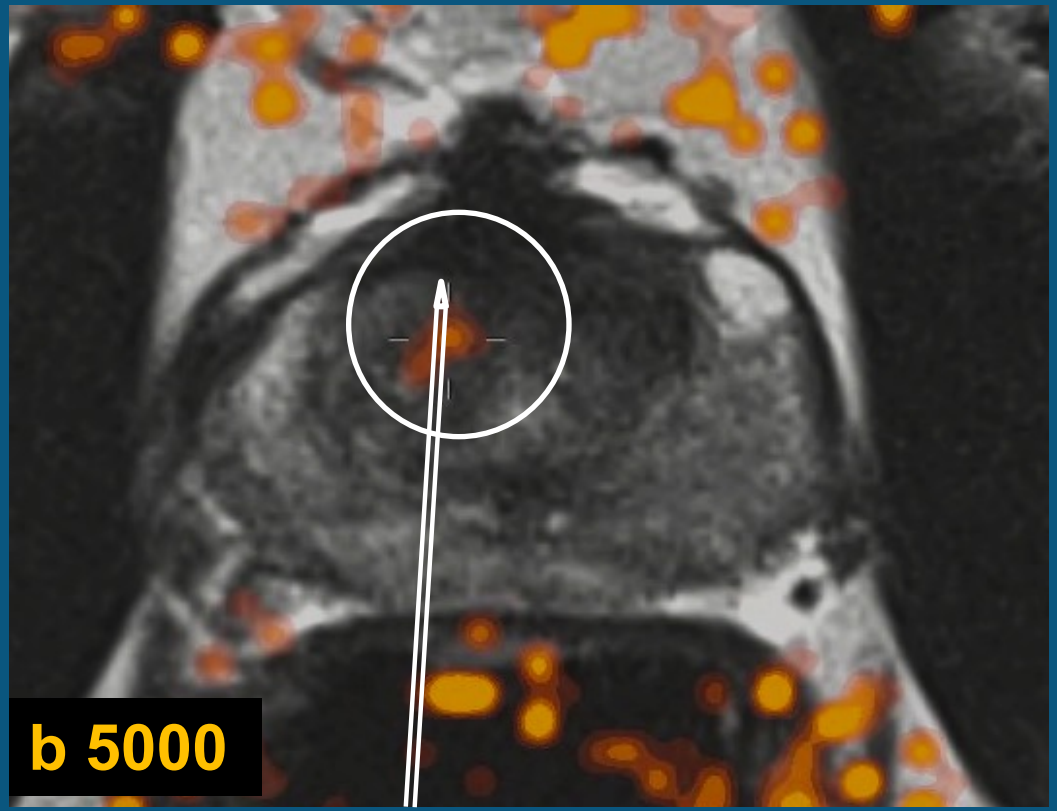

Calc b1400

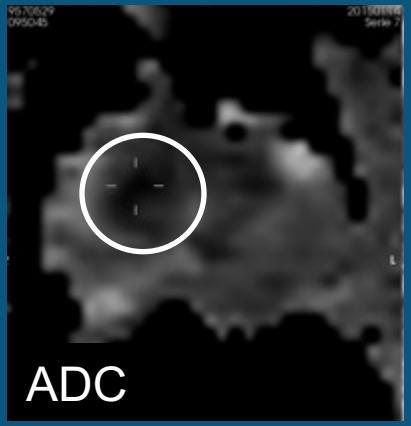

T2W

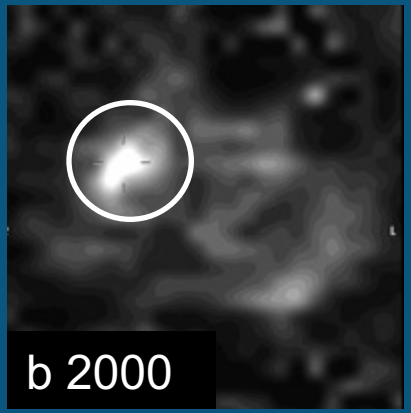

Calc b2000


Calc b5000

MRDB: Gl 3+5







DOES mp-MRI MISS SIGNIFICANT PCA?

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European Association of Urology

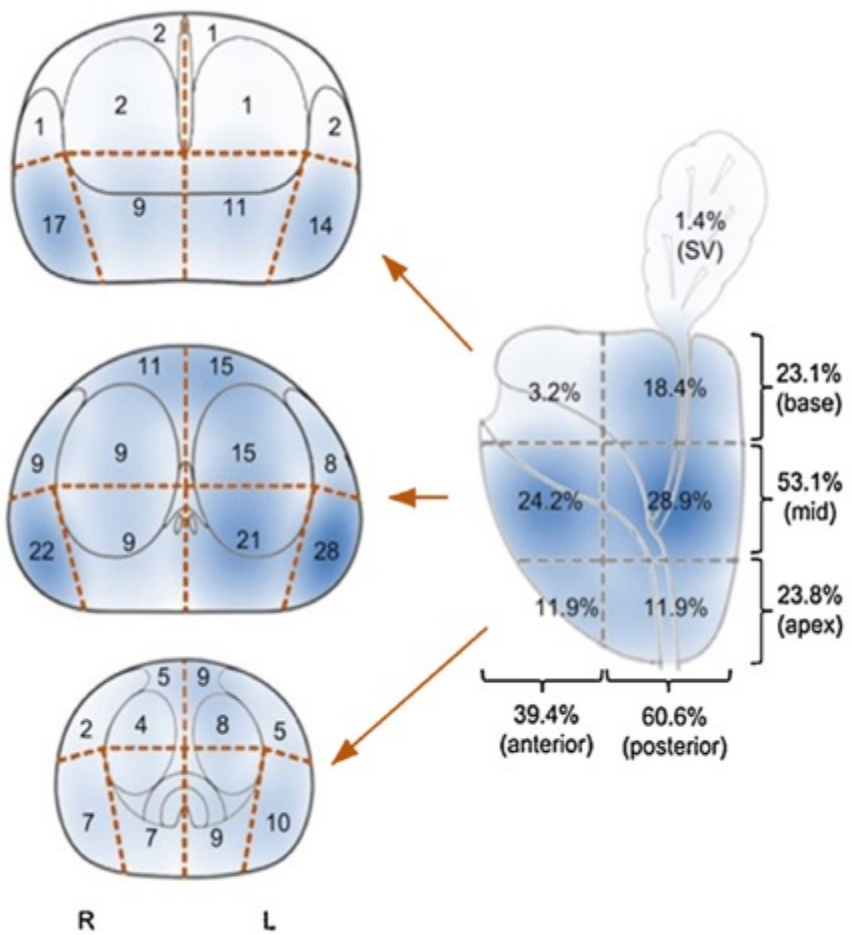
Platinum Priority – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

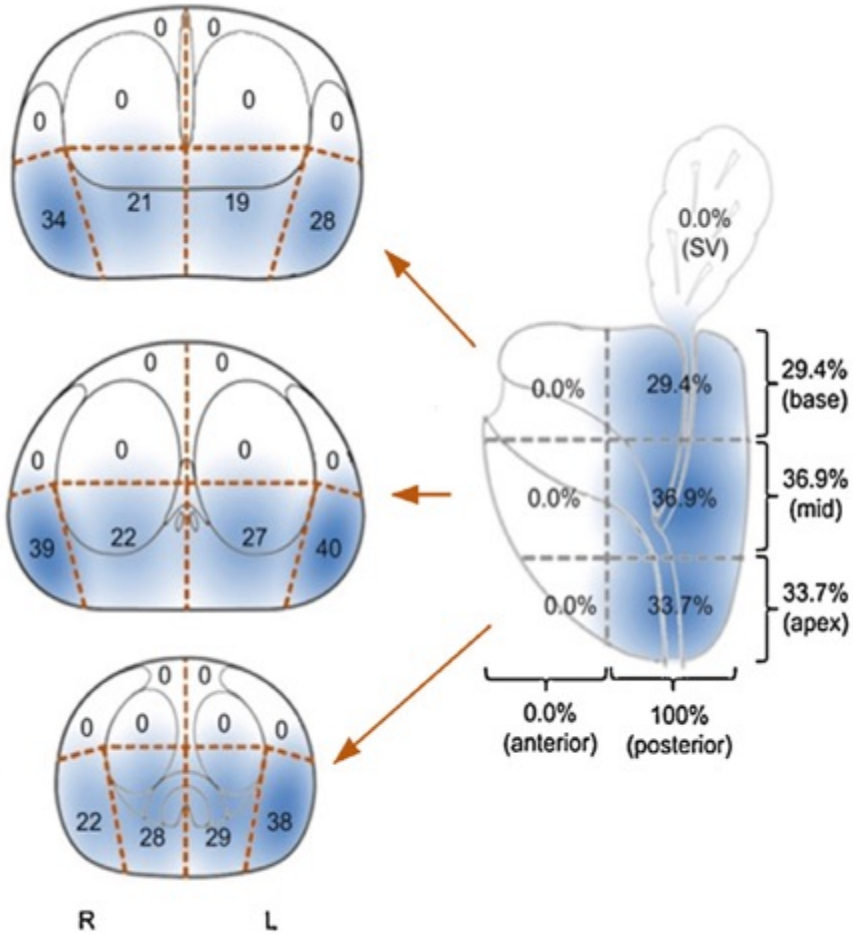
Why and Where do We Miss Significant Prostate Cancer with Multi-parametric Magnetic Resonance Imaging followed by Magnetic Resonance-guided and Transrectal Ultrasound-guided Biopsy in Biopsy-naïve Men?

Martijn G. Schouten [a,], Marloes van der Leest [a], Morgan Pokorny [b], Martijn Hoogenboom [a], Jelle O. Barentsz [a], Les C. Thompson [b], Jurgen J. Fütterer [a]*

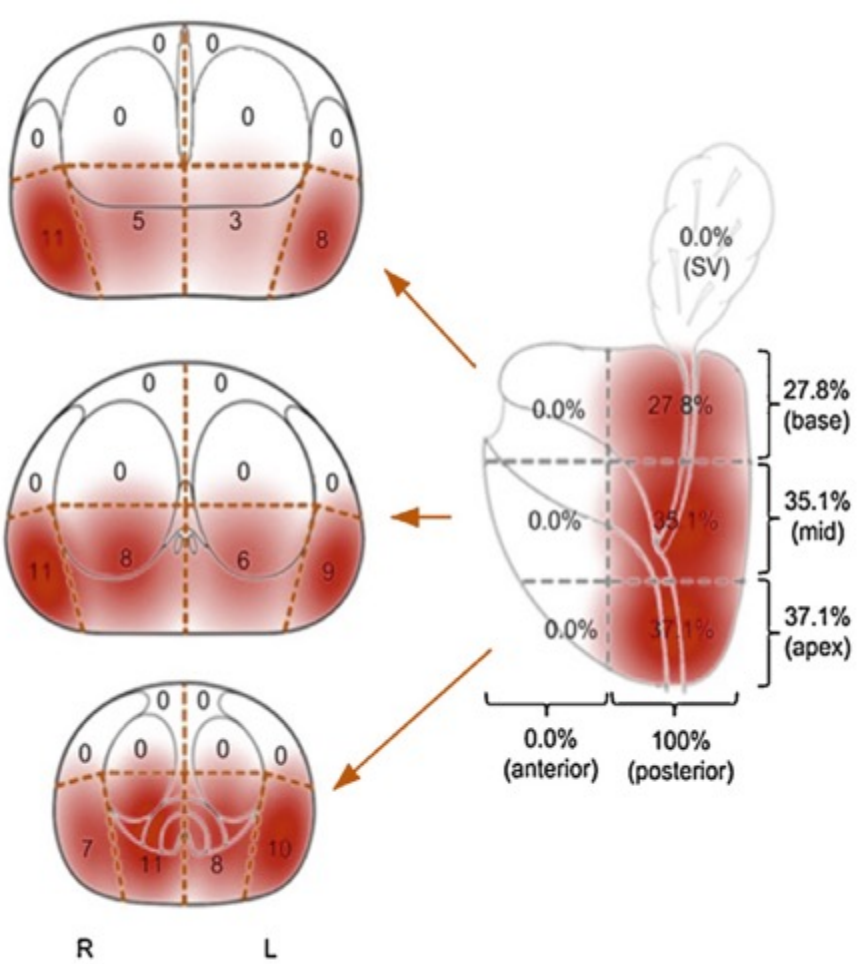
[a] *Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Nijmegen, The Netherlands;* [b] *Department of Urology, The Wesley Hospital, Brisbane, Australia*



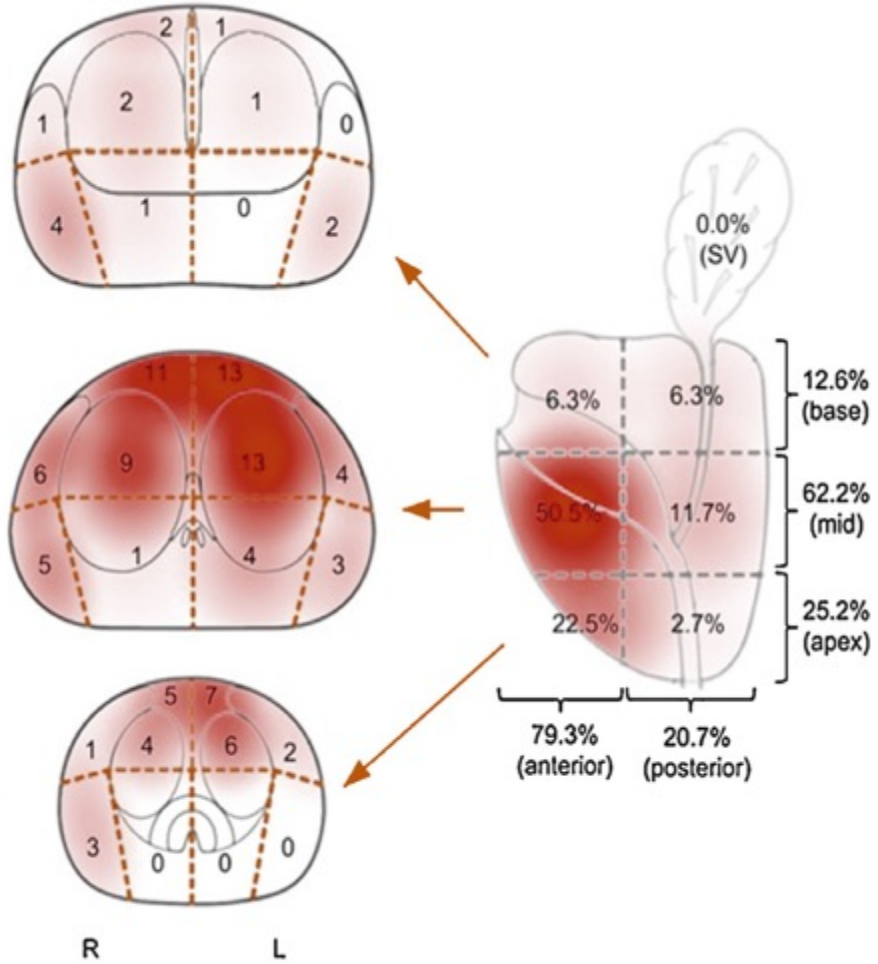
Cancer positive on MR-Bx



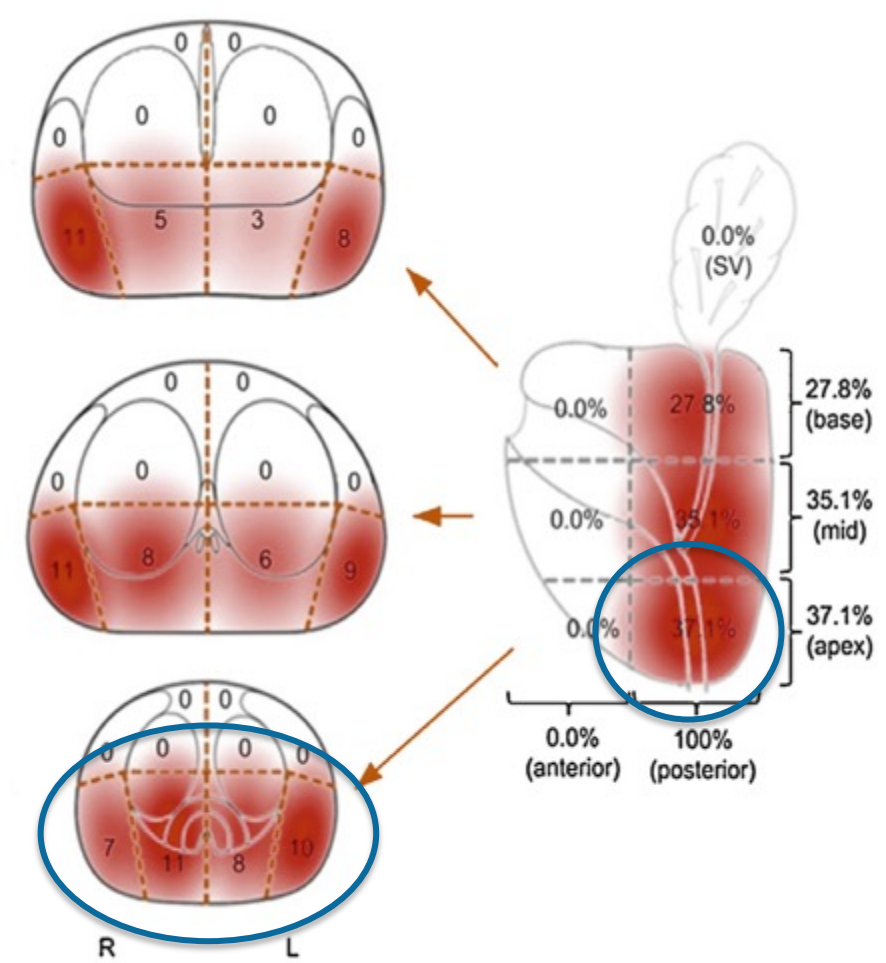
Cancer positive on TRUS-Bx



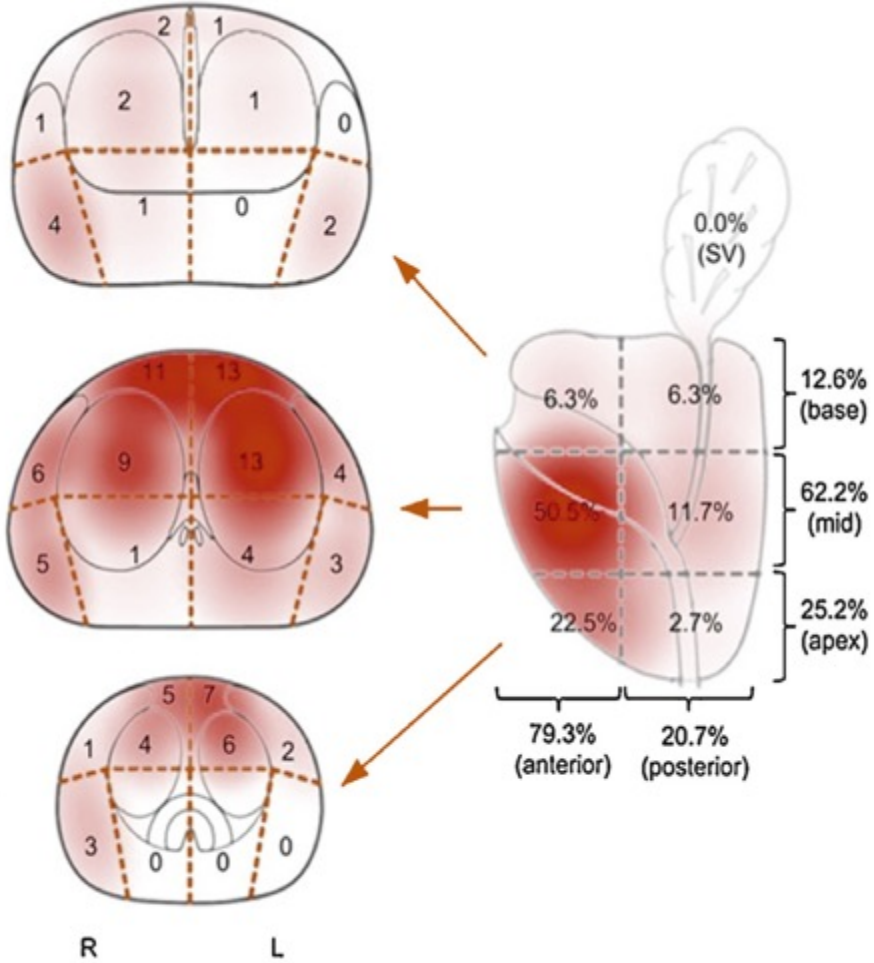
Missed segments with MR-Bx



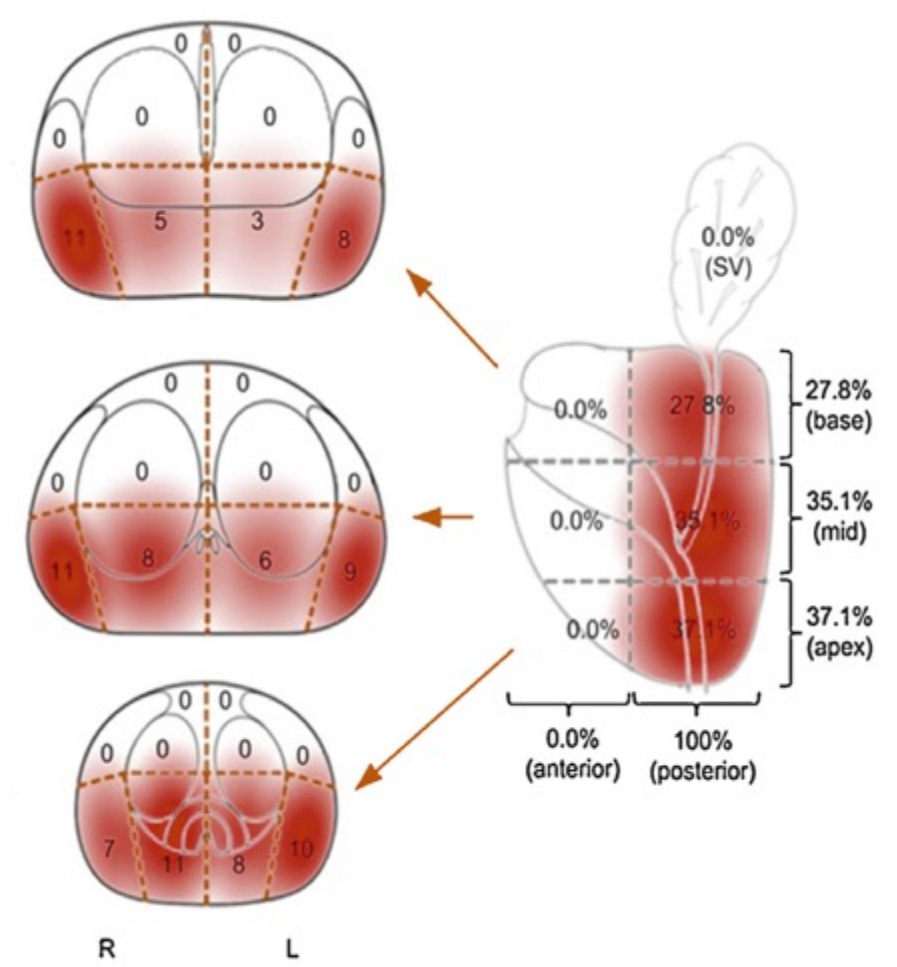
Missed segments with TRUS-Bx



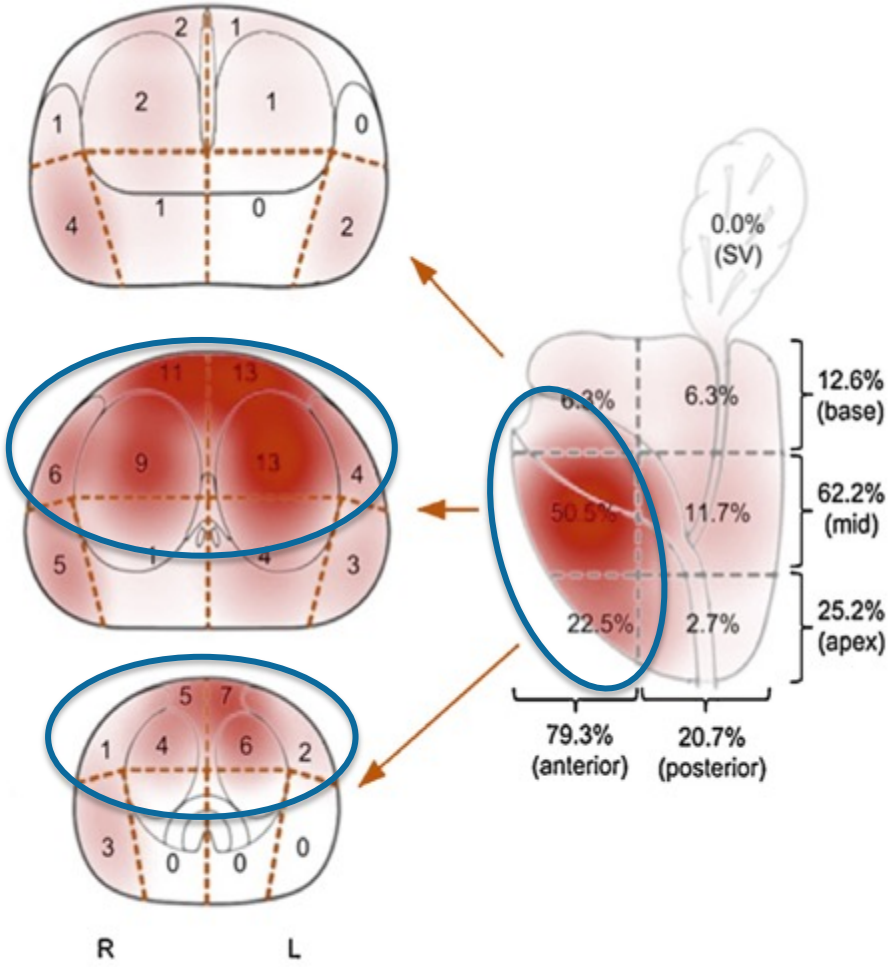
Missed segments with MR-Bx



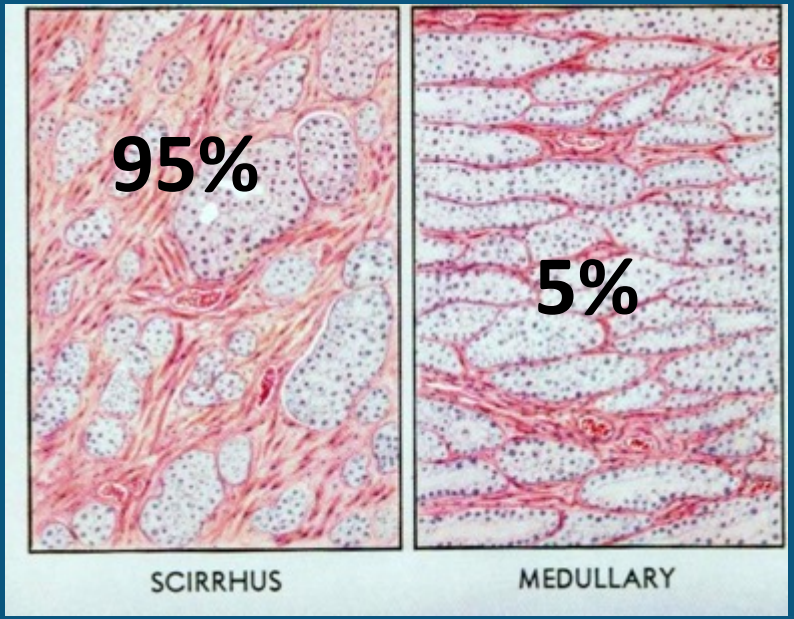
Missed segments with TRUS-Bx



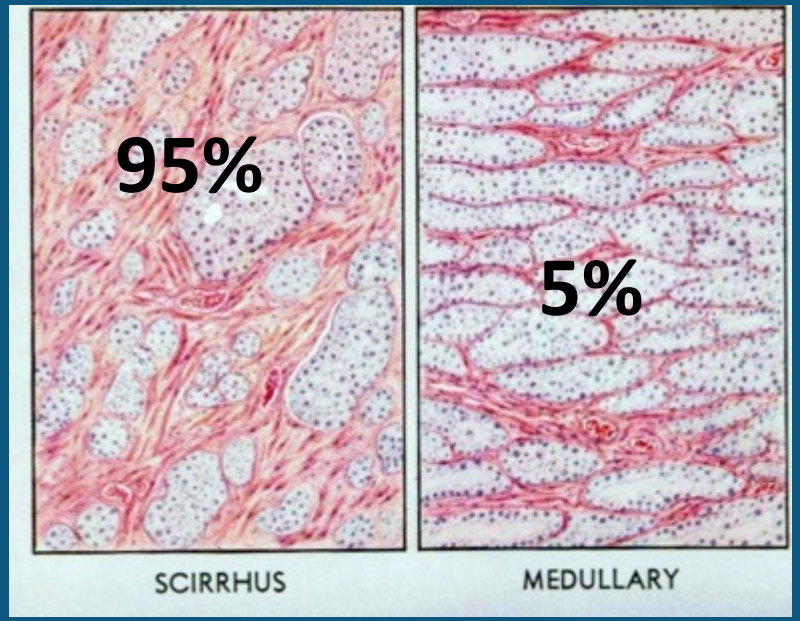
Missed segments with MR-Bx



Missed segments with TRUS-Bx



1954 - FEEL A HARD LUMP

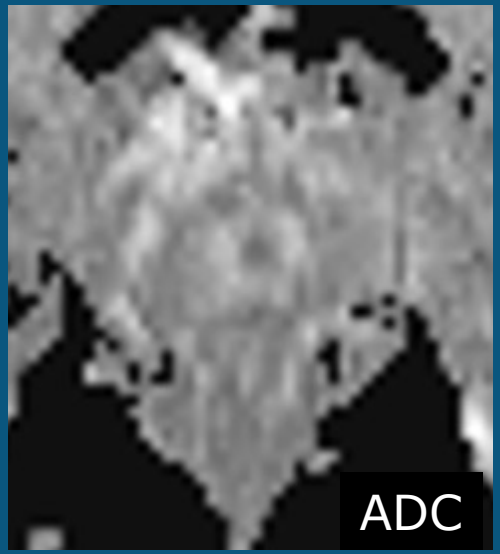


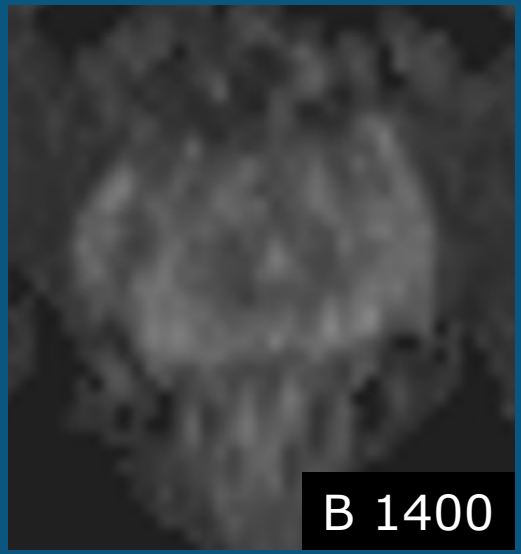
1954 - FEEL A HARD LUMP

2014 - SEE A HARD LUMP:

DWI - finds the scirrhus tumors

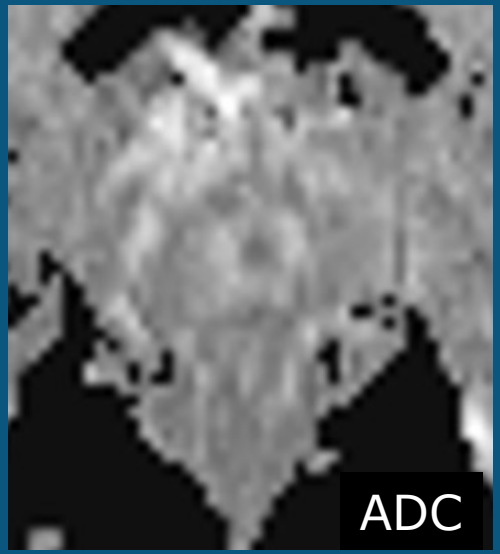
What sPCa do we miss with mpMRI?

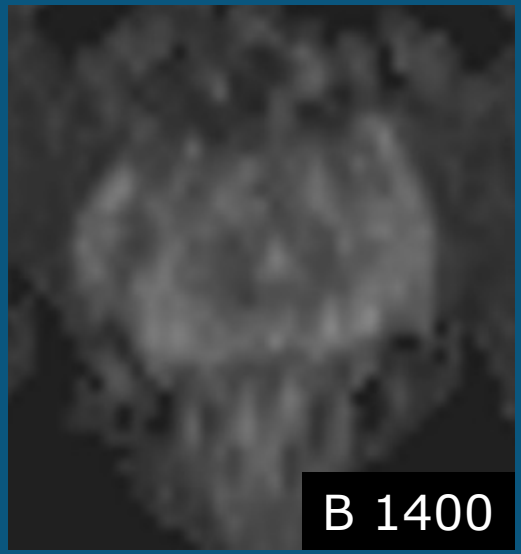




- ✓ **Gleason 3+4, large 3+3**

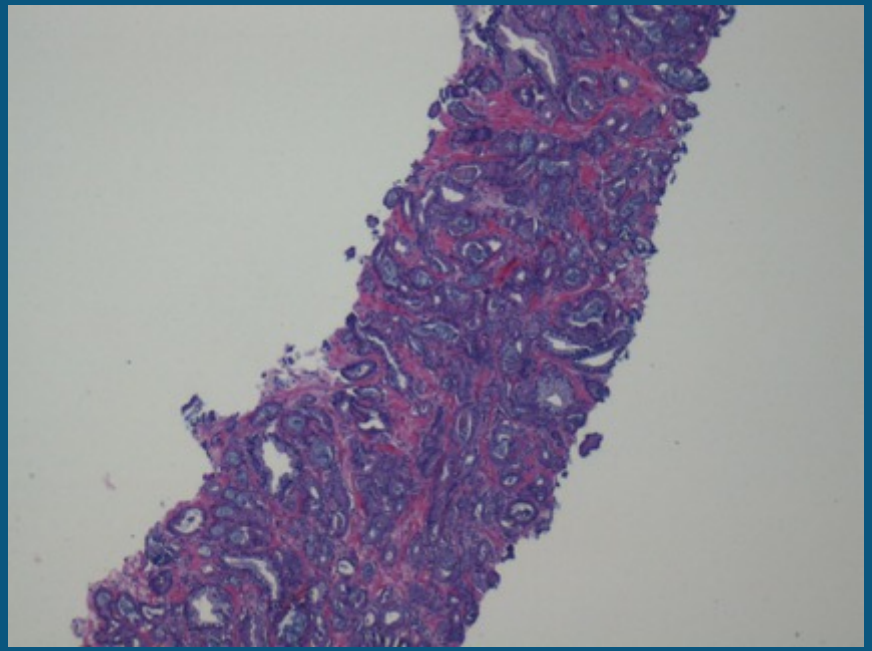
What sPCa do we miss with mpMRI?

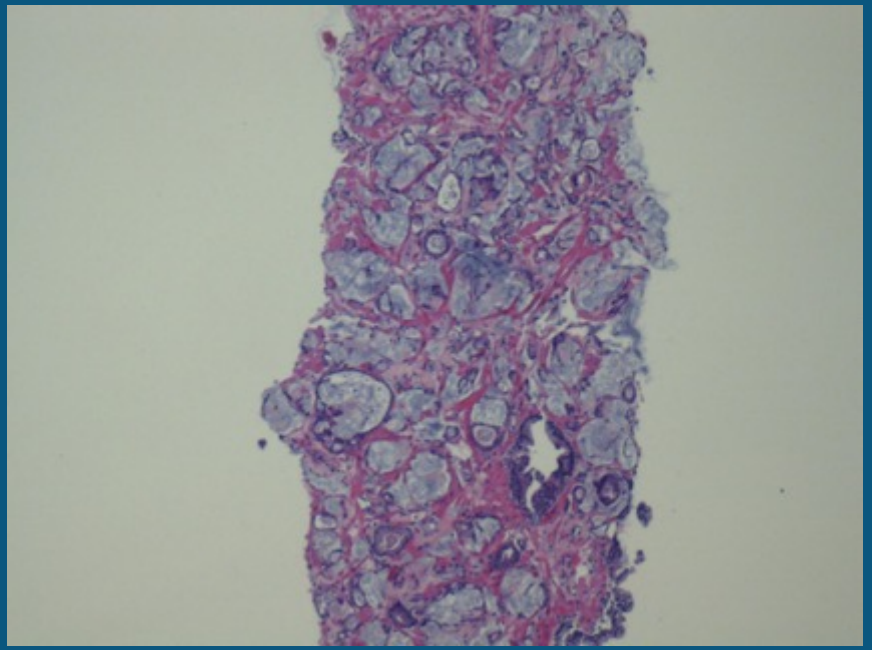




- ✓ **Gleason 3+4, large 3+3 (>75%)**

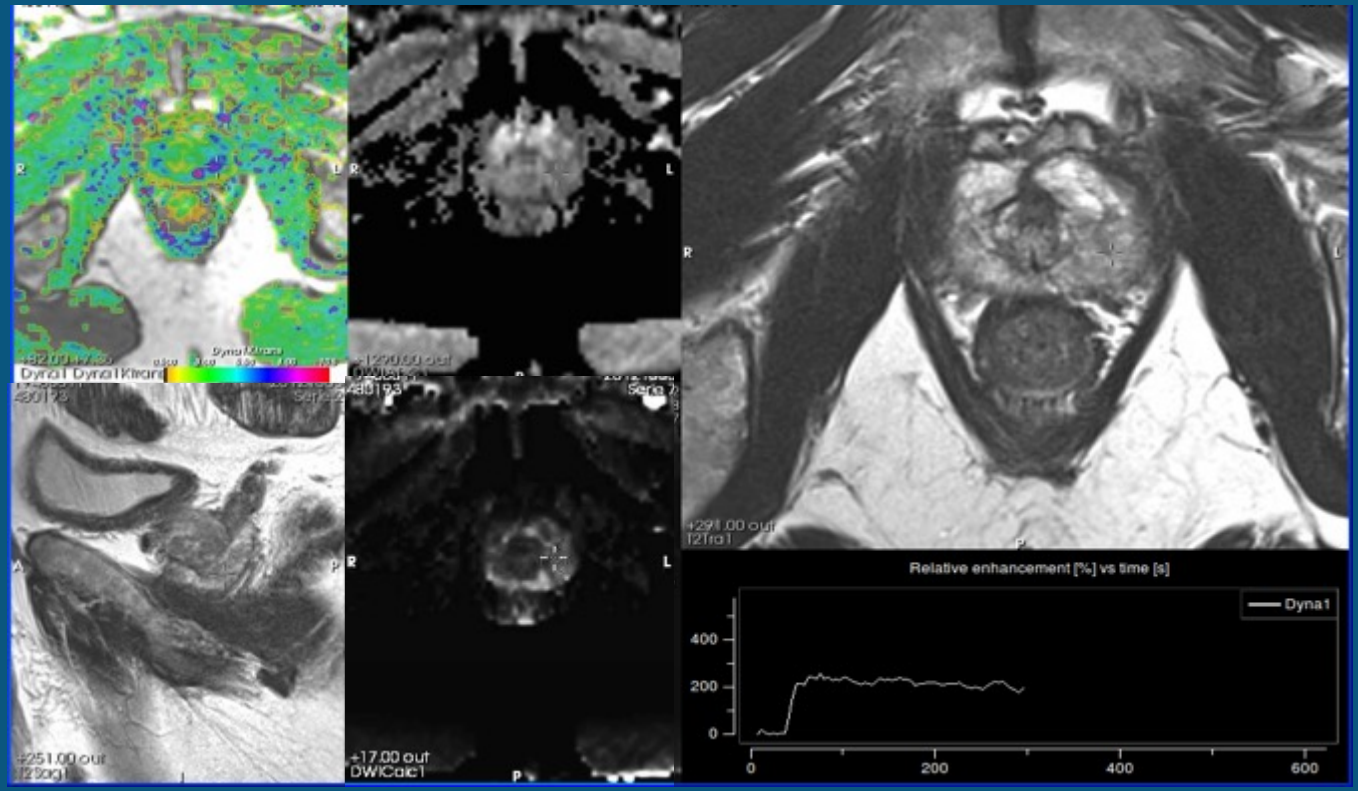
What sPCa do we miss with mpMRI?





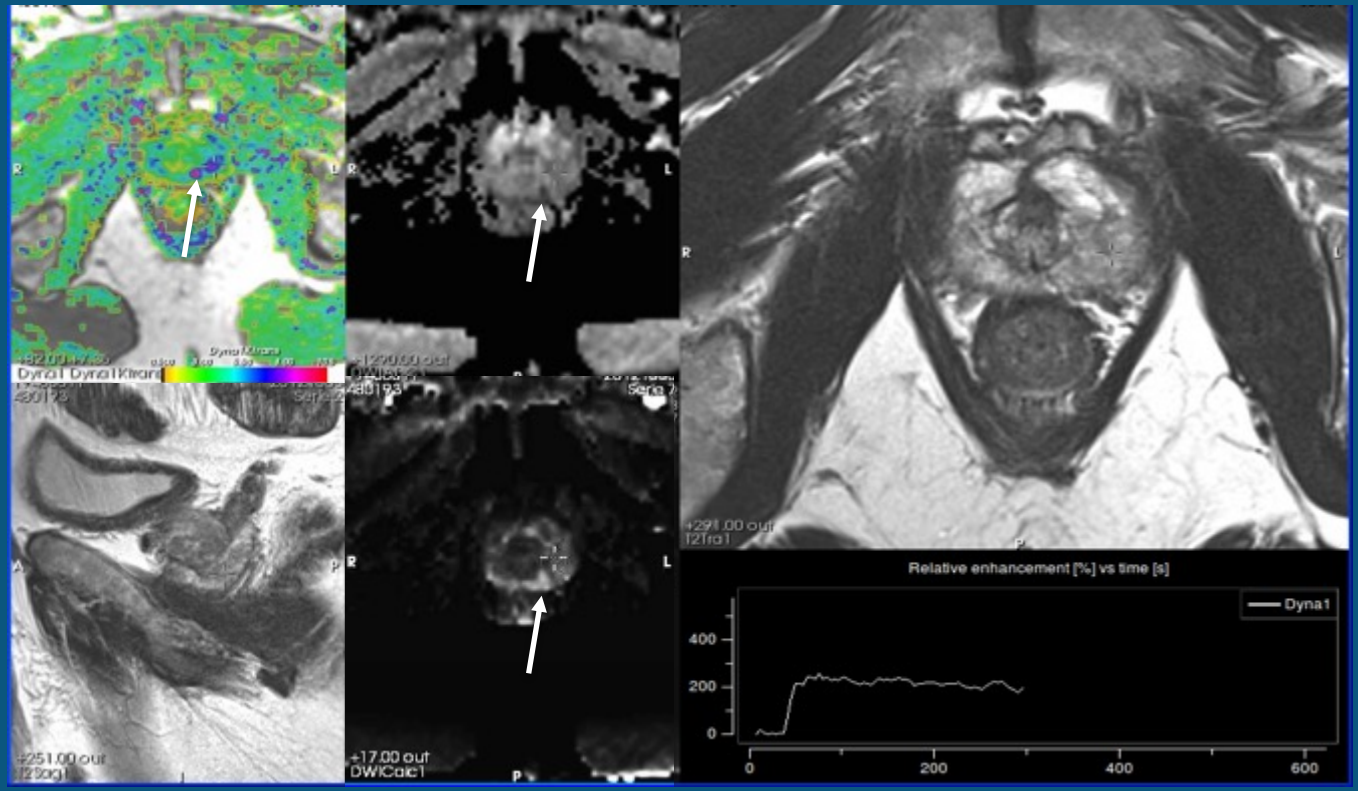
- ✓ Gleason ≥4+3 with areas of MUCIN production

What sPCa do we miss with mpMRI?



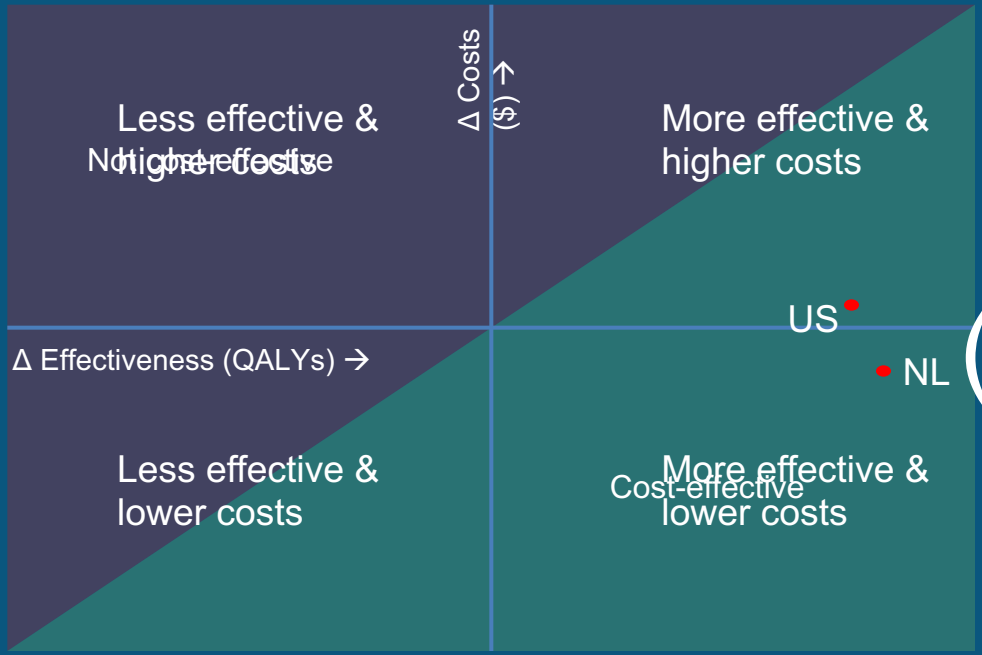
✓ **Small lesions:** misdiagnosis, and/or missed biopsy

What sPCa do we miss with mpMRI?



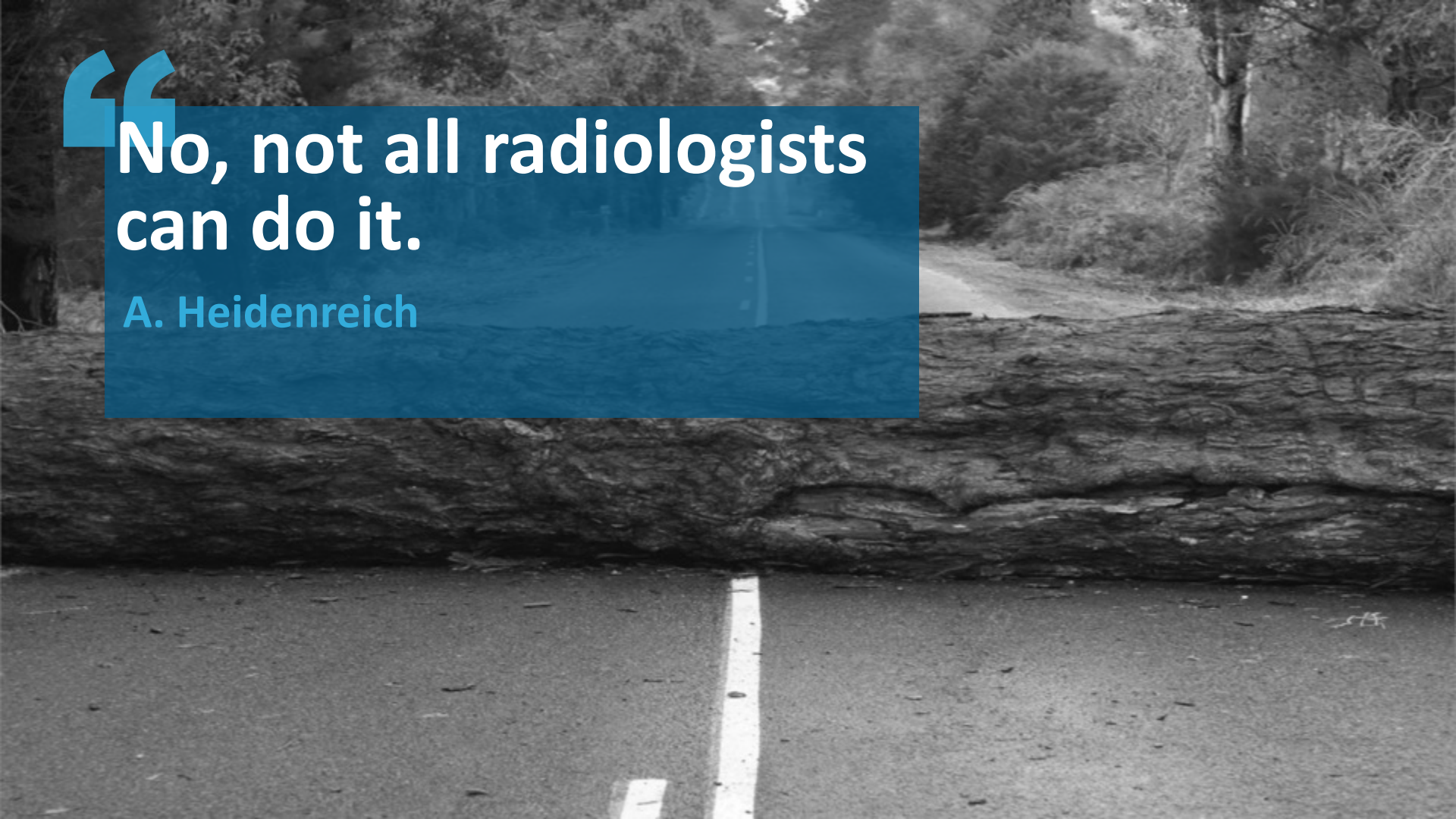
✓ Misdiagnosis

Cost-effectiveness



De Rooij, Eur Urol 2014

WHAT ARE THE CHALLENGES OF MP-MRI?


No, not all radiologists can do it.
A. Heidenreich

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European Association of Urology

Collaborative Review – Prostate Cancer

Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature

Jurgen J. Fütterer [a,*], *Alberto Briganti* [b], *Pieter De Visschere* [c], *Mark Emberton* [d], *Gianluca Giannarini* [e], *Alex Kirkham* [f], *Samir S. Taneja* [g], *Harriet Thoeny* [h], *Geert Villeirs* [c], *Arnauld Villers* [i]

Detection rate significant PCa	**44-87%**
NPV of significant PCa	**63-98%**

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European Association of Urology

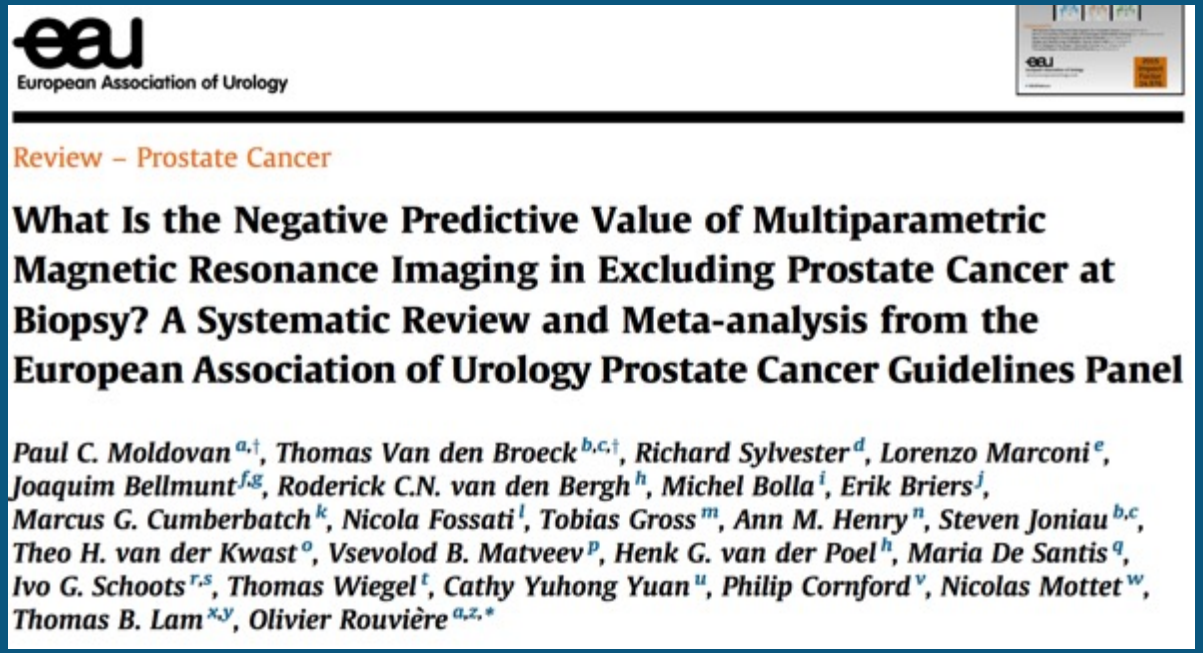
Collaborative Review – Prostate Cancer

Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature

Jurgen J. Fütterer [a,*], *Alberto Briganti* [b], *Pieter De Visschere* [c], *Mark Emberton* [d], *Gianluca Giannarini* [e], *Alex Kirkham* [f], *Samir S. Taneja* [g], *Harriet Thoeny* [h], *Geert Villeirs* [c], *Arnauld Villers* [i]

Detection rate significant PCa 44-87%

NPV of significant PCa 63-98%



European Association of Urology

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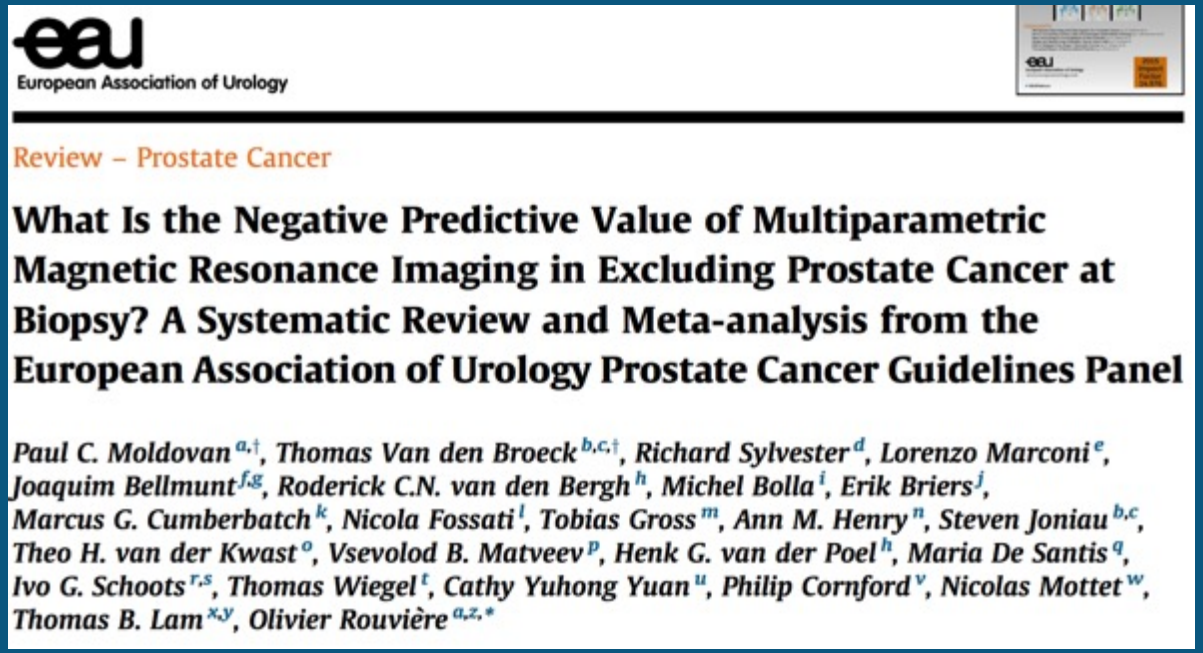
Large variability NPV for S-PK (56-99%)



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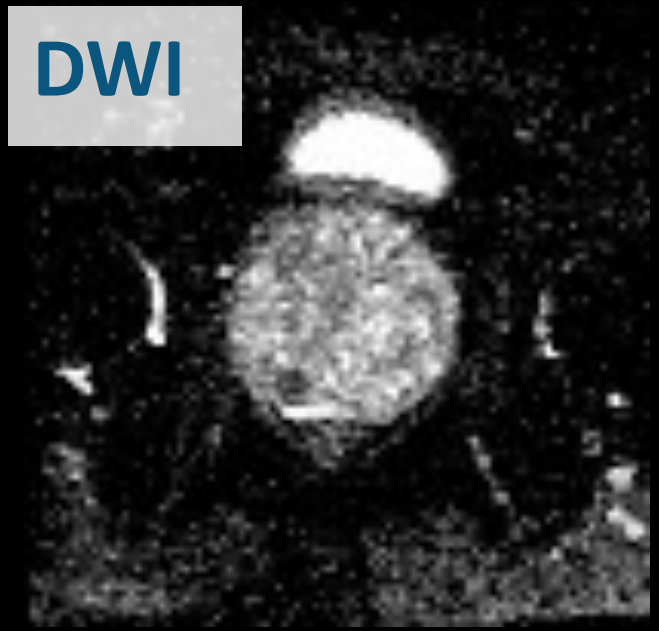
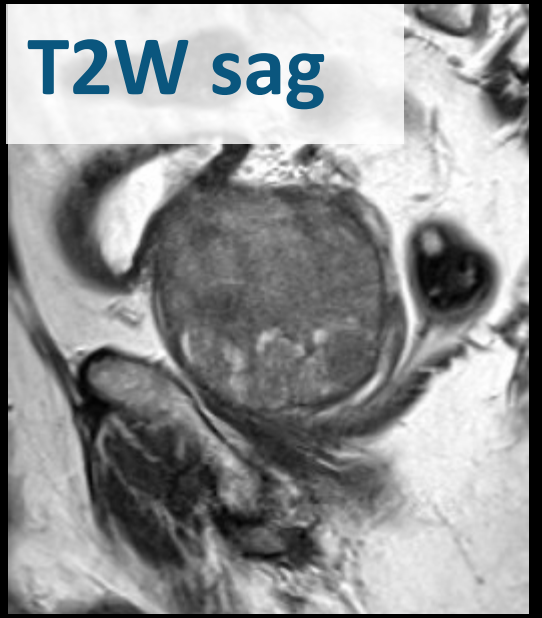
Variability of acquiring, interpretation and biopsy should ↓

“A case we see too often

65 Y; PSA 32 ng/ml; 2x negative TRUS-Bx, T1c





Report: CZ lesion, perform biopsy of this lesion,
or do so if you see another lesion

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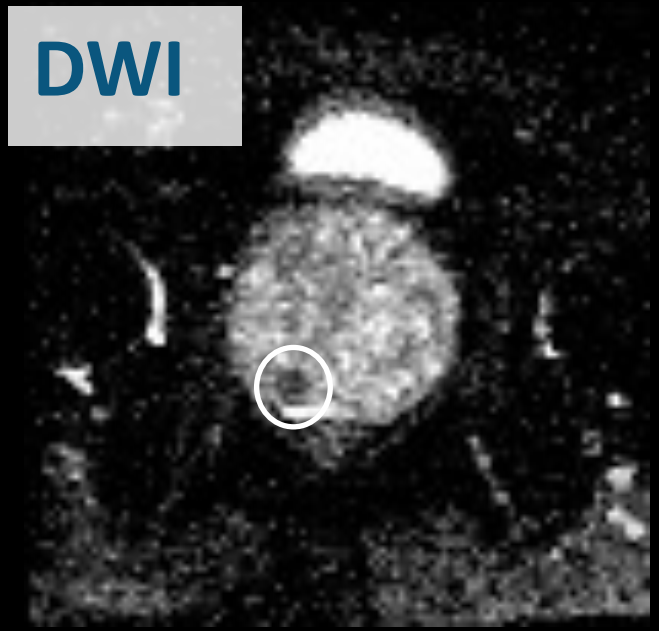

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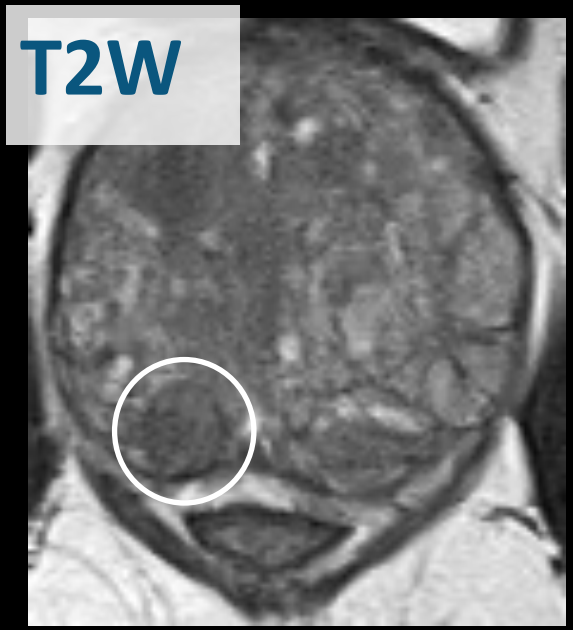

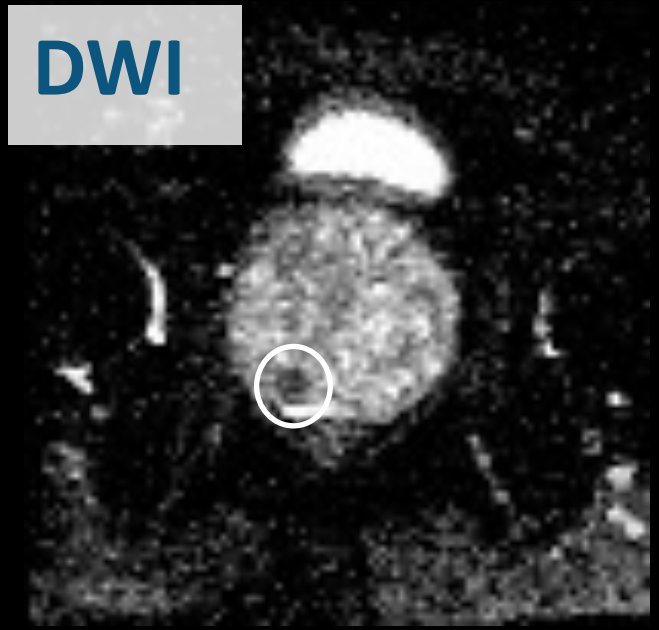

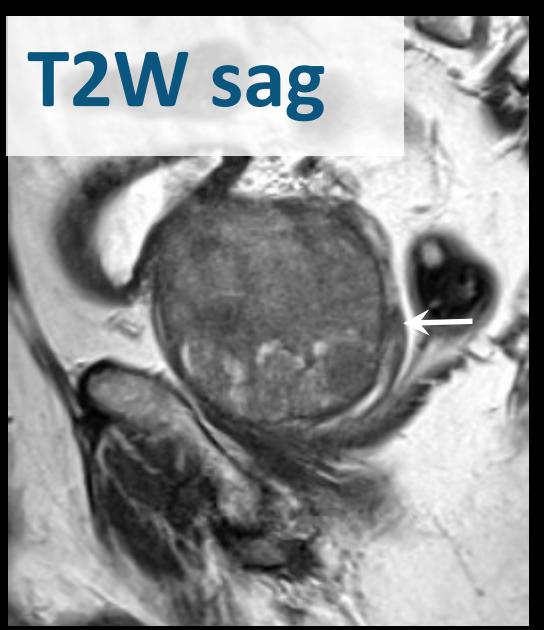

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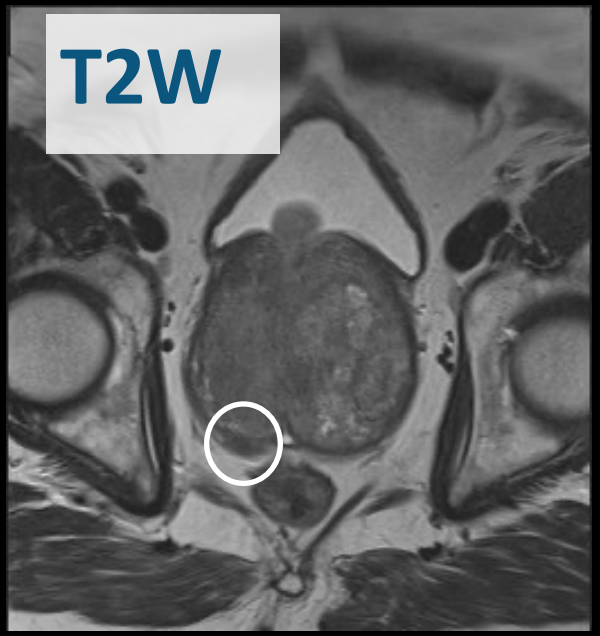

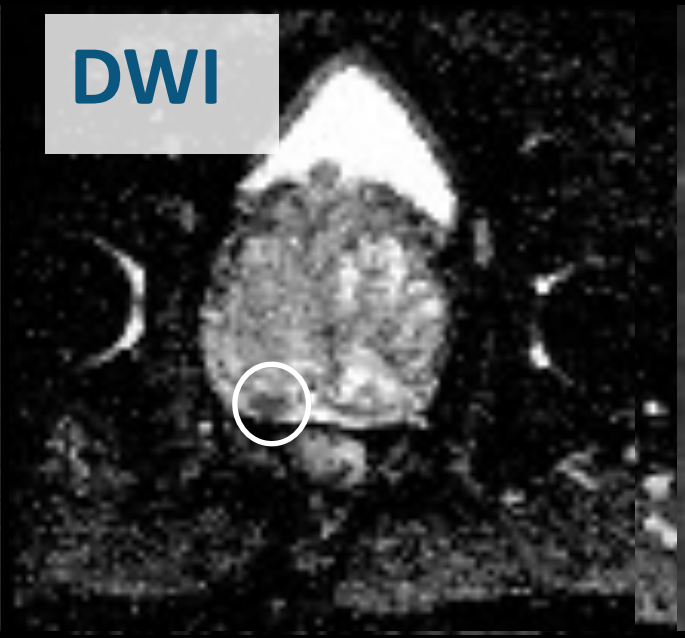

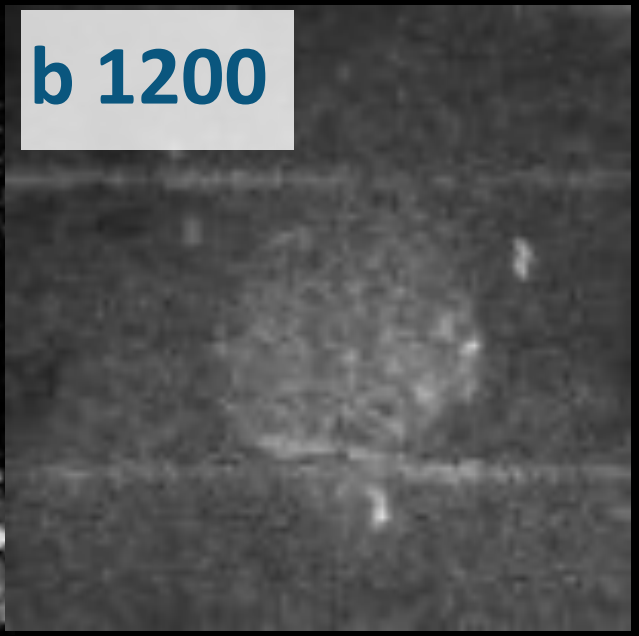

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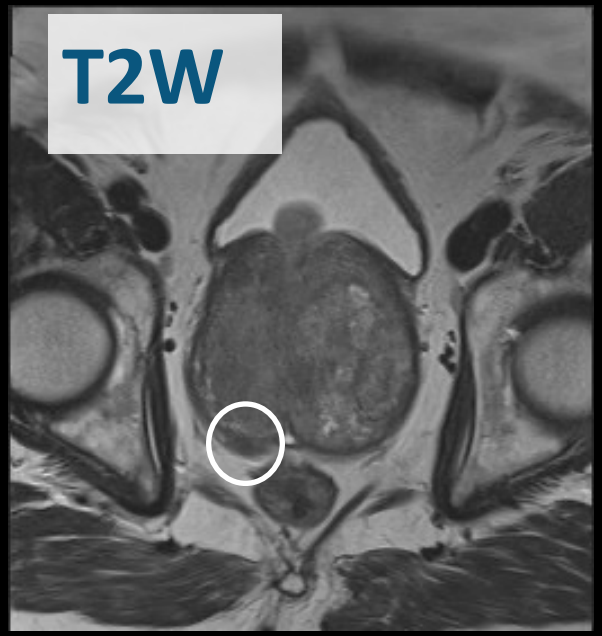

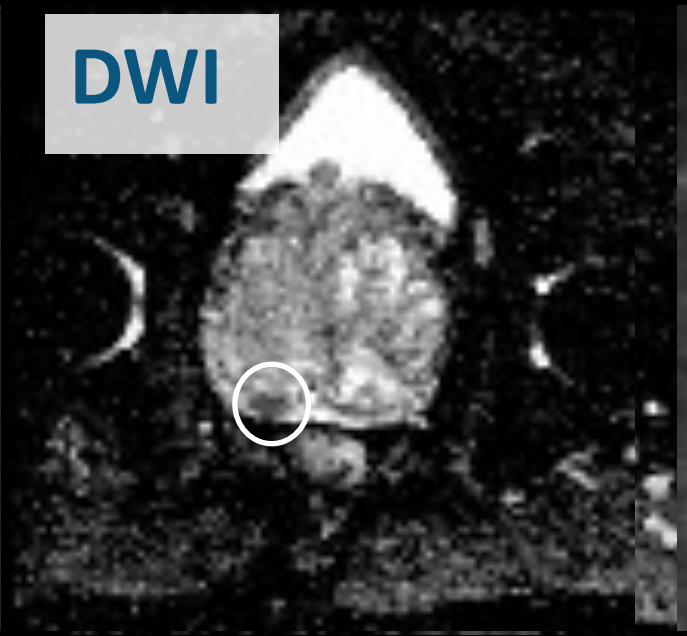

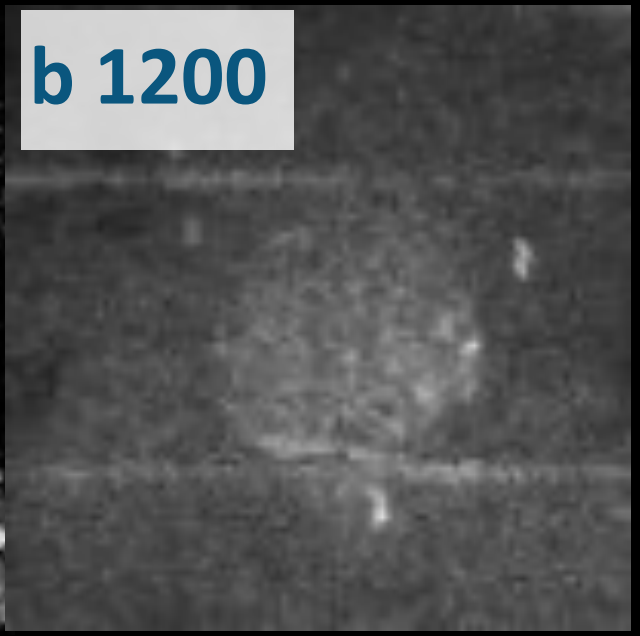

MR-GB: Gleason: 5+4

Accuracy and Agreement of PIRADSv2 for Prostate Cancer mpMRI: A Multireader Study

Matthew D. Greer BS,[1,2] Anna M. Brown BSE, MPhil,[1,3] Joanna H. Shih PhD,[4] Ronald M. Summers MD, PhD,[5] Jamie Marko MD,[6] Yan Mee Law MD,[7] Sandeep Sankineni MD,[1] Arvin K. George MD,[8] Maria J. Merino MD,[9] Peter A. Pinto MD,[8] Peter L. Choyke MD,[1] and Baris Turkbey MD[1]*

Specialists had less PI-RADS 3 diagnoses

Greer JMRI 2016

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Specialist >2000 MRI's

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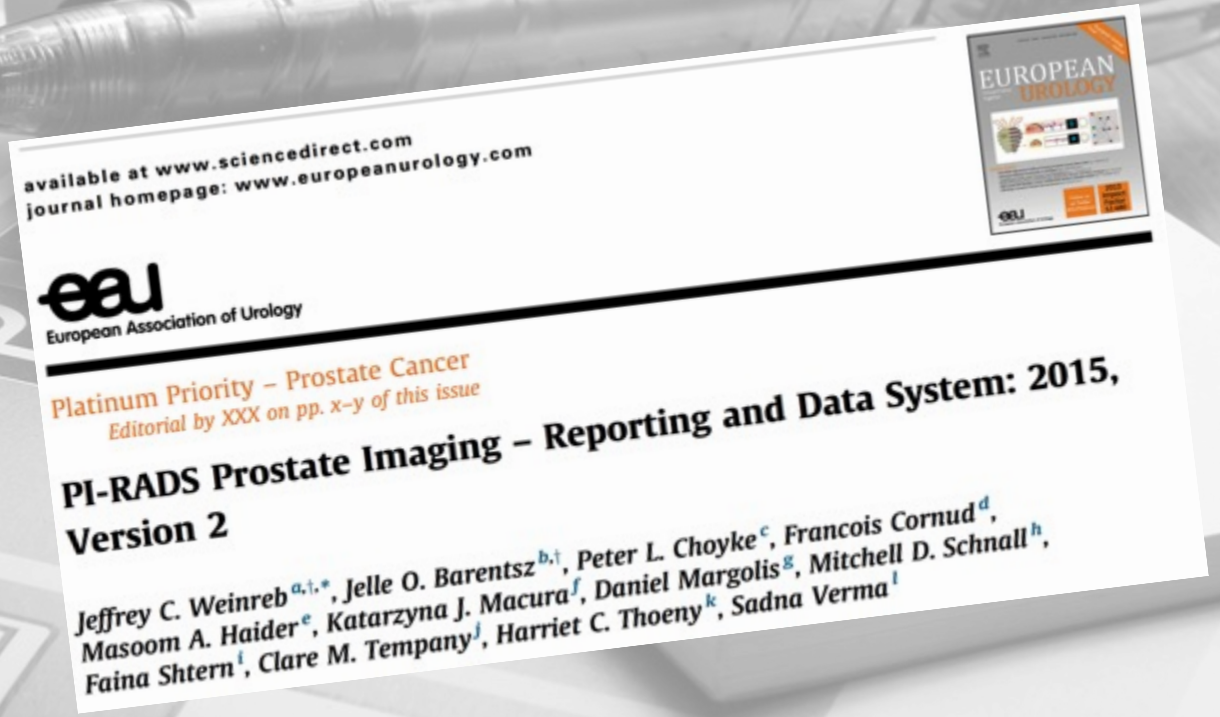
GUIDELINES



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European Association of Urology

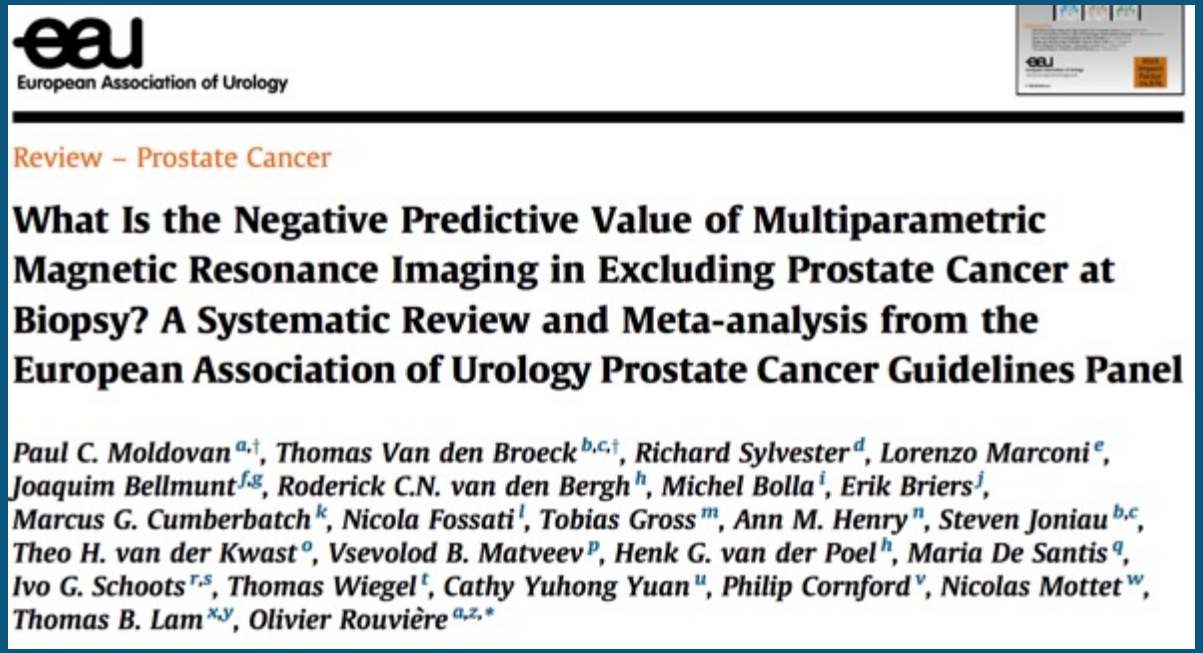
EUROPEAN UROLOGY

Platinum Priority – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

PI-RADS Prostate Imaging – Reporting and Data System: 2015, Version 2

Jeffrey C. Weinreb[a,†,*], Jelle O. Barentsz[b,†], Peter L. Choyke[c], Francois Cornud[d], Masoom A. Haider[e], Katarzyna J. Macura[f], Daniel Margolis[g], Mitchell D. Schnall[h], Faina Shtern[i], Clare M. Tempany[j], Harriet C. Thoeny[k], Sadna Verma[l]



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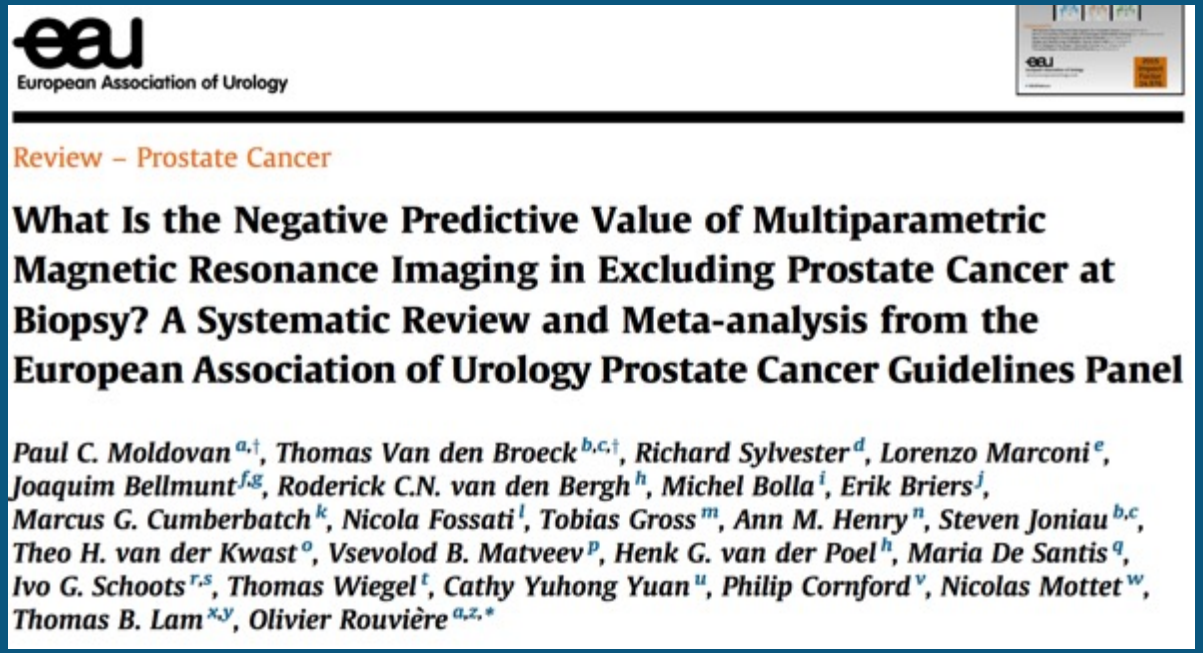
Large variability NPV for csPCa (56-99%)



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6% vs 28%

Greer JMRI 2016

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Specialists had less PI-RADS 3 diagnoses

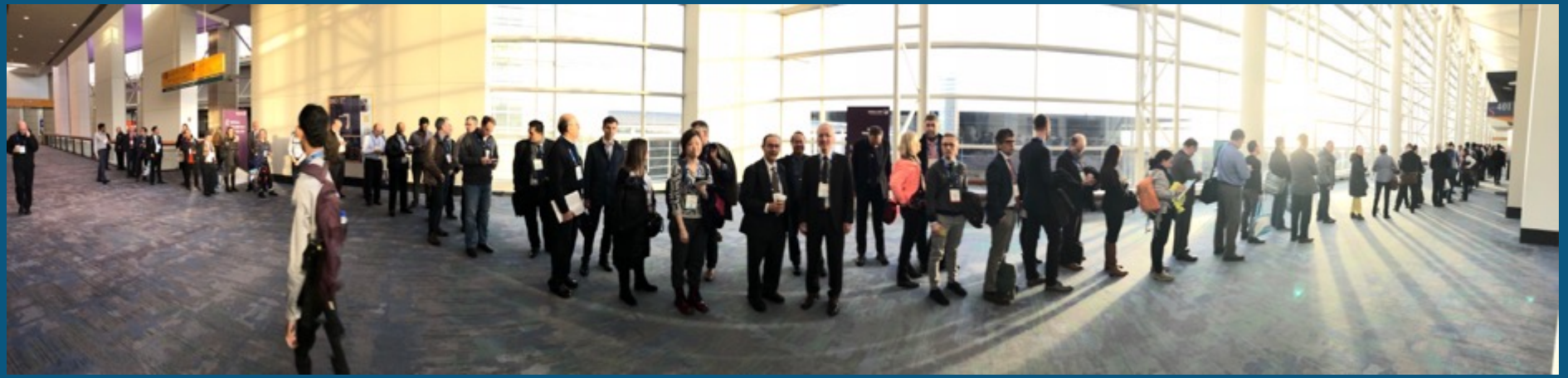
Specialist >2000 MRI's

Non-Specialists 300-500 MRI's

Greer JMRI 2016


TRAINING
LEARNER DRIVER

Hands-on PI-RADS Courses



4-days Hands-on-Course (100 cases) +
100 Double-Read cases with feed-back

K .77

Agreement: 93%

CIRCLE OF LEARNING


Teacher


Unaware
incompetent
Teacher


Unaware
incompetent
Aware
incompetent
Teacher

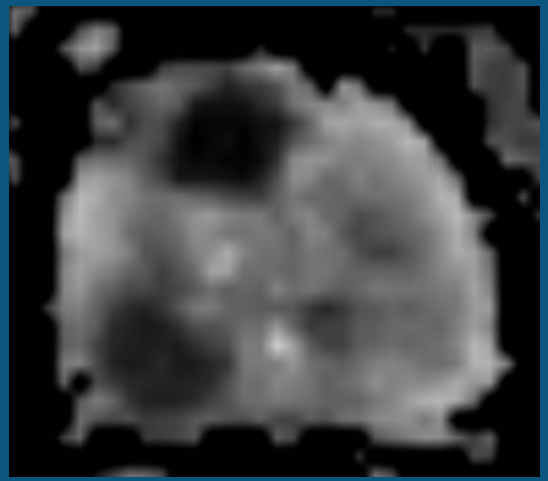

Unaware
incompetent
Aware
incompetent
Teacher
Aware
competent


Unaware incompetent
Aware incompetent
Teacher
Aware competent
Unaware competent

QUALITY CONTROLS

Quality Controls

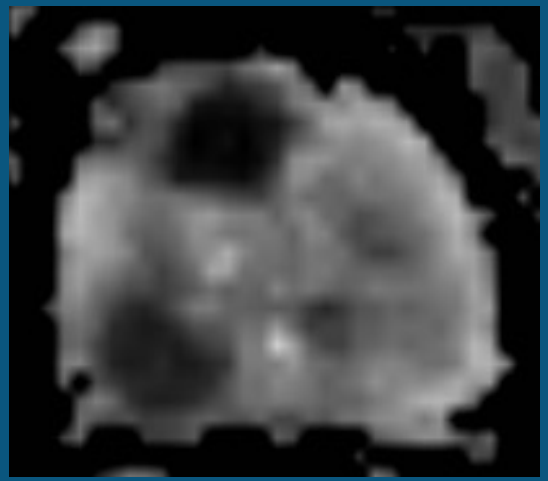
Copy-paste breast screening:



Quality Controls

Copy-paste breast screening:

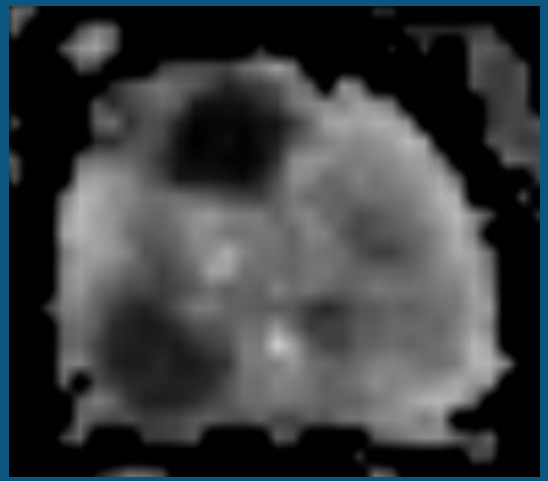
1. **Extensive teaching course**



Quality Controls

Copy-paste breast screening:

1. **Extensive teaching course**
2. **Validation of personal quality (double-reads, examination)**



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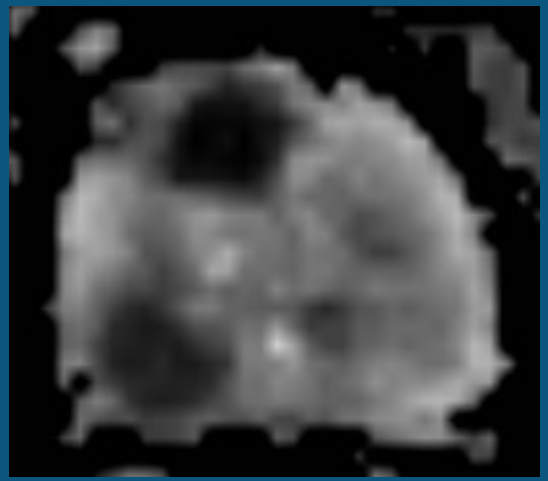
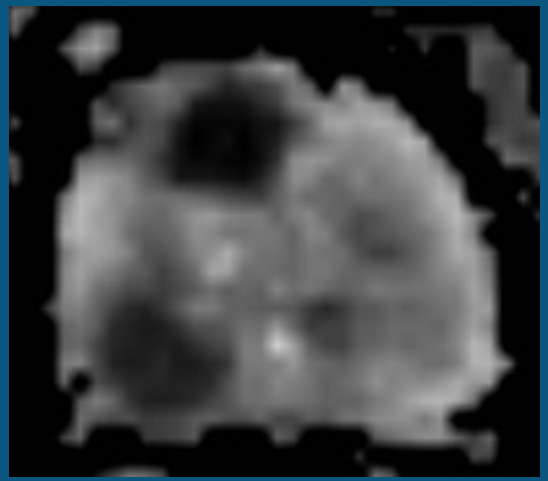
3. **Personal certification**



Quality Controls

Copy-paste breast screening:

1. **Extensive teaching course**
2. **Validation of personal quality (double-reads, examination)**
3. **Personal certification**
4. **Quality-Visitation**



We must develop Quality Criteria: WIP

1. Go yearly to accredited courses

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2. Read ≥ 10 prostate MRI/week (+ <1 day)

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3. **Your PI-RADS 3 diagnoses should be <15%**

We must develop Quality Criteria: WIP

1. Go yearly to accredited courses
2. Read ≥ 10 prostate MRI/week (+ <1 day)
3. Your PI-RADS 3 diagnoses should be <15%
4. **PI-RADS 4-5 should yield cs-PCa >65%**

We must develop Quality Criteria: WIP

1. Go yearly to accredited courses
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3. Your PI-RADS 3 diagnoses should be <15%
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5. **Be at MDT: compare PI-RADS with pathology**

We must develop Quality Criteria: suggestion

1. Go yearly to accredited courses
2. Read ≥ 10 prostate MRI/week (+ <1 day)
3. Your PI-RADS 3 diagnoses should be <15%
4. PI-RADS 4-5 should yield cs-PCa >65%
5. Be at MDT: compare PI-RADS with pathology
6. **Show your your outcome data: Q-visitation**

PI-RADS mpMRI-MRI-directed pathway limitations

50% of men with positive MRI undergoing biopsy have negative histology or insignificant cancers

Performance of radiologists in practise does not match that seen in high volume centers

Steep learning curve for MRI interpretations and biopsy performance (Expertise >300 cases)

30-50% don't benefit from Gd contrast medium injections

Time intensive to review, report & lesion contour for MRI-fusion biopsy

Multiple quality issues from image acquisition, interpretations and MRI-directed biopsies

@ProfPadhani

PI-RADS Steering Committee: The PI-RADS mpMRI and MRI-directed Biopsy Pathway – Padhani AR, et al. Radiology 2019 [epub]

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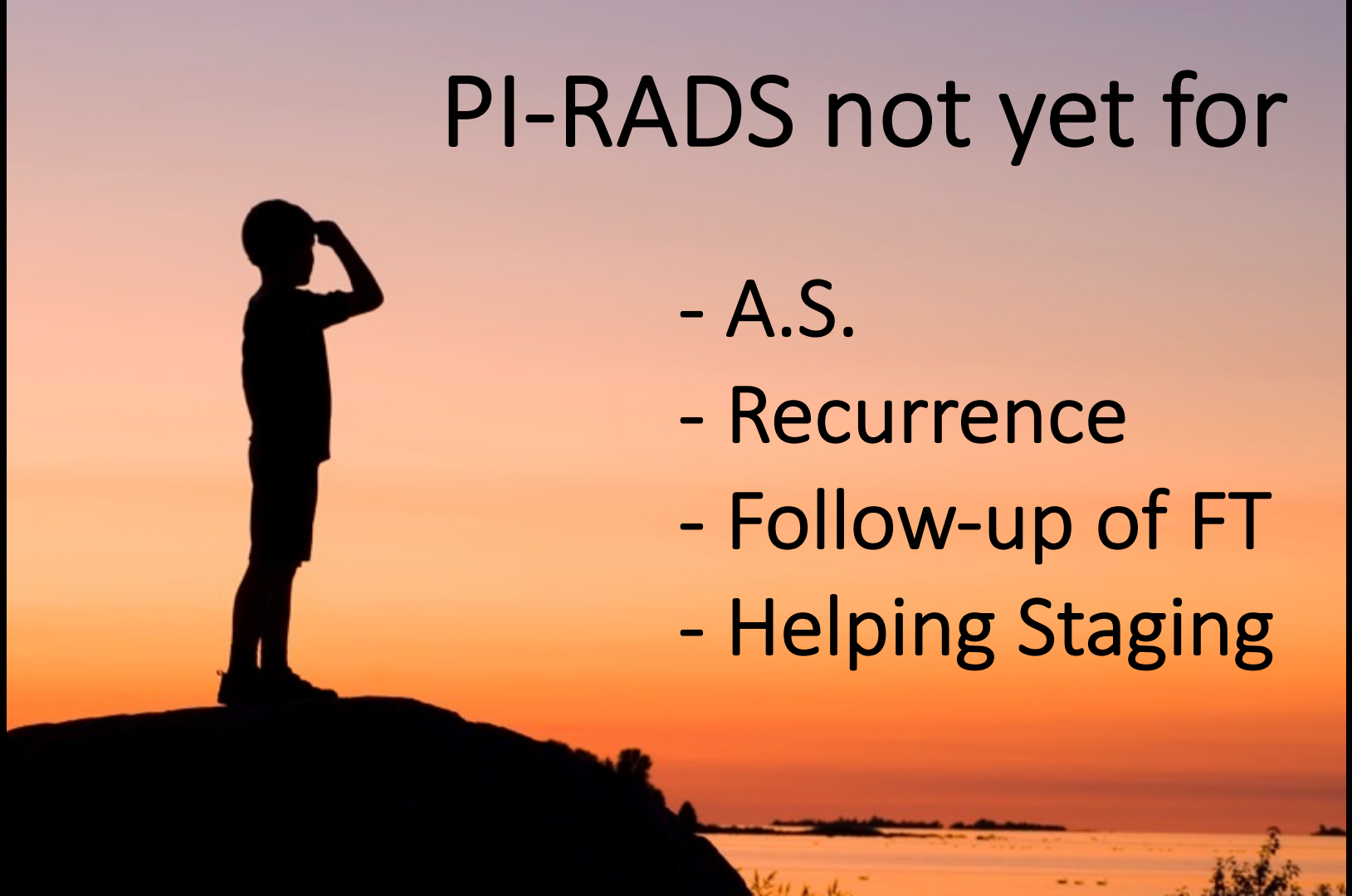
PI-RADS not yet for
- A.S.
- Recurrence
- Follow-up of FT
- Helping Staging

Prostate mpMRI is there to stay

Only if we provide good quality

DRE

for Radiologists

Develop

Develop Radiological

Develop Radiological Expertise

www.mri-prostate-barentsz.nl

Jelle Barentsz

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