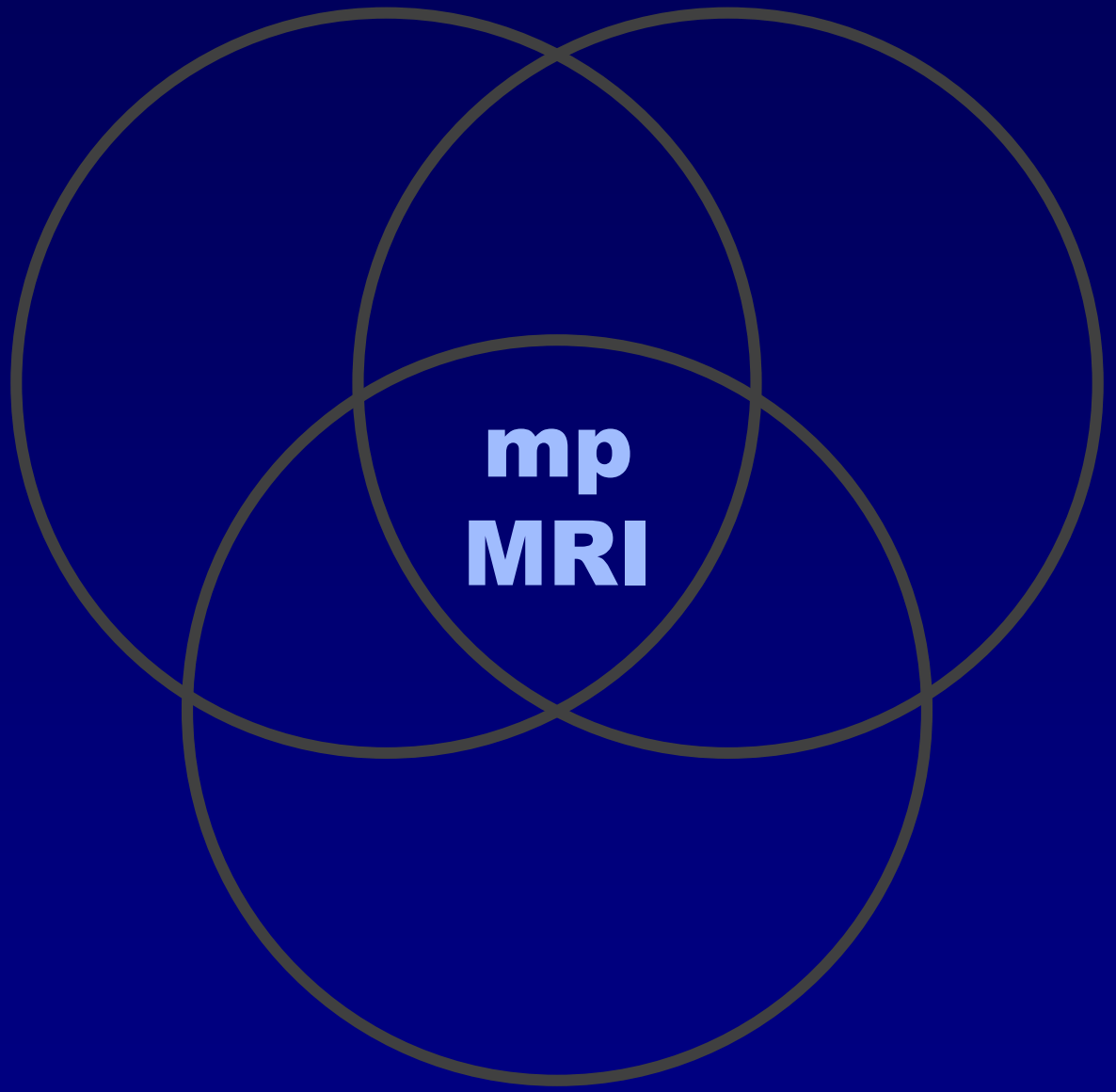
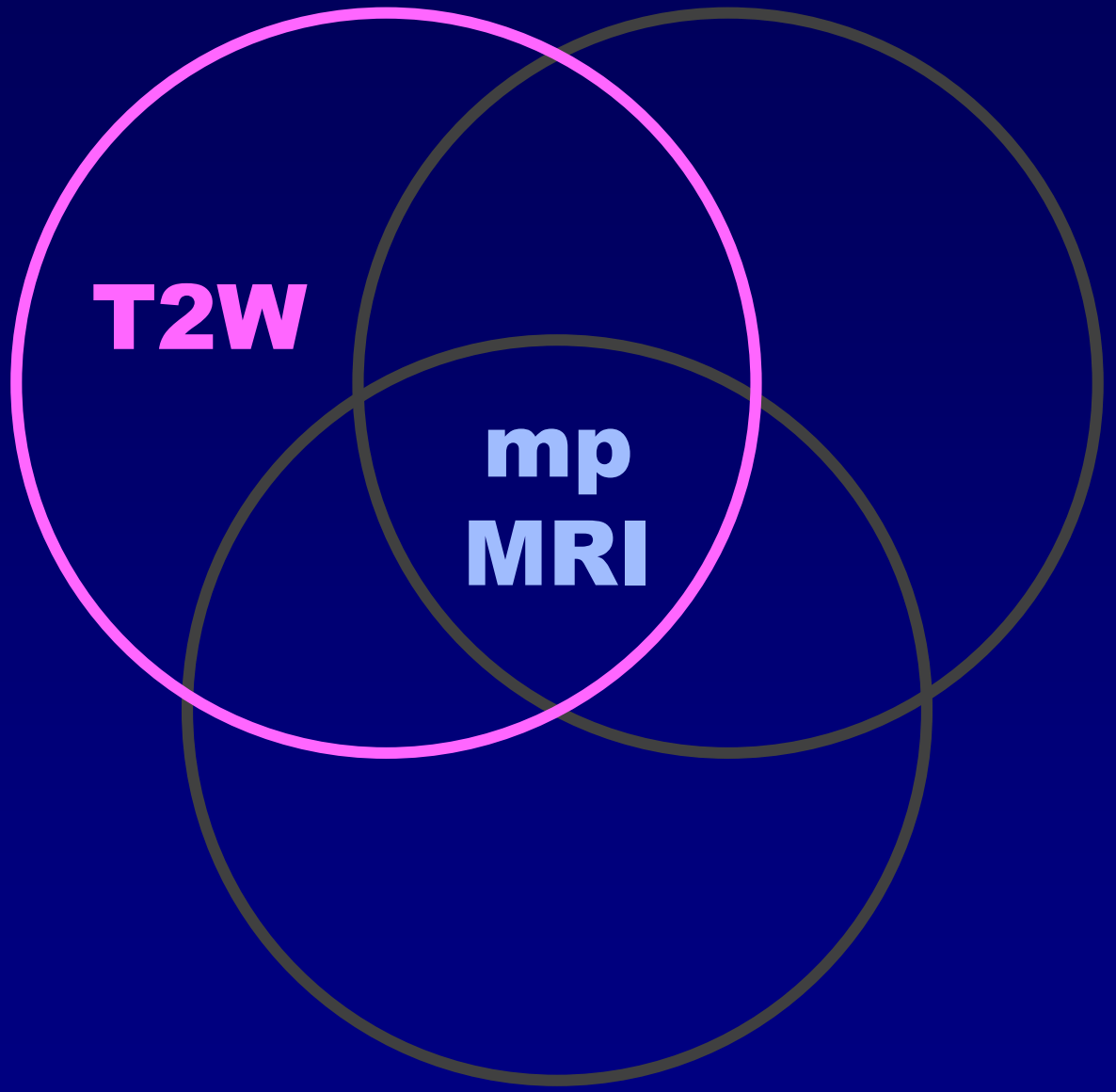
mpMRI IN DIAGNOSIS OF PROSTATE CANCER

Prof. Geert M. Villeirs

Genitourinary Radiology
Ghent University Hospital, Belgium

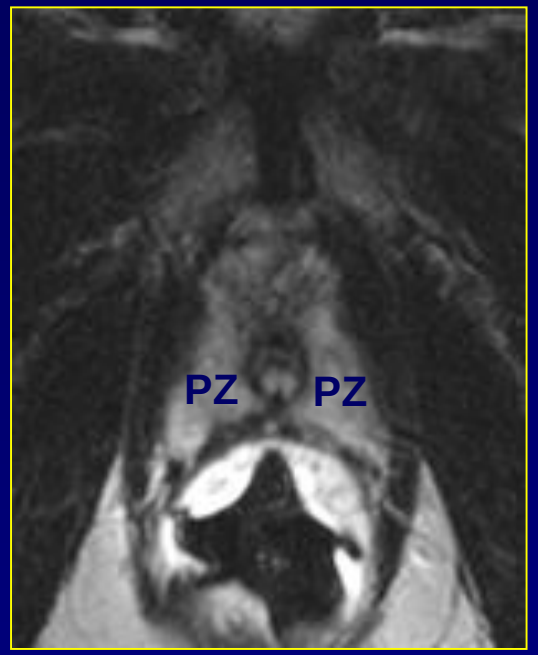
1 Introduction


mp
MRI

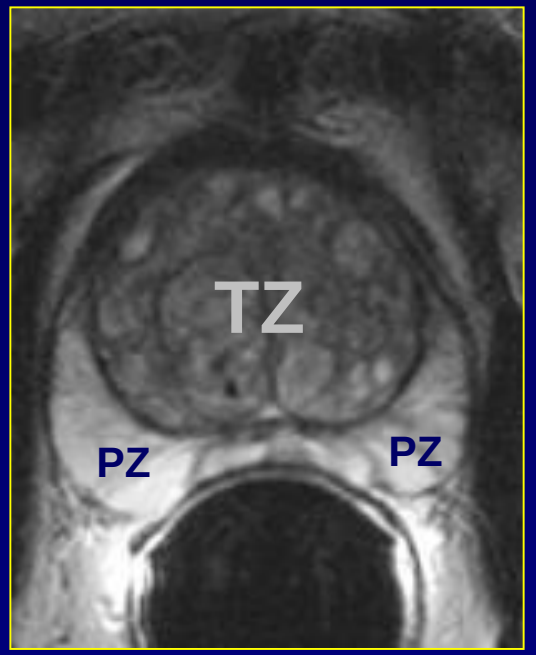

T2W
mp
MRI

T2-weighted MRI

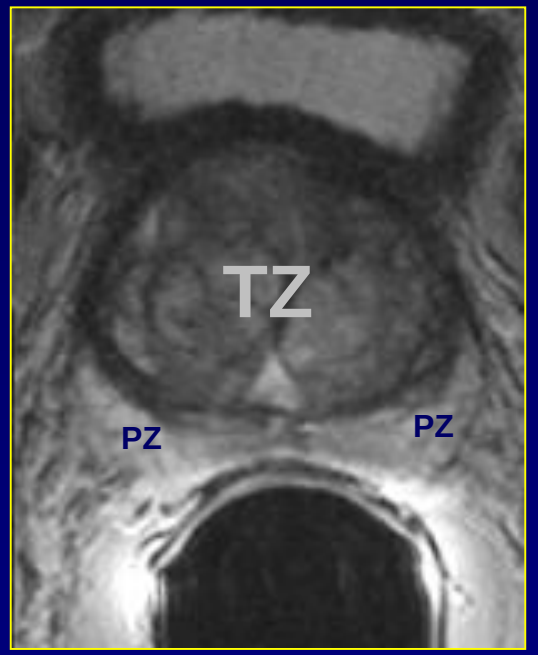
Anatomy



Prostatic Apex



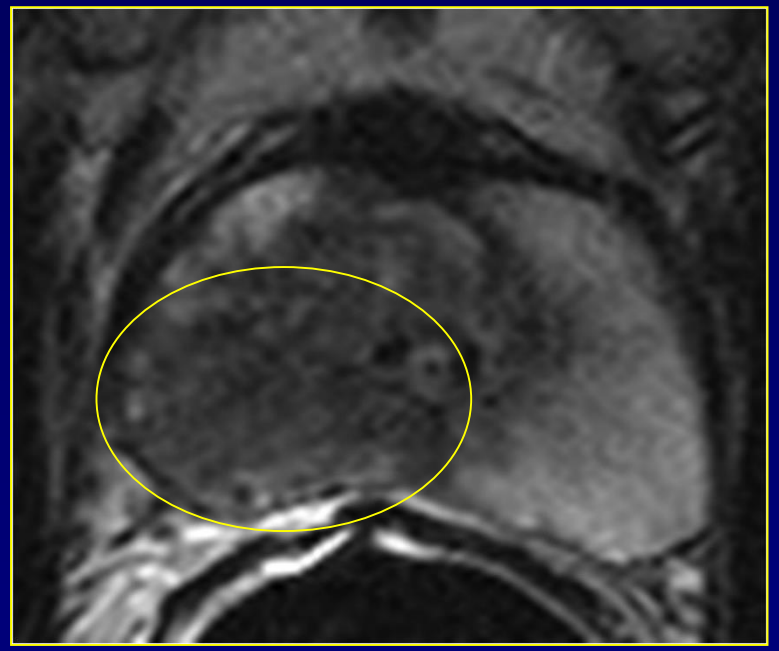
Midprostate

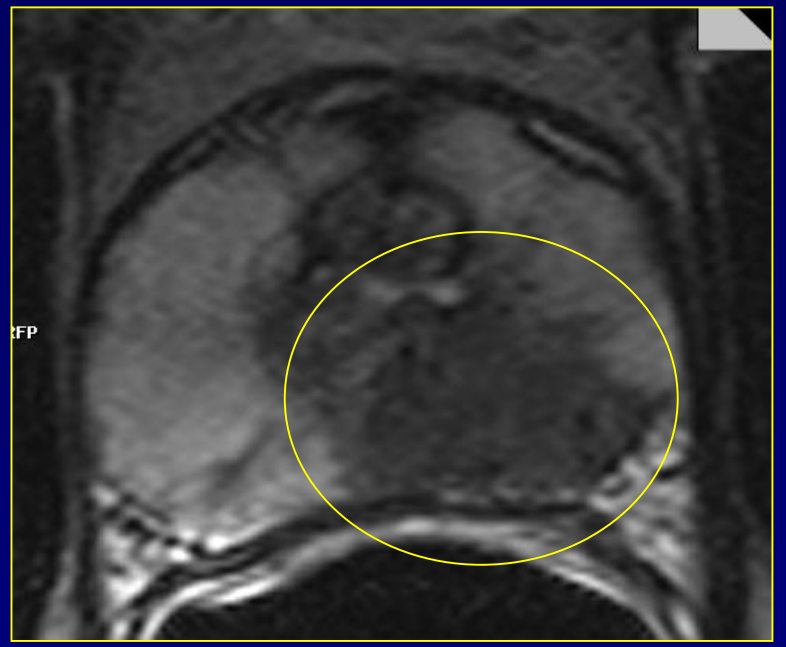


Prostatic Base

T2-weighted MRI

Peripheral zone cancer

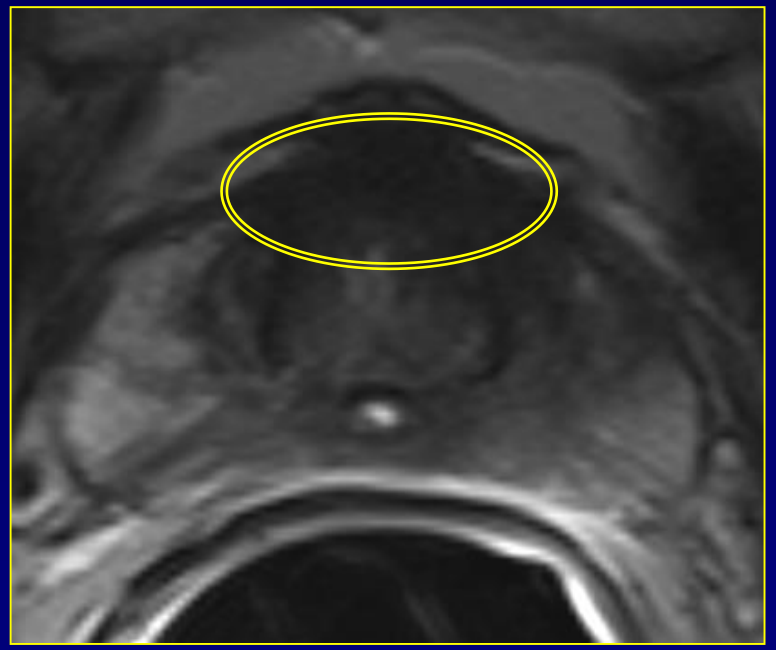


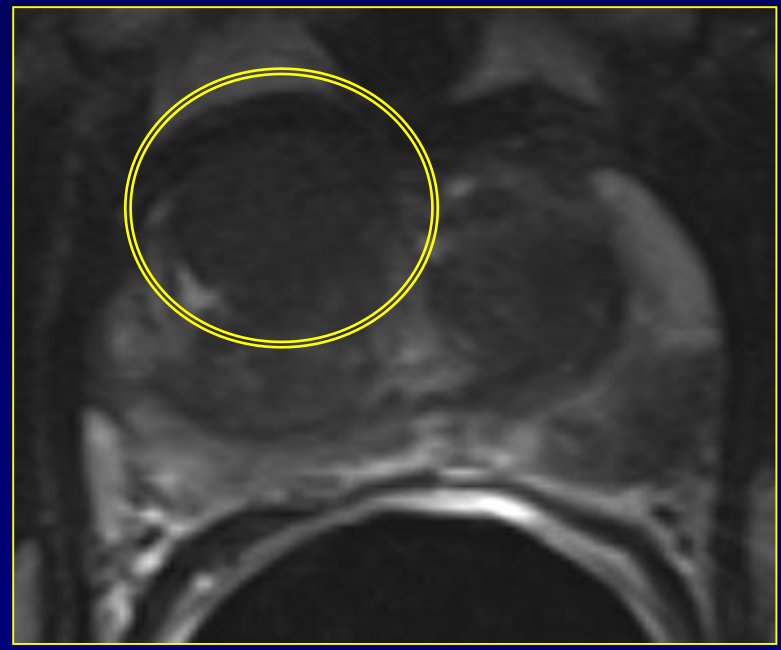


Low signal intensity area

T2-weighted MRI

Transition zone cancer

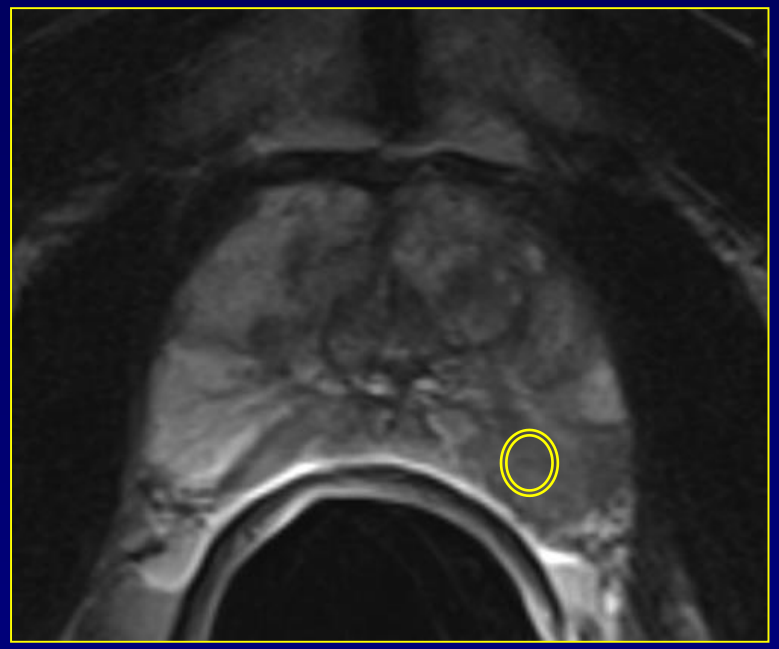




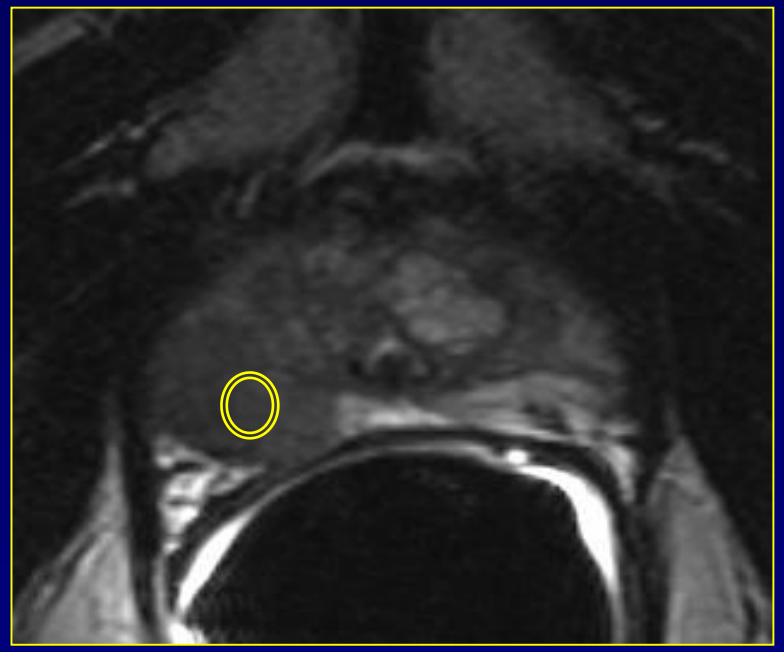
Area of uniform signal intensity decrease

T2-weighted MRI

Assessment of aggressiveness



Gleason 3+3

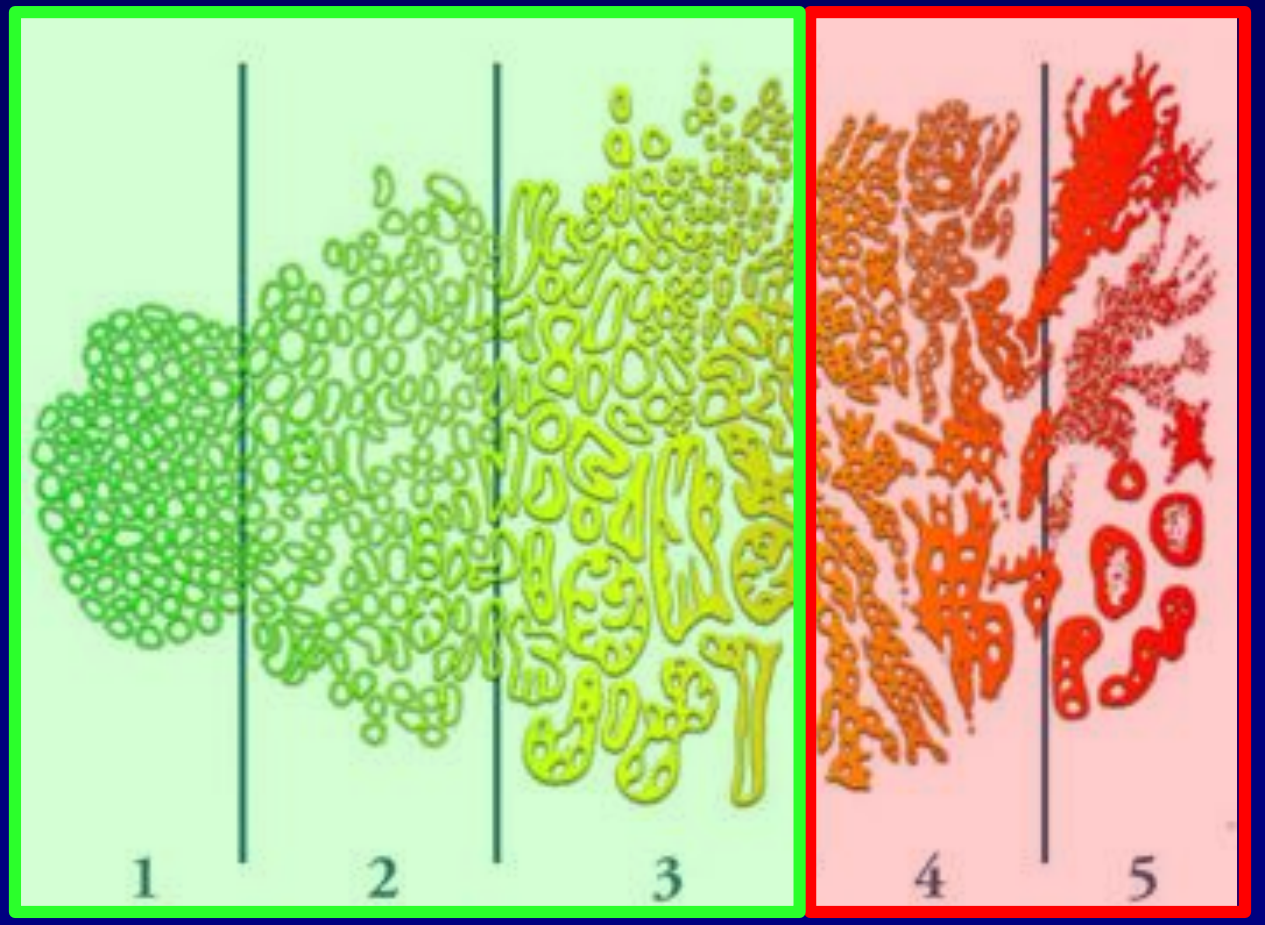


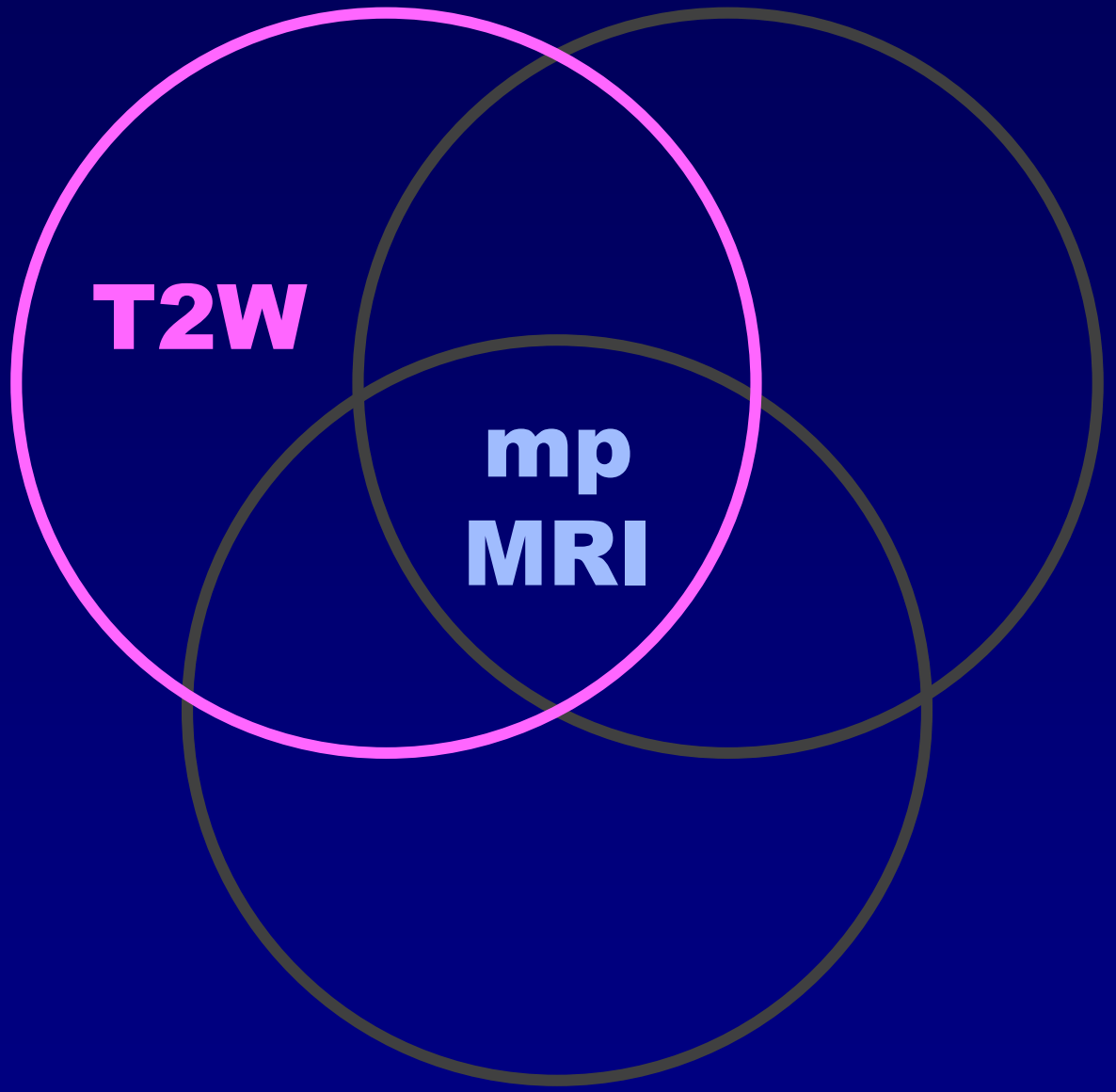
Gleason 4+5

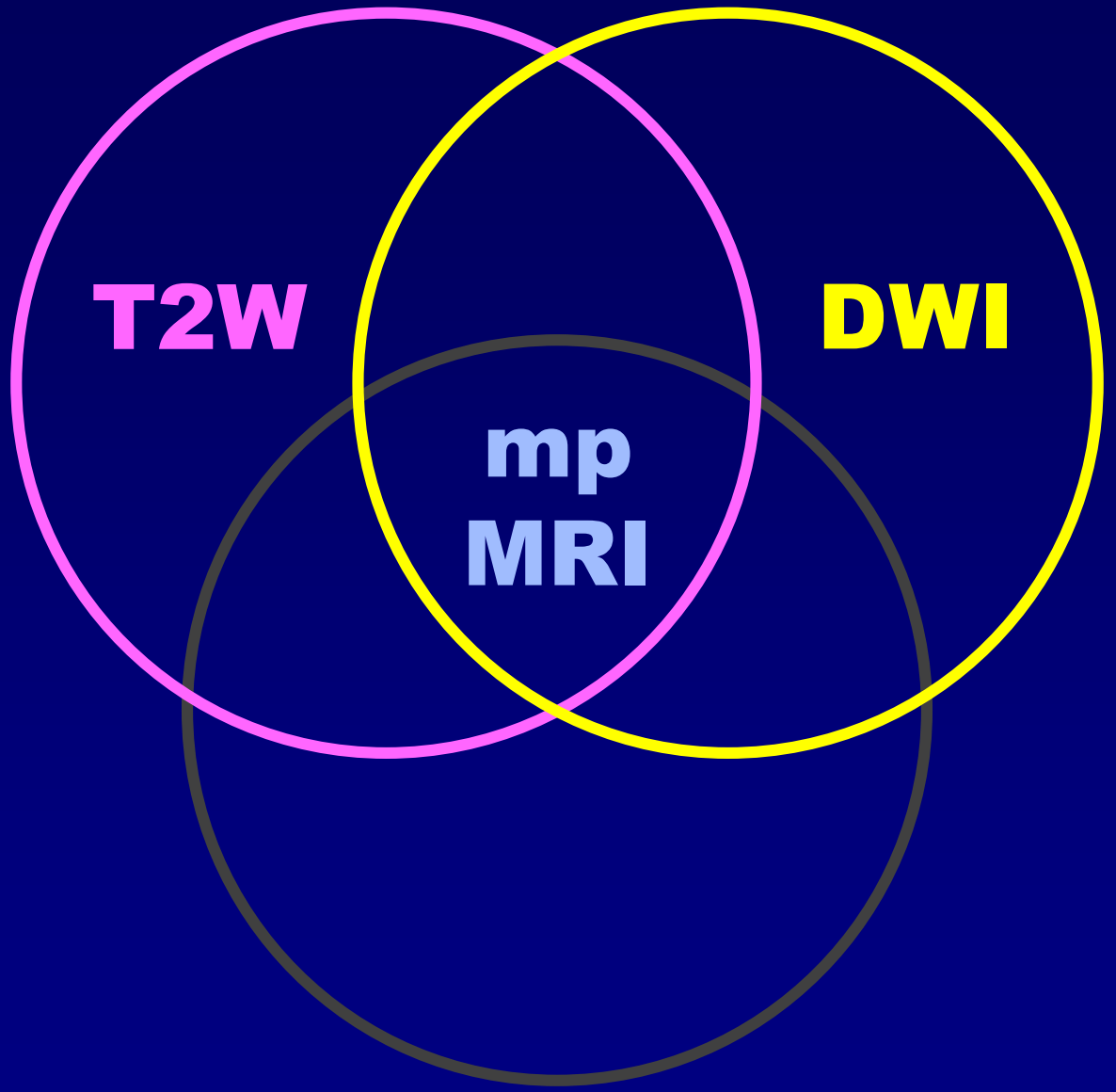
Wang, Radiology 2008;246:168
May, Invest Radiol 2019;54:146

T2-weighted MRI

Assessment of aggressiveness




T2W
mp
MRI


T2W
DWI
mp
MRI

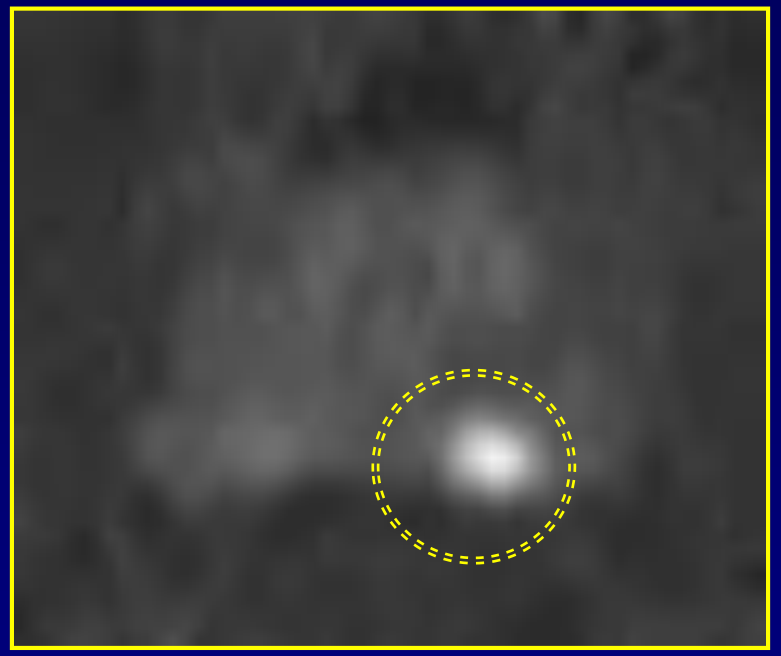
Diffusion-Weighted Imaging

Phenotype

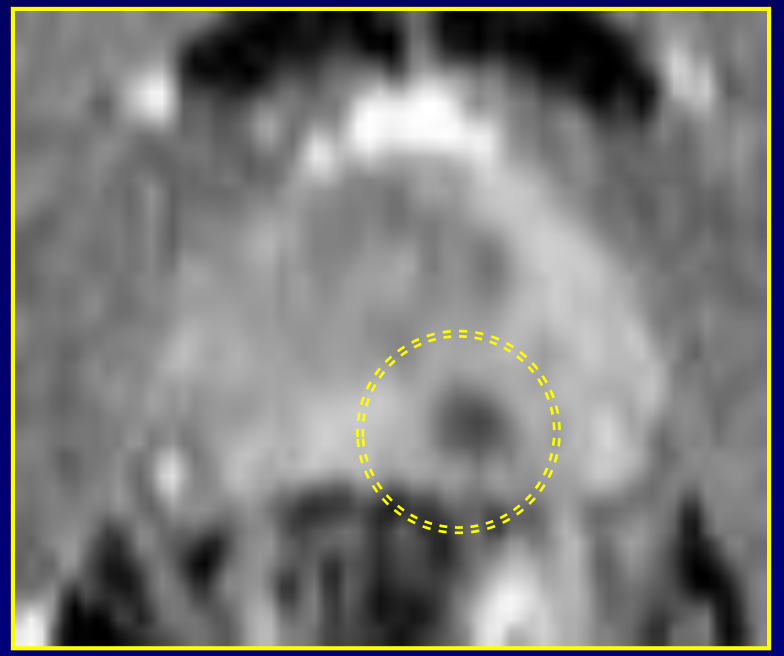
- Principle = INHIBITION OF WATER DIFFUSION
  - No inhibition in normal tissue (fluid filled ducts, low/intermediate cellular density)
  - Much inhibition in tumour lesions (vast tumoral sheats, high cellular density)

Diffusion-Weighted Imaging

Peripheral zone cancer



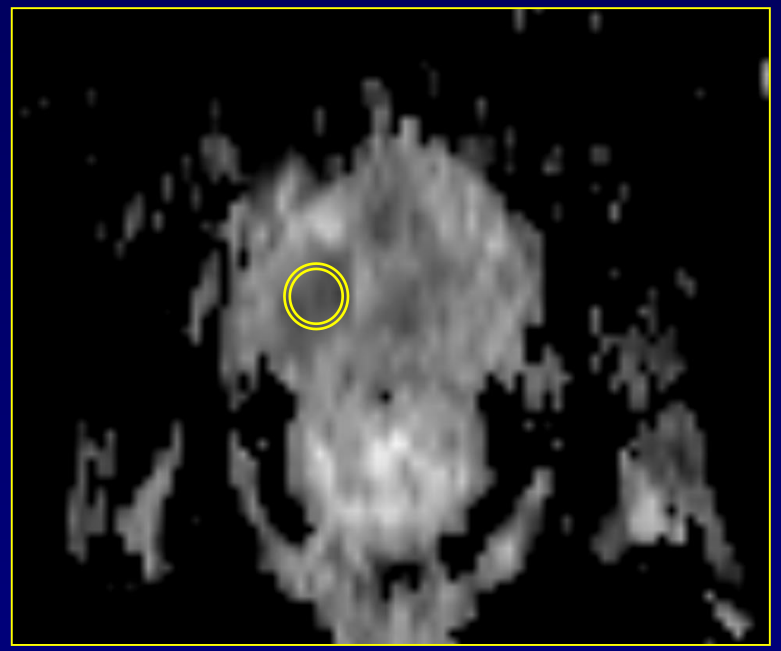
b1400



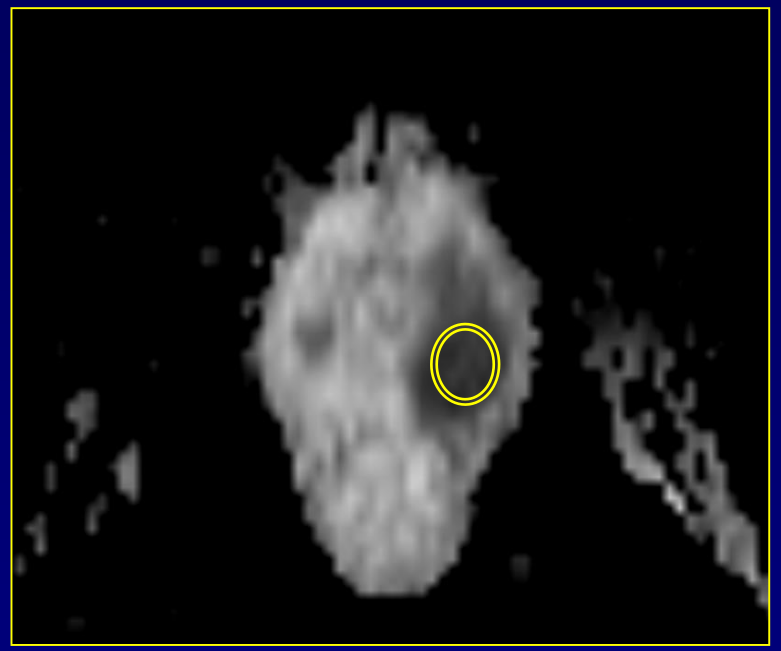
ADC

Diffusion-Weighted Imaging

Assessment of aggressiveness

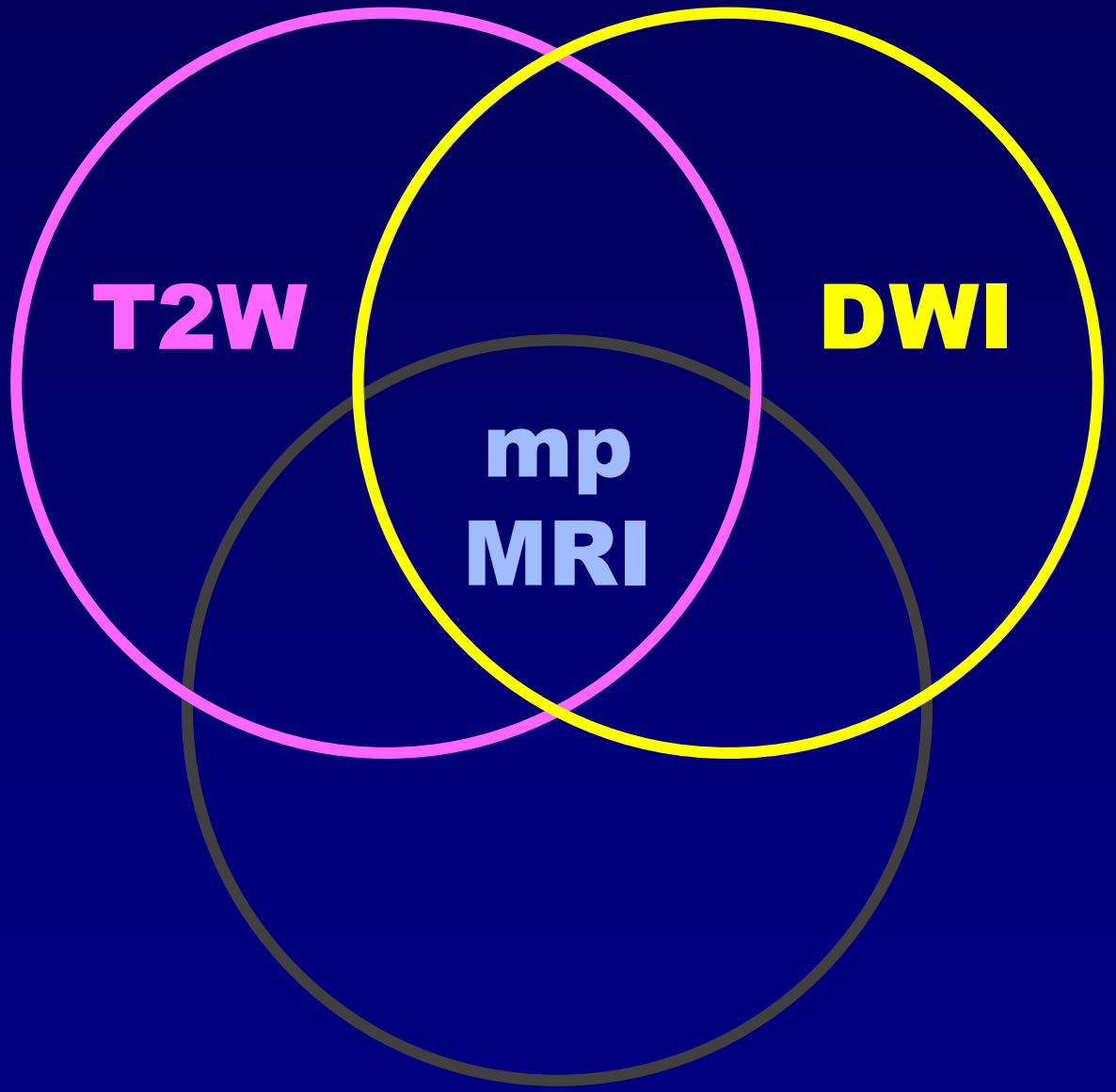


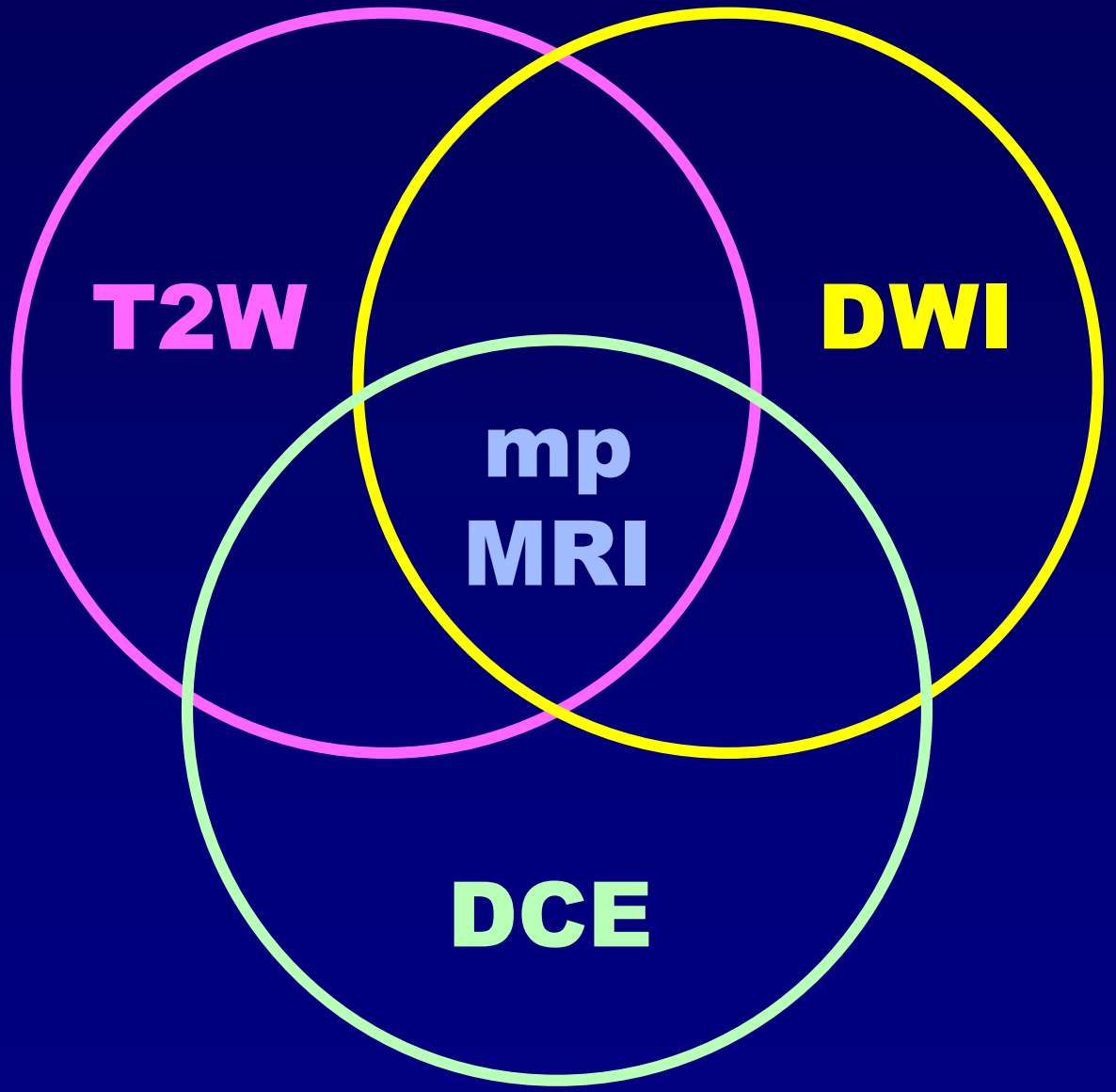
ADC 762
Gleason 3+4



ADC 518
Gleason 5+4

*Hambrock, Eur Urol. 2012 Jan;61(1):177-84


T2W
DWI
mp
MRI


T2W
DWI
mp
MRI
DCE

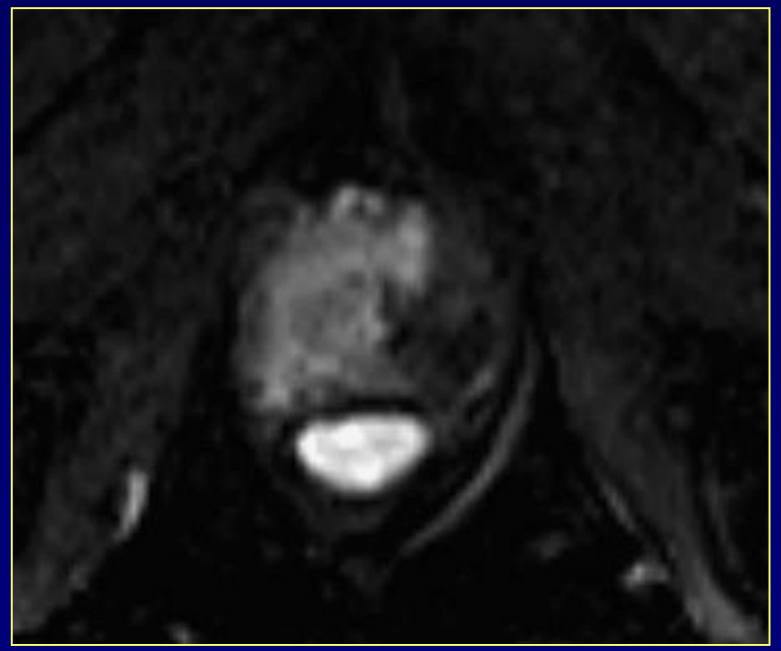
Dynamic Contrast-Enhanced MRI

Phenotype

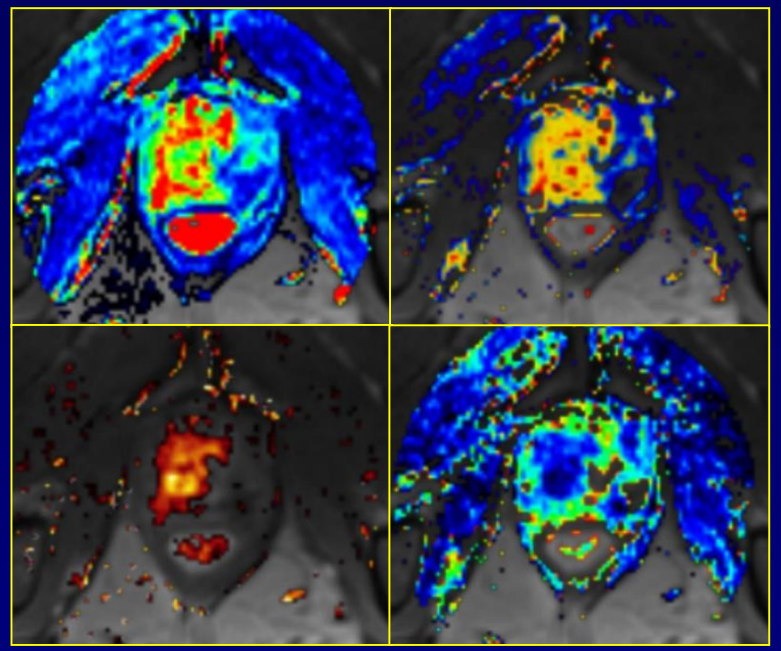
- Principle = DEMONSTRATION OF NEOANGIOGENESIS

Dynamic Contrast-Enhanced MRI

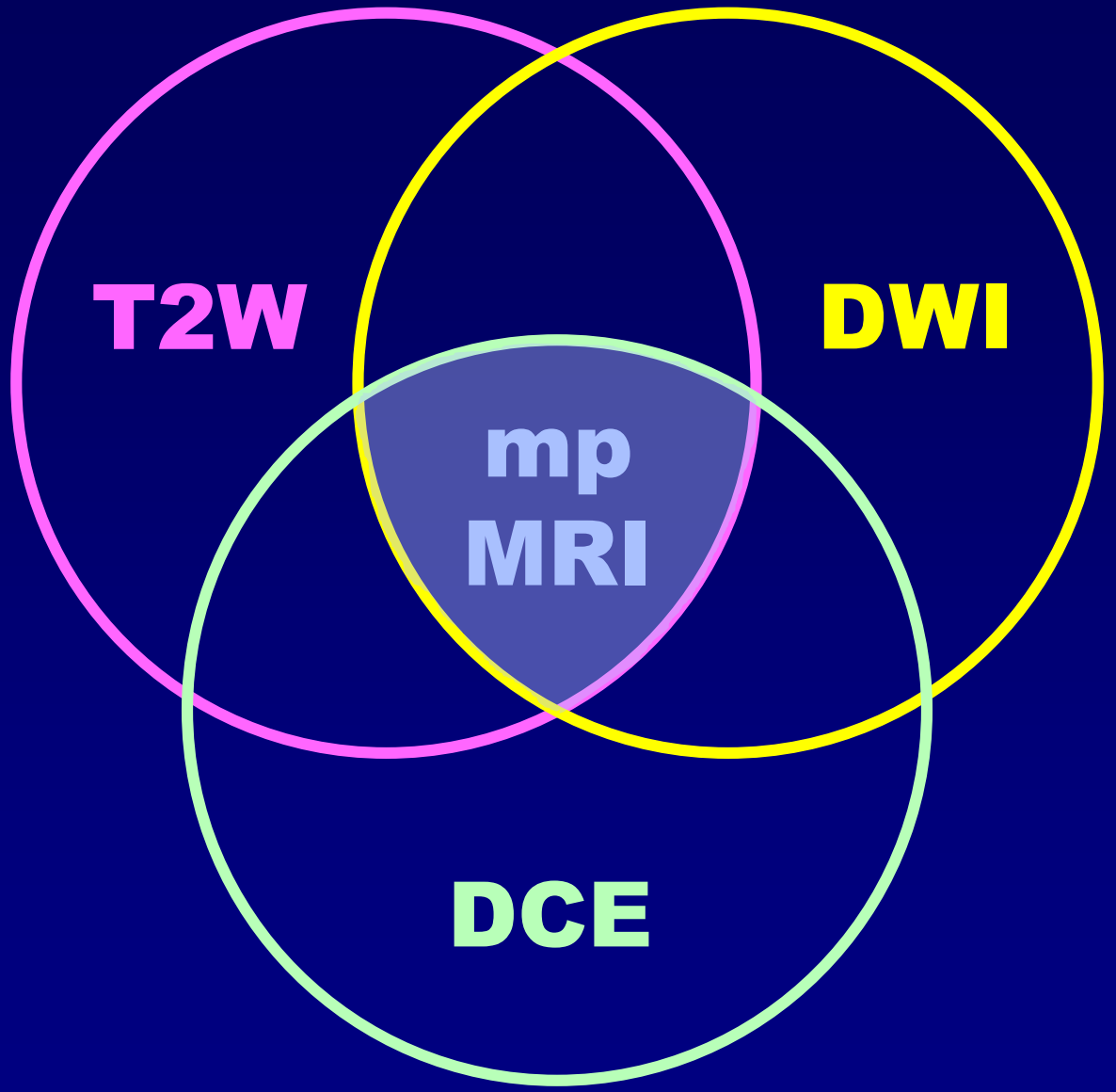
Phenotype



Subtraction image



Tofts Model
(iAUC, K^{trans}, v_e, k_{ep})


T2W
DWI
mp
MRI
DCE

mpMRI

How?

2

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

Received: 16 October 2011 / Revised: 23 November 2011 / Accepted: 2 December 2011 / Published online: 10 February 2012

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

Key Points

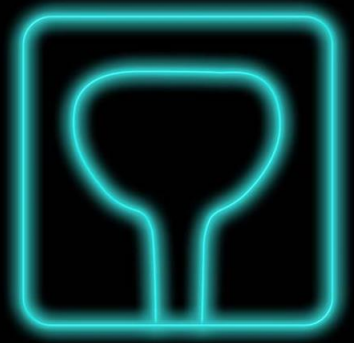
- *This report provides guidelines for magnetic resonance imaging (MRI) in prostate cancer.*
- *Clinical indications, and minimal and optimal imaging acquisition protocols are provided.*
- *A structured reporting system (PI-RADS) is described.*

GV

PI-RADS™

Prostate Imaging – Reporting and Data System

2015
version 2



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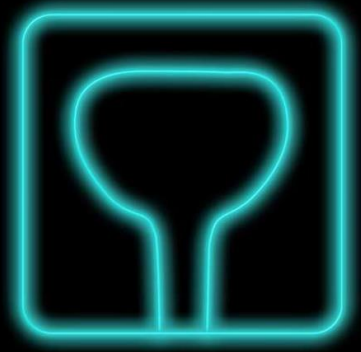
PI-RADS®

Prostate Imaging – Reporting and Data System

2019
Version 2.1



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Multiparametric MRI

PI-RADS™ v2

SECTION IV: MULTIPARAMETRIC MRI (MPMRI)

A. T1-Weighted (T1W) and T2-Weighted (T2W)

Both T1W and T2W sequences should be obtained for all prostate MR exams. T1W images are used primarily to determine the presence of hemorrhage within the prostate and seminal vesicles and to delineate the outline of the gland. T1W images may also useful for detection of nodal and skeletal metastases, especially following intravenous administration of a gadolinium-based contrast agent (GBCA).

T2W images are used to discern prostatic zonal anatomy, assess abnormalities within the gland, and to evaluate for seminal vesicle invasion, EPE, and nodal involvement.

On T2W images, clinically significant cancers in the PZ usually appear as round or ill-defined hypointense focal lesions. However, this appearance is not specific and can be seen in various conditions such as prostatitis, hemorrhage, glandular atrophy, benign hyperplasia, biopsy related scars, and after therapy (hormone, ablation, etc.).

The T2W features of TZ tumors include non-circumscribed homogeneous, moderately hypointense lesions ("erased charcoal" or "smudgy fingerprint" appearance), spiculated margins, lenticular shape, absence of a complete hypointense capsule, and invasion of the urethral sphincter and anterior fibromuscular stroma. The more features present, the higher the likelihood of a clinically significant TZ cancer.

TZ cancers may be difficult to identify on T2W images since the TZ is often composed of variable amounts of glandular (T2-hyperintense) and stromal (T2-hypointense) tissue intermixed with each other, thus demonstrating heterogeneous signal intensity. Areas where benign stromal elements predominate may mimic or obscure clinically significant cancer.

Both PZ and TZ cancers may extend across anatomical boundaries. Invasive behavior is noted when there is extension within the gland (i.e. across regional parts of the prostate), into the seminal vesicles, or outside the gland (EPE).

1. **Technical Specifications**

T2W

Multiplanar (axial, coronal, and sagittal) T2W images are usually obtained with 2D RARE (rapid acquisition with relaxation enhancement) pulse sequences, more commonly known as fast-spin-echo (FSE) or turbo-spin-echo (TSE). In order to avoid blurring, excessive echo train lengths should be avoided.

- Slice thickness: 3mm, no gap. Locations should be the same as those used for DWI and DCE
- FOV: generally 12-20 cm to encompass the entire prostate gland and seminal vesicles
- In plane dimension: ≤0.7mm (phase) x ≤0.4mm (frequency)

3D axial acquisitions may be used as an adjunct to 2D acquisitions. If acquired using isotropic voxels, 3D acquisitions may be particularly useful for visualizing detailed anatomy and

Multiparametric MRI

distinguishing between genuine lesions and partial volume averaging effects. However, the soft tissue contrast is not identical and in some cases may be inferior to that seen on 2D T2W images, and the in-plane resolution may be lower than their 2D counterpart.

T1W

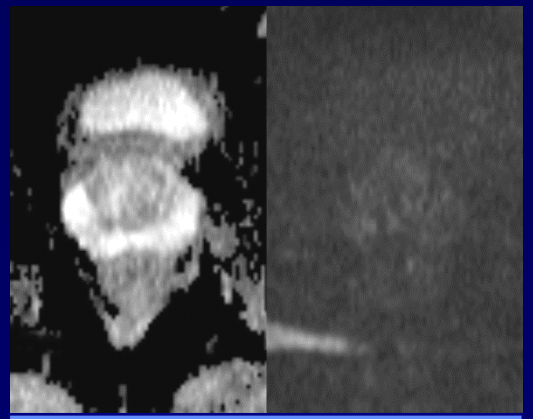
Axial T1W images of the prostate may be obtained with or without fat suppression using spin echo or gradient echo sequences. Locations should be the same as those used for DWI and DCE, although lower spatial resolution compared to T2W may be used to decrease acquisition time or increase anatomic coverage.

2. **PI-RADS Assessment for T2W**

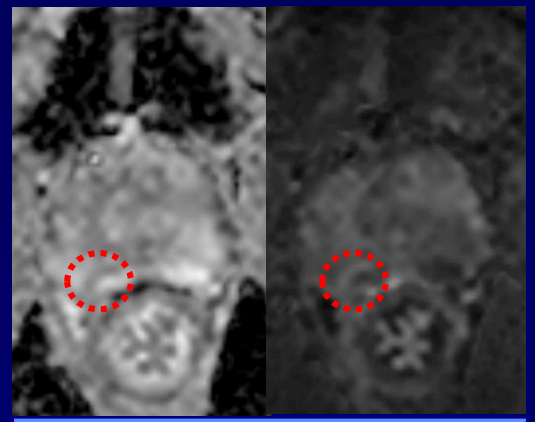
Score	Peripheral Zone (PZ)
1	Uniform hyperintense signal intensity (normal)
2	Linear or wedge-shaped hypointensity or diffuse mild hypointensity, usually indistinct margin
3	Heterogeneous signal intensity or non-circumscribed, rounded, moderate hypointensity Includes others that do not qualify as 2, 4, or 5
4	Circumscribed, homogenous moderate hypointense focus/mass confined to prostate and <1.5 cm in greatest dimension
5	Same as 4 but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

Score	Transition Zone (TZ)
1	Homogeneous intermediate signal intensity (normal)
2	Circumscribed hypointense or heterogeneous encapsulated nodule(s) (BPH)
3	Heterogeneous signal intensity with obscured margins Includes others that do not qualify as 2, 4, or 5
4	Lenticular or non-circumscribed, homogeneous, moderately hypointense, and <1.5 cm in greatest dimension
5	Same as 4, but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

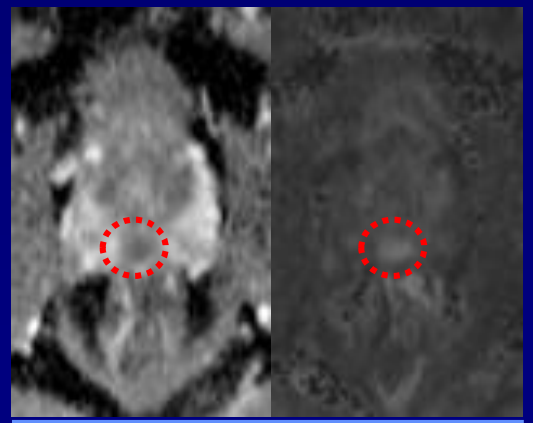
DWI in PERIPHERAL ZONE



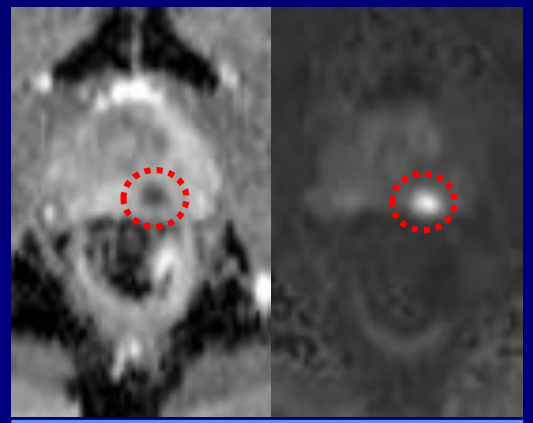
PI-RADS 1



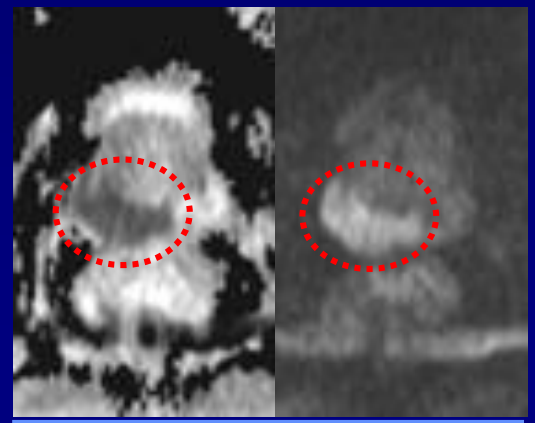
PI-RADS 2



PI-RADS 3

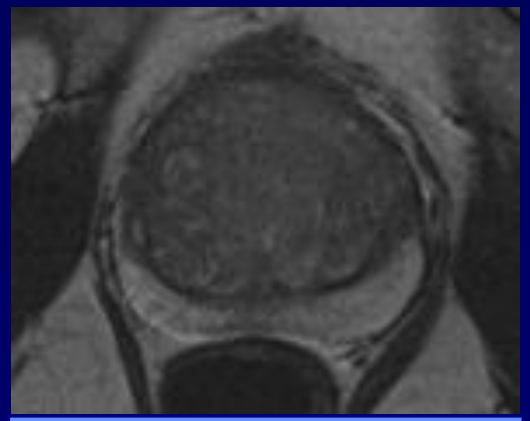


PI-RADS 4

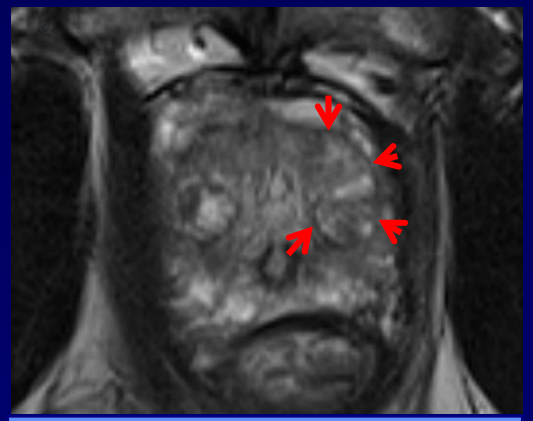


PI-RADS 5

T2 in TRANSITION ZONE



PI-RADS 1



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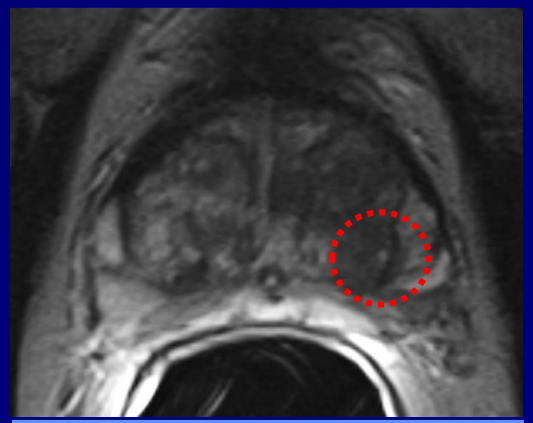
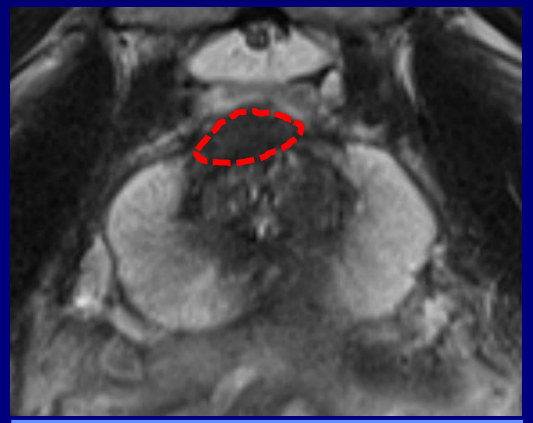


PI-RADS 3



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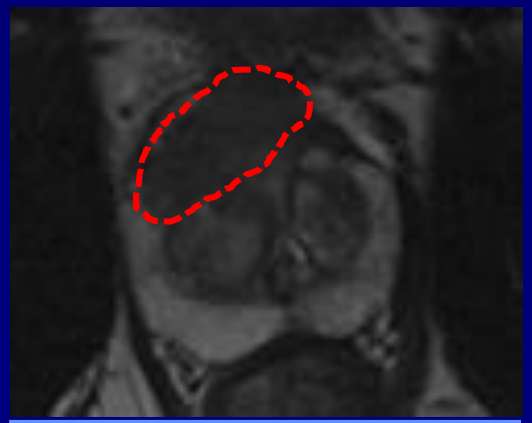
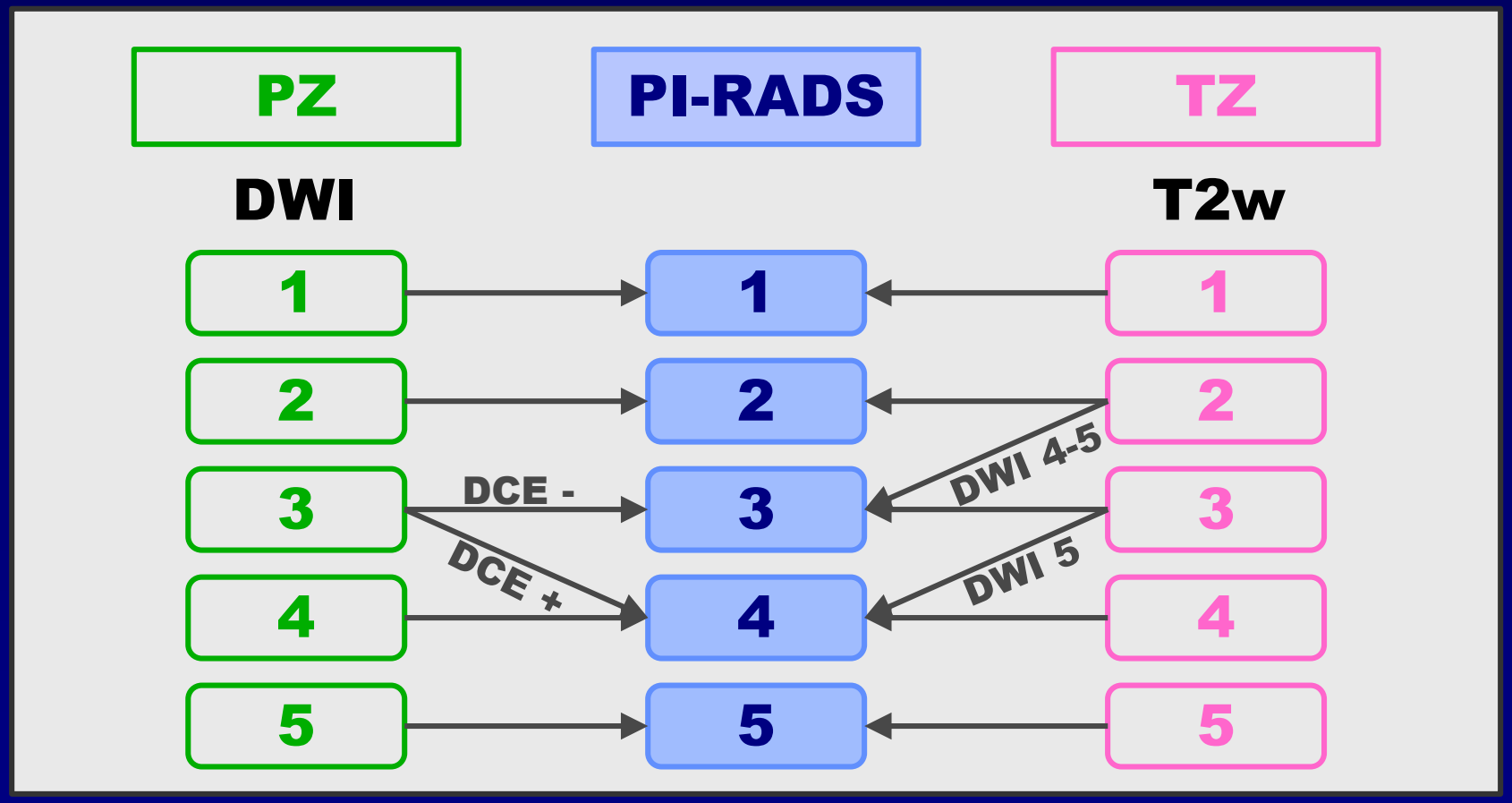


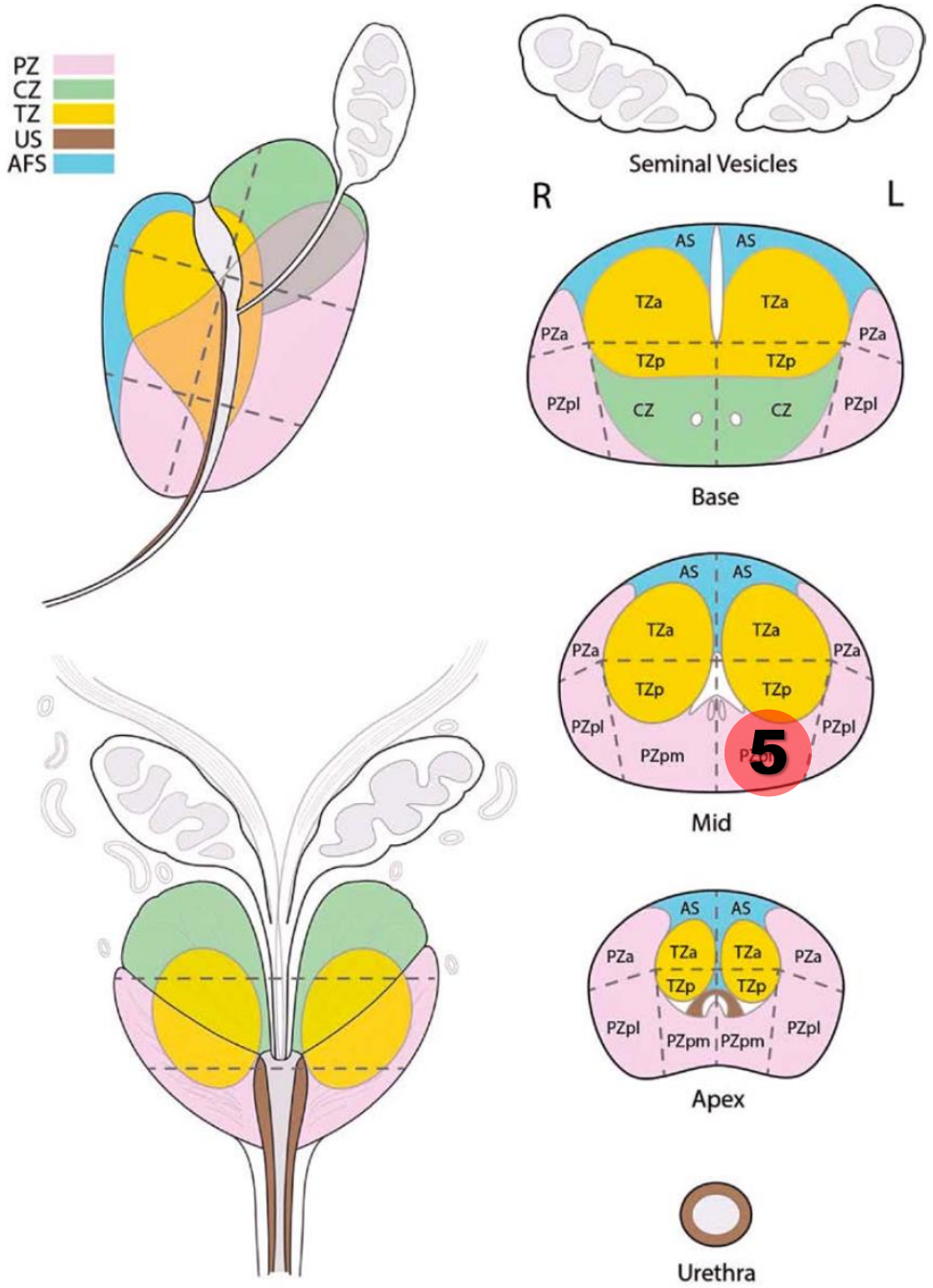
PI-RADS 5

PI-RADS



PI-RADS

PI-RADS	mpMRI probability of clinically significant disease
1	Clinically significant disease is **very unlikely**
2	Clinically significant disease is **unlikely**
3	Clinically significant disease is **equivocal**
4	Clinically significant disease is **likely**
5	Clinically significant disease is **very likely**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PZpm
PZpm
PZpl
Apex
Urethra

mpMRI *Performance*

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journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Prostate Cancer

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

Diagnostic Performance of Prostate Imaging Reporting and Data System Version 2 for Detection of Prostate Cancer: A Systematic Review and Diagnostic Meta-analysis

Sungmin Woo [a,†], *Chong Hyun Suh* [b,c,†], *Sang Youn Kim* [a,*], *Jeong Yeon Cho* [a,d], *Seung Hyup Kim* [a,d]

[a] *Department of Radiology, Seoul National University College of Medicine, Seoul, Korea;* [b] *Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea;* [c] *Department of Radiology, Namwon Medical Center, Jeollabuk-do, Republic of Korea;* [d] *Institute of Radiation Medicine and Kidney Research Institute, Seoul National University Medical Research Center, Seoul, Korea*

Article info

Article history:

Abstract

Context: In 2015, the updated Prostate Imaging Reporting and Data System version 2

Eur Urol 2017;72:177

GV

Validation of PI-RADS

- Meta-analysis of 21 single-institution studies, including 3857 patients
  - pooled sensitivity: **89%** (range: 73% - 100%)
  - pooled specificity: **73%** (range: 8% - 100%)

Woo, Eur Urol 2017;72:177

Validation of PI-RADS

- What is the impact of:
  - technical parameters (magnet strength, coil use, …)
  - definition of prostate cancer (all cancers versus clinically significant cancers only)
  - clinical scenario (biopsy naive, prior negative biopsy, known cancer)
  - reader expertise

I.
Impact of technical parameters

Impact of technique

- Do we need a 3T with ERC?
  - no difference between 1.5T and 3.0T
  - no difference between ERC or no ERC
    - → good results also possible on state-of-the-art (strong gradients, multiple channels) 1.5T system without ERC
- Technical standardization according to PI-RADS v2.1

Woo, Eur Urol 2017;72:177

II.
Definition of prostate cancer

mpMRI vs. cancer aggressiveness

ISUP 1

ISUP 2

ISUP 3-5

Prospective Evaluation of PI-RADS™ Version 2 Using the International Society of Urological Pathology Prostate Cancer Grade Group System

Sherif Mehralivand,* Sandra Bednarova,* Joanna. H. Shih, Francesca V. Mertan, Sonia Gaur, Maria J. Merino, Bradford J. Wood,† Peter A. Pinto,‡ Peter L. Choyke and Baris Turkbey§

From the Department of Urology and Pediatric Urology, University Medical Center (SM), Mainz, Germany, Urologic Oncology Branch (SM, PAP), Molecular Imaging Program (SM, SB, FVM, SG, PLC, BT), Center for Interventional Oncology (SB, BJW), Laboratory of Pathology, National Cancer Institute (MJM) and Radiology and Imaging Sciences, Clinical Center (SB, BJW), National Institutes of Health, Bethesda and Biometric Research Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health (JHS), Rockville, Maryland, and Institute of Diagnostic Radiology, Department of Medical and Biological Sciences, University of Udine (SB), Udine, Italy

Purpose: The PI-RADS™ (Prostate Imaging Reporting and Data System), version 2 scoring system, introduced in 2015, is based on expert consensus. In the same time frame ISUP (International Society of Urological Pathology) introduced a new pathological scoring system for prostate cancer. Our goal was to prospectively evaluate the cancer detection rates for each PI-RADS, version 2 category and compare them to ISUP group scores in patients undergoing systematic biopsy and magnetic resonance imaging-transrectal ultrasound fusion guided biopsy.

Materials and Methods: A total of 339 treatment naïve patients prospectively underwent multiparametric magnetic resonance imaging evaluated with PI-RADS, version 2 with subsequent systematic and fusion guided biopsy from May 2015 to May 2016. ISUP scores were applied to pathological specimens. An

Abbreviations and Acronyms

CDR = cancer detection rate

CS = clinically significant

DCE = dynamic contrast enhanced

DWI = diffusion-weighted imaging

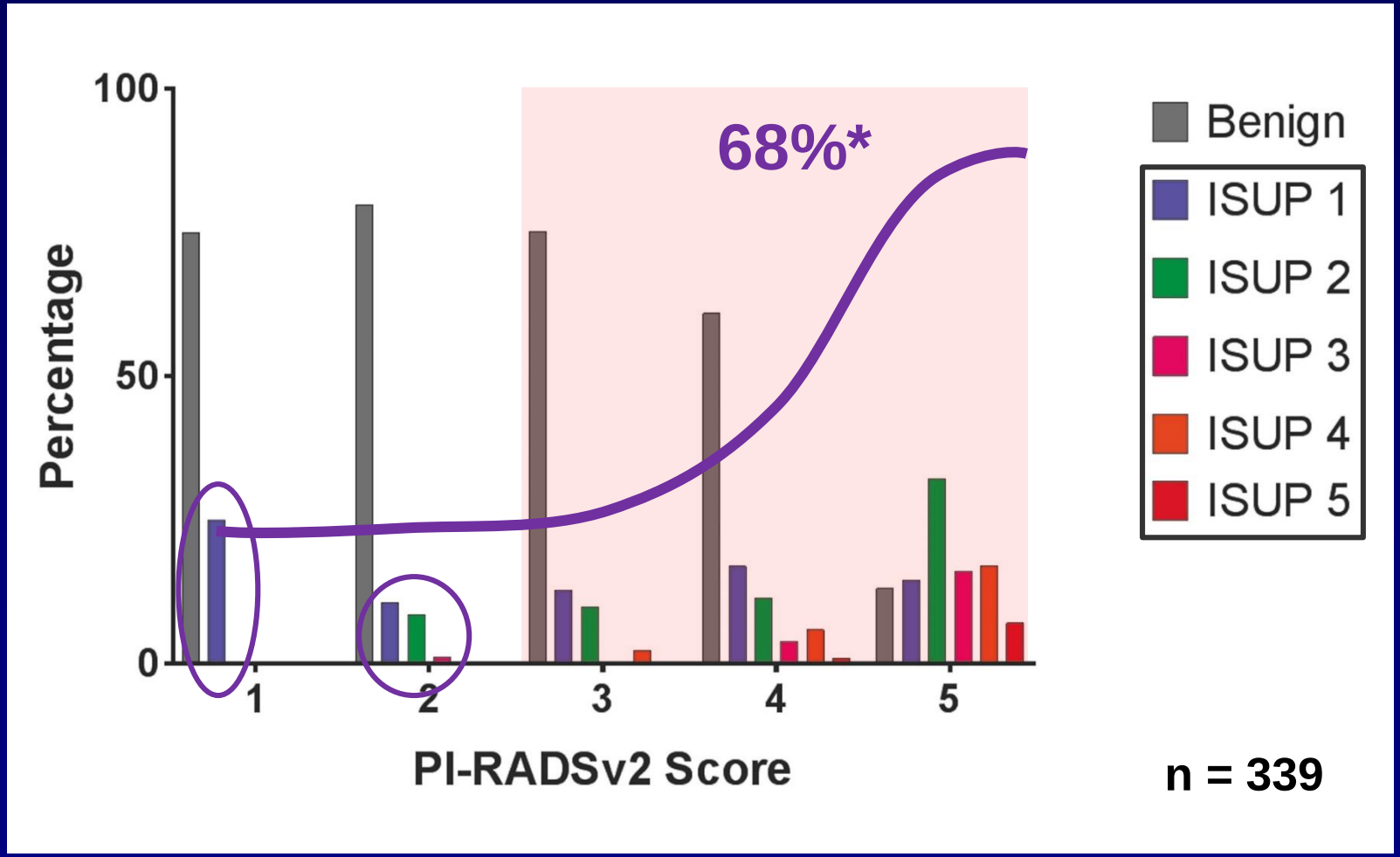
ISUP = International Society of Urological Pathology

mpMRI = multiparametric MRI

Mehralivand, J Urol 2017;198:583

GV

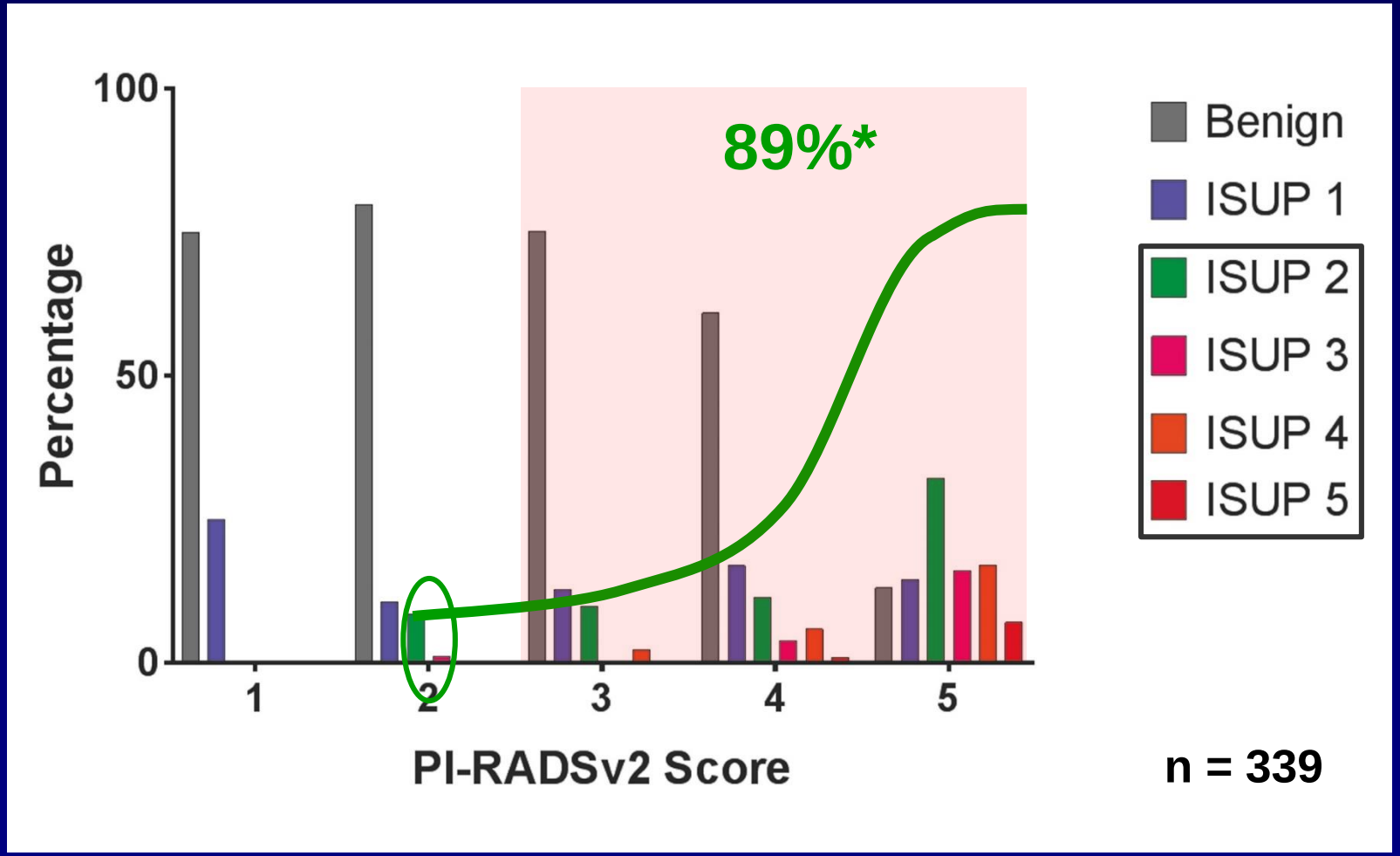
mpMRI vs. cancer aggressiveness



Mehralivand, J Urol 2017;198:583

*Drost, Cochrane Database Syst Rev 2019;4:CD012663

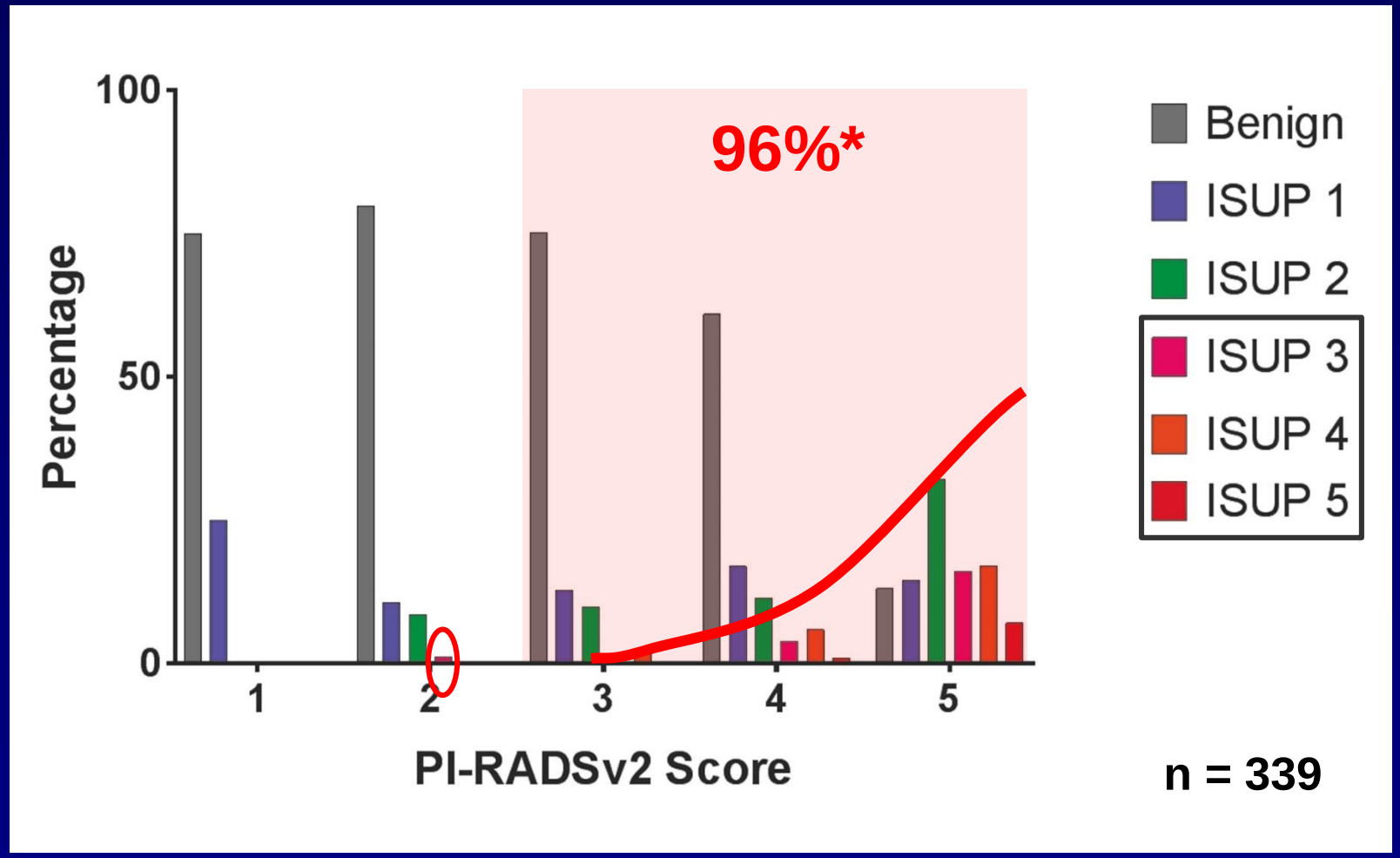
mpMRI vs. cancer aggressiveness



Mehralivand, J Urol 2017;198:583

*Drost, Cochrane Database Syst Rev 2019;4:CD012663

mpMRI vs. cancer aggressiveness



Mehralivand, J Urol 2017;198:583

*Drost, Cochrane Database Syst Rev 2019;4:CD012663

Rationale of mpMRI

- If mpMRI is negative (PI-RADS 1-2): **do not biopsy** (high NPV for excluding clinically significant cancer)
- If mpMRI is positive (PI-RADS 3-5): **target** biopsy needle towards mpMRI visible lesion

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Review – Prostate Cancer

What Is the Negative Predictive Value of Multiparametric Magnetic Resonance Imaging in Excluding Prostate Cancer at Biopsy? A Systematic Review and Meta-analysis from the European Association of Urology Prostate Cancer Guidelines Panel

Paul C. Moldovan[a,†], *Thomas Van den Broeck*[b,c,†], *Richard Sylvester*[d], *Lorenzo Marconi*[e], *Joaquim Bellmunt*[f,g], *Roderick C.N. van den Bergh*[h], *Michel Bolla*[i], *Erik Briers*[j], *Marcus G. Cumberbatch*[k], *Nicola Fossati*[l], *Tobias Gross*[m], *Ann M. Henry*[n], *Steven Joniau*[b,c], *Theo H. van der Kwast*[o], *Vsevolod B. Matveev*[p], *Henk G. van der Poel*[h], *Maria De Santis*[q], *Ivo G. Schoots*[r,s], *Thomas Wiegel*[t], *Cathy Yuhong Yuan*[u], *Philip Cornford*[v], *Nicolas Mottet*[w], *Thomas B. Lam*[x,y], *Olivier Rouvière*[a,z,*]

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GV

NPV of mpMRI

- Meta-analysis of 48 studies (9613 patients)
  - **82%** median NPV for **any** cancer exclusion
  - **88%** median NPV for **clinically significant** (ISUP 2-5) cancer exclusion

Moldovan, Eur Urol 2017;72:250

Rationale of mpMRI

- If mpMRI is negative (PI-RADS 1-2): **do not biopsy** (high NPV for excluding clinically significant cancer)
- If mpMRI is positive (PI-RADS 3-5): **target** biopsy needle towards mpMRI visible lesion

EUROPEAN UROLOGY 68 (2015) 1045–1053

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

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]

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Article info

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Abstract

Context: Detection of clinically significant prostate cancer (PCa) is a major challenge. It has been shown that multiparametric magnetic resonance imaging (mpMRI) facilitates localisa-

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PPV of mpMRI

- Systematic review of 12 studies (1981 patients)*
  - PPV range 34%- 68% for csPCA
    - higher PPV for more aggressive tumors
    - higher PPV for more targeted biopsies (as opposed to systematic biopsy)

*Fütterer, Eur Urol 2015;68:1045

JAMA Network Open

Original Investigation | Imaging

Comparison of Multiparametric Magnetic Resonance Imaging and Targeted Biopsy With Systematic Biopsy Alone for the Diagnosis of Prostate Cancer

A Systematic Review and Meta-analysis

Martha M. C. Elwenspoek, PhD; Athena L. Sheppard, MSc; Matthew D. F. McInnes, MD, PhD; Samuel W. D. Merriel, MSc; Edward W. J. Rowe, MD; Richard J. Bryant, FRCS(Urol), PhD; Jenny L. Donovan, PhD; Penny Whiting, PhD

Abstract

IMPORTANCE The current diagnostic pathway for patients with suspected prostate cancer (PCa) includes prostate biopsy. A large proportion of individuals who undergo biopsy have either no PCa or low-risk disease that does not require treatment. Unnecessary biopsies may potentially be avoided with prebiopsy imaging.

OBJECTIVE To compare the performance of systematic transrectal ultrasonography–guided prostate biopsy vs prebiopsy biparametric or multiparametric magnetic resonance imaging (MRI) followed by targeted biopsy with or without systematic biopsy.

DATA SOURCES MEDLINE, Embase, Cochrane, Web of Science, clinical trial registries, and reference lists of recent reviews were searched through December 2018 for randomized clinical trials using the terms "prostate cancer" and "MRI."

STUDY SELECTION Randomized clinical trials comparing diagnostic pathways including prebiopsy

Key Points

Question Is prebiopsy magnetic resonance imaging combined with targeted biopsy associated with improved detection of clinically significant prostate cancer compared with transrectal ultrasonography–guided systematic prostate biopsy alone?

Findings This systematic review and meta-analysis of 7 randomized clinical trials (2582 patients) demonstrates that prebiopsy magnetic resonance imaging combined with targeted biopsy is associated with improved detection of

mpMRI-guided biopsy

- Meta-analysis of 7 single-institution studies, including 2582 patients
  - 57% more detection of csPCa
  - 77% reduction of cores taken
  - adding systematic biopsy to mpMRI-guided biopsy does not seem to improve csPCa detection

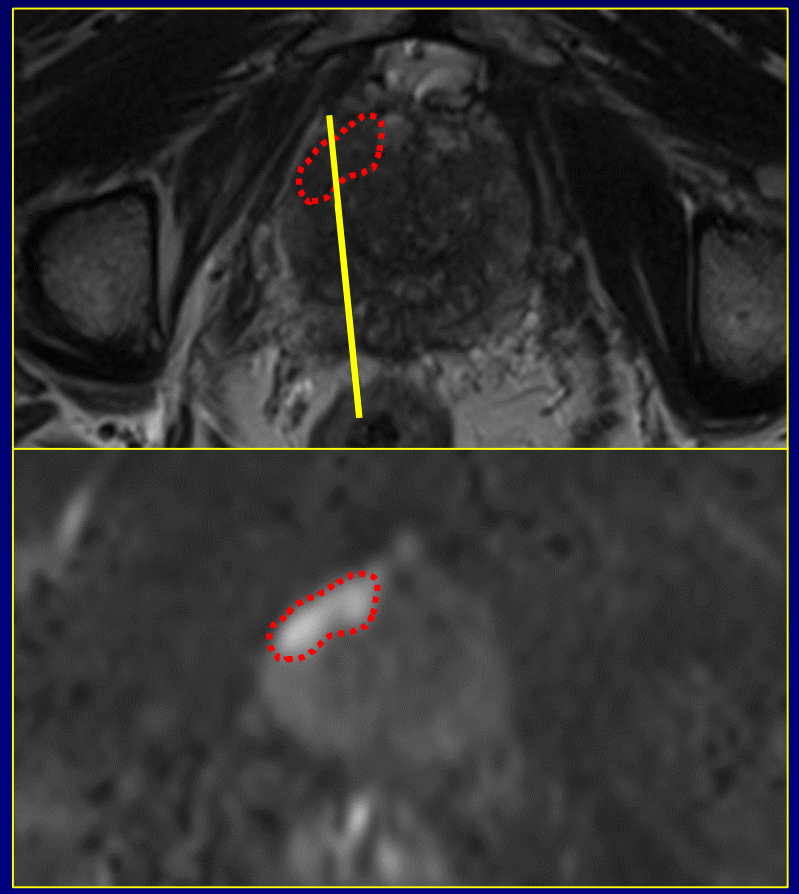
*Elwenspoek, JAMA Network Open. 2019;2(8):e198427

Rationale of mpMRI

- If mpMRI is negative (PI-RADS 1-2): **do not biopsy** (high NPV for excluding clinically significant cancer)
- If mpMRI is positive (PI-RADS 3-5): **target** biopsy needle towards mpMRI visible lesion

A chain is as strong as its weakest link…

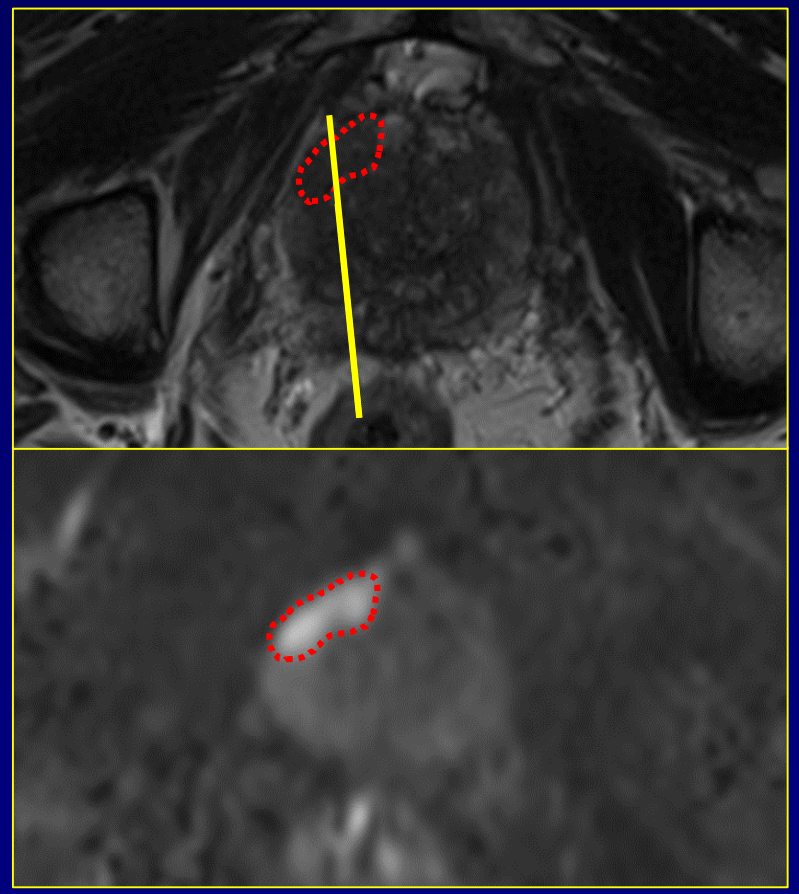
mpMRI-guided biopsy



- Operator skills*
  - learning curve effect up to 60 procedures
  - flattening after 80 procedures
  - optimal number of procedures > 100

*Gaziev, BJU Int 2016;117:80
Mager, Int Urol Nephrol 2017;49:1
Stabile, Eur Urol Oncol 2018;1:120
Halstuch, Prostate Cancer Prostatic Dis 2019; doi: 10.1038/s41391-019-0137-2

mpMRI-guided biopsy



- Technical options
  - Cognitive fusion
  - MRI-US fusion
  - In bore biopsy
- No significant difference in csPCA detection*

*Wegelin, Eur Urol 2017;71:517

III.
Impact of clinical scenario

Guidelines
Repeat biopsy

Recommendations in patients with prior negative biopsy	LE	Strength rating
Perform mpMRI before prostate biopsy.	1a	Strong
When mpMRI is positive (i.e. PI-RADS ≥ 3), perform targeted biopsy only.	2a	Weak
When mpMRI is negative (i.e. PI-RADS ≤ 2), and clinical suspicion of prostate cancer is high, perform systematic biopsy based on shared decision making with the patient.	2a	Strong

Relative sensitivity of MRI-guided biopsy versus TRUS-guided biopsy in the repeat setting is **1.45 -1.62***

*Schoots, Eur Urol 2015;68:438
Stabile, Prost Cancer and Prost Dis 2018;21:473

Guidelines
Initial biopsy

Recommendations in biopsy naïve patients	LE	Strength rating
Perform mpMRI before prostate biopsy.	1a	Weak
When mpMRI is positive (i.e. PI-RADS ≥ 3), combine targeted and systematic biopsy.	2a	Strong
When mpMRI is negative (i.e. PI-RADS ≤ 2), and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient.	2a	Weak

Relative sensitivity of MRI-guided biopsy versus TRUS-guided biopsy in the biopsy naïve setting is **0.97 – 1.15***

*Schoots, Eur Urol 2015;68:438
Stabile, Prost Cancer and Prost Dis 2018;21:473

mpMRI as triage test

- In the biopsy naïve setting, use of mpMRI is 5% more likely to make the correct diagnosis (relative sensitivity **1.05**)
- In the prior negative biopsy setting, us of mpMRI is 44% more likely to make the correct diagnosis (relative sensitivity **1.44**)

*Drost, Cochrane Database Syst Rev 2019;4:CD012663
doi: 10.1002/14651858.CD012663.pub2

mpMRI as triage test

- Incremental cancer detection is one thing…
- Other important questions in the screening setting:
  - how many biopsies do we deem appropriate? (“primum non nocere”)
  - do we really want to find ALL cancers?

mpMRI as triage test

ISUP 1

ISUP 2

ISUP 3-5

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

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

Summary

Background Men with high serum prostate specific antigen usually undergo transrectal ultrasound-guided prostate biopsy (TRUS-biopsy). TRUS-biopsy can cause side-effects including bleeding, pain, and infection. Multi-parametric magnetic resonance imaging (MP-MRI) used as a triage test might allow men to avoid unnecessary TRUS-biopsy and improve diagnostic accuracy.

Methods We did this multicentre, paired-cohort, confirmatory study to test diagnostic accuracy of MP-MRI and TRUS-biopsy against a reference test (template prostate mapping biopsy [TPM-biopsy]). Men with prostate-specific antigen concentrations up to 15 ng/mL, with no previous biopsy, underwent 1·5 Tesla MP-MRI followed by both TRUS-biopsy and TPM-biopsy. The conduct and reporting of each test was done blind to other test results. Clinically significant cancer was defined as Gleason score ≥4+3 or a maximum cancer core length 6 mm or longer. This study is registered on ClinicalTrials.gov, NCT01292291.

Findings Between May 17, 2012, and November 9, 2015, we enrolled 740 men, 576 of whom underwent 1·5 Tesla MP-MRI followed by both TRUS-biopsy and TPM-biopsy. On TPM-biopsy, 408 (71%) of 576 men had cancer with 230 (40%) of 576 patients clinically significant. For clinically significant cancer, MP-MRI was more sensitive (93%, 95% CI 88–96%) than TRUS-biopsy (48%, 42–55%; p<0·0001) and less specific (41%, 36–46% for MP-MRI *vs* 96%, 94–98% for TRUS-biopsy; p<0·0001). 44 (5·9%) of 740 patients reported serious adverse events, including 8 cases of sepsis.

Lancet 2017; 389: 815–22

Published Online
January 19, 2017
http://dx.doi.org/10.1016/S0140-6736(16)32401-1

See Comment page 767

*These authors contributed equally

†For a complete list of members of the PROMIS study group see appendix

Division of Surgery and Interventional Science, Faculty of Medical Sciences, University College London, London, UK (H Ahmed FRCS, A El-Shater Bosaily MBBCh, Prof M Emberton FRCS); **Department of Urology, UCLH**

GV

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

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

ABSTRACT

BACKGROUND

Multiparametric magnetic resonance imaging (MRI), with or without targeted biopsy, is an alternative to standard transrectal ultrasonography–guided biopsy for prostate-cancer detection in men with a raised prostate-specific antigen level who have not undergone biopsy. However, comparative evidence is limited.

METHODS

In a multicenter, randomized, noninferiority trial, we assigned men with a clinical suspicion of prostate cancer who had not undergone biopsy previously to undergo MRI, with or without targeted biopsy, or standard transrectal ultrasonography–guided biopsy. Men in the MRI-targeted biopsy group underwent a targeted biopsy (without standard biopsy cores) if the MRI was suggestive of prostate cancer; men whose MRI results were not suggestive of prostate cancer were not offered biopsy.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Kasivisvanathan at the Division of Surgery and Interventional Science, UCL, 3rd Fl., Charles Bell House, 43-45 Foley St., London W1W 7TS, United Kingdom, or at veeru.kasi@ucl.ac.uk.

*A complete list of members of the PRECISION Study Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on March 19,

GV

EUROPEAN UROLOGY 75 (2019) 570–578

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Prostate Cancer – Editor's Choice

Editorial by Derek J. Rosario, Thomas J. Walton and Steven J. Kennish on pp. 579–581 of this issue

Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study

Marloes van der Leest [a], Erik Cornel [b], Bas Israël [a], Rianne Hendriks [c], Anwar R. Padhani [d], Martijn Hoogenboom [a], Patrik Zamecnik [a], Dirk Bakker [b], Anglita Yanti Setiasti [e], Jeroen Veltman [f], Huib van den Hout [f], Hans van der Lelij [g], Inge van Oort [c], Sjoerd Klaver [h], Frans Debruyne [i], Michiel Sedelaar [c], Gerjon Hannink [j], Maroeska Rovers [j], Christina Hulsbergen-van de Kaa [e,†], Jelle O. Barentsz [a,†,]*

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GV

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

*Olivier Rouvière, Philippe Puech, Raphaële Renard-Penna, Michel Claudon, Catherine Roy, Florence Mège-Lechevallier, Myriam Decaussin-Petrucci, Marine Dubreuil-Chambardel, Laurent Magaud, Laurent Remontet, Alain Ruffion, Marc Colombel, Sébastien Crouzet, Anne-Marie Schott, Laurent Lemaitre, Muriel Rabilloud, Nicolas Grenier, for the MRI-FIRST Investigators**

Lancet Oncol 2019; 20: 100–09

Published Online November 20, 2018 http://dx.doi.org/10.1016/S1470-2045(18)30569-2

See Comment page 9

*All MRI-FIRST investigators are listed in the appendix

Service d'Imagerie Urinaire et Vasculaire (Prof O Rouvière MD, M Dubreuil-Chambardel PhD), **Service d'Anatomo-Pathologie** (F Mège-Lechevallier MD), **and Service d'Urologie** (Prof M Colombel MD, Prof S Crouzet MD), **Hôpital Edouard Herriot, Service d'Urologie** (Prof A Ruffion MD), **Service d'Anatomo-Pathologie** (M Decaussin-Petrucci MD), **Center Hospitalier Lyon Sud, Pôle de Santé Publique** (L Magaud PhD, Prof A-M Schott MD), **and Service de Biostatistique et Bioinformatique** (L Remontet MD, M Rabilloud MD), **Hospices Civils de Lyon, Lyon, France; Faculté de Médecine Lyon Est**

Summary

Background Whether multiparametric MRI improves the detection of clinically significant prostate cancer and avoids the need for systematic biopsy in biopsy-naive patients remains controversial. We aimed to investigate whether using this approach before biopsy would improve detection of clinically significant prostate cancer in biopsy-naive patients.

Methods In this prospective, multicentre, paired diagnostic study, done at 16 centres in France, we enrolled patients aged 18–75 years with prostate-specific antigen concentrations of 20 ng/mL or less, and with stage T2c or lower prostate cancer. Eligible patients had been referred for prostate multiparametric MRI before a first set of prostate biopsies, with a planned interval of less than 3 months between MRI and biopsies. An operator masked to multiparametric MRI results did a systematic biopsy by obtaining 12 systematic cores and up to two cores targeting hypoechoic lesions. In the same patient, another operator targeted up to two lesions seen on MRI with a Likert score of 3 or higher (three cores per lesion) using targeted biopsy based on multiparametric MRI findings. Patients with negative multiparametric MRI (Likert score ≤2) had systematic biopsy only. The primary outcome was the detection of clinically significant prostate cancer of International Society of Urological Pathology grade group 2 or higher (csPCa-A), analysed in all patients who received both systematic and targeted biopsies and whose results from both were available for pathological central review, including patients who had protocol deviations. This study is registered with ClinicalTrials.gov, number NCT02485379, and is closed to new participants.

Findings Between July 15, 2015, and Aug 11, 2016, we enrolled 275 patients. 24 (9%) were excluded from the analysis. 53 (21%) of 251 analysed patients had negative (Likert ≤2) multiparametric MRI. csPCa-A was detected in 94 (37%) of 251 patients. 13 (14%) of these 94 patients were diagnosed by systematic biopsy only, 19 (20%) by targeted biopsy only, and 62 (66%) by both techniques. Detection of csPCa-A by systematic biopsy (29·9%, 95% CI 24·3–36·0) and targeted biopsy (32·3%, 26·5–38·4) did not differ significantly (p=0·38). csPCa-A would have been missed in 5·2% (95% CI 2·8–8·7) of patients had systematic biopsy not been done, and in 7·6% (4·6–11·6) of patients had targeted biopsy not been done. Four grade 3 post-biopsy adverse events were reported (3 cases of prostatitis, and 1 case of urinary retention with haematuria).

GV

Cochrane Library

Cochrane Database of Systematic Reviews

Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer (Review)

Drost FJH, Osses DF, Nieboer D, Steyerberg EW, Bangma CH, Roobol MJ, Schoots IG

GV

mpMRI as triage test?

	PROMIS	PRECISION	4M	MRI First	COCHRANE
# patients	576	500	626	251	-
PSA	≤ 15 ng/mL	≤ 20 ng/mL	≥ 3 ng/mL	≤ 20 ng/mL	-
Biopsies	-27%	-28%	-49%	-18%	**-33%**
Insignificant cancers	-5%	-13%	-11%	-13%	**-8%**
Significant cancers	+18%	+12%	+2%	+2%	**+2%**

PROMIS - Ahmed, Lancet 2017;389:815
PRECISION - Kasivisvanathan, NEJM 2018;378:1767
4M – van der Leest, Eur Urol 2019;75:570
MRI First – Lancet Oncol 2019; 20: 100–09
Cochrane Review – Drost, Cochrane Database Syst Rev 2019;4:CD012663
doi: 10.1002/14651858.CD012663.pub2

mpMRI as triage test?

- Main objective of mpMRI in…
  - biopsy-naive setting: **decrease number of unnecessary biopsies (-33%)**
  - prior negative biopsy setting: **increase number of significant cancer detections (+40%)**

JAMA Network Open

Original Investigation | Urology

Assessment of the Diagnostic Accuracy of Biparametric Magnetic Resonance Imaging for Prostate Cancer in Biopsy-Naive Men

The Biparametric MRI for Detection of Prostate Cancer (BIDOC) Study

Lars Boesen, MD, PhD; Nis Nørgaard, MD; Vibeke Løgager, MD; Ingegerd Balslev, MD; Rasmus Bisbjerg, MD; Karen-Cecilie Thestrup, MD; Mads D. Winther; Henrik Jakobsen, MD; Henrik S. Thomsen, DMC

Abstract

IMPORTANCE Multiparametric magnetic resonance imaging (MRI) enhances detection and risk stratification for significant prostate cancer but is time-consuming (approximately 40 minutes) and expensive. Rapid and simpler (approximately 15-minute) biparametric MRI (bpMRI) using fewer scan sequences could be implemented as a prostate MRI triage test on a larger scale before performing biopsies.

OBJECTIVES To assess the diagnostic accuracy and negative predictive value (NPV) of a novel bpMRI method in biopsy-naive men in detecting and ruling out significant prostate cancer in confirmatory biopsies.

DESIGN, SETTING, AND PARTICIPANTS A single-institutional, paired, prospective cohort study of biopsy-naive men with clinical suspicion of prostate cancer from November 1, 2015, to June 15, 2017.

INTERVENTIONS All patients underwent bpMRI (T2-weighted and diffusion-weighted imaging) followed by standard transrectal ultrasound-guided biopsies (all men) and targeted biopsies of men with suspicious bpMRI findings.

MAIN OUTCOMES AND MEASURES Suspicion grades of bpMRI, biopsy results, and NPV of bpMRI

Key Points

Question What are the diagnostic accuracy and negative predictive value of novel biparametric magnetic resonance imaging (MRI) in biopsy-naive men in detecting and ruling out significant prostate cancer?

Findings In this cohort study of 1020 men who underwent both biparametric targeted and standard transrectal ultrasound-guided biopsies, low-suspicion biparametric MRI had a high negative predictive value (97%) in ruling out significant prostate cancer on confirmatory biopsies.

Meaning The biparametric MRI used as a triage test in this study was associated with improved prostate cancer risk stratification and may be used to

bpMRI as triage test?

- Bidoc trial: prospective paired-cohort study, PSA ≥ 4 ng/mL or abnormal DRE
  - 1020 biopsy-naïve men
  - bpMRI @ 3T (15 mins)
    - ax/sag T2w + ax DWI (b0, b100, b800, b2000)
    - modified PI-RADS: DWI 3 final
  - standard biopsy + bpMRI-targeted biopsy as reference

Boesen, JAMA Network open 2018;1:e180219

bpMRI as triage test?

	BIDOC					
# patients	1020					
PSA	≥ 4 ng/mL					
Biopsies	-30%					
Insignificant cancers	-40%					
Significant cancers	+11%					

Boesen, JAMA Network open 2018;1:e180219

bpMRI as triage test?

	BIDOC	PROMIS	PRECISION	4M	MRI First	Cochrane
# patients	1020	576	500	626	251	-
PSA	≥ 4 ng/mL	≤ 15 ng/mL	≤ 20 ng/mL	≥ 3 ng/mL	≤ 20 ng/mL	-
Biopsies	-30%	-27%	-28%	-49%	-18%	-33%
Insignificant cancers	-40%	-5%	-13%	-11%	-13%	-8%
Significant cancers	+11%	+18%	+12%	+2%	+2%	+2%

PROMIS - Ahmed, Lancet 2017;389:815
PRECISION - Kasivisvanathan, NEJM 2018;378:1767
4M – van der Leest, Eur Urol 2019;75:570
MRI First – Lancet Oncol 2019; 20: 100–09
Cochrane Review – Drost, Cochrane Database Syst Rev 2019;4:CD012663
doi: 10.1002/14651858.CD012663.pub2

bpMRI as triage test?

- Yes, but…
  - only in case of high quality DWI
  - not in case of recurrence detection

IV.
Effect of expertise

Effect of expertise

	PROMIS	PRECISION	4M	MRI First	COCHRANE
		500	626		
		≤ 20 ng/mL	≥ 3 ng/mL		
		-28%	**-49%**		
cancers		-13%	-11%		
Significant cancers	+18%	+12%	+2%	+2%	+2%

- 25 centers in 11 countries
- “modest experience”
- no central double reading

- 4 centers in 1 country
- highly experienced high-volume academic center + 3 sattelites
- central double reading

PROMIS - Ahmed, Lancet 2017;389:815
PRECISION - Kasivisvanathan, NEJM 2018;378:1767
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Effect of expertise

- Prostate MRI is a great tool for prostate cancer diagnosis, but highest quality is mandatory
  - we need to standardize mpMRI (PI-RADS v2.1)
  - we need to train, expand knowledge and maximize expertise

NOVEMBER 29, 2016

TUESDAY

INSIDE: Exhibitor Products

BEYOND IMAGING RSNA 2016

Daily Bulletin

THE OFFICIAL NEWSPAPER OF THE RSNA ANNUAL MEETING • ONLINE AT *RSNA.ORG/BULLETIN*

New Hands-on Prostate MRI Course is a Hit

A NEW COURSE ON PROSTATE IMAGING is among the many popular hands-on courses being presented at RSNA 2016. The course, using the American College of Radiology's MRI Prostate Imaging Reporting and Data System (PI-RADS) was introduced on Monday and filled to capacity.

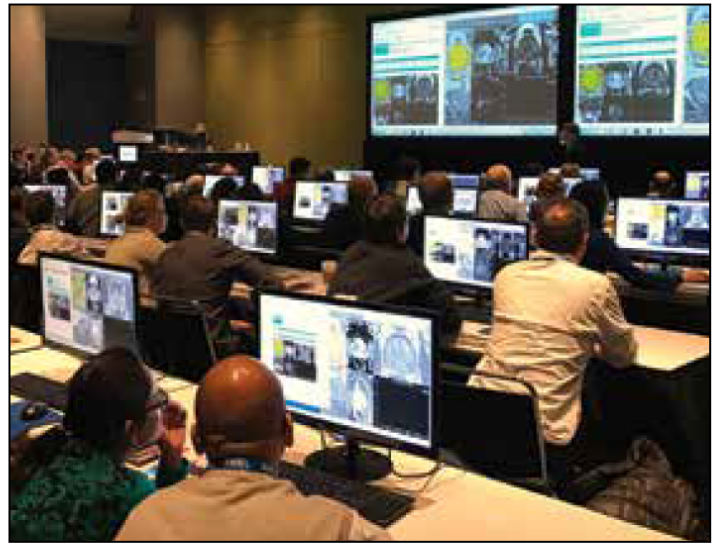
The course was co-organized by Jelle Barentsz, MD, PhD. He and a team of 10 international experts delivered interactive, individualized training on PI-RADS using 50 computers, which allowed optimal training of 30 cases from daily practice.

"I have never seen so many enthusiastic and active participants," said Dr. Barentsz, professor of radiology and chair of the Radboud Prostate MR-Referencing Center of Radboud University Medical Center, the Netherlands. "MRI of the prostate is booming, which shows the enthusiasm and need for training PI-RADS. More and more urologists are requesting prostate MRIs, and they expect good quality."

The course repeats Tuesday through Thursday, from 8 to 10 a.m.

PROSTATE MRI (HANDS-ON)

Tuesday	8–10 a.m.	RCA31	Room S401AB
Wednesday	8–10 a.m.	RCA41	Room S401AB
Thursday	8–10 a.m.	RCA51	Room S401AB



Monday's Prostate MRI course was filled to capacity.

GV

esur

European Society of Urogenital Radiology

10th Prostate MRI Teaching Course

April 24-25, 2020

Fribourg, Switzerland

GV

Effect of expertise

- Prostate MRI is a great tool for prostate cancer diagnosis, but highest quality is mandatory
  - we need to standardize mpMRI (PI-RADS v2.1)
  - we need to train, expand knowledge and maximize expertise
  - we need quality criteria and certification (ESUR)

Take Home Messages

Take Home Messages

- mpMRI is a combination of T2 + DWI + DCE (if no DCE: bpMRI)
- mpMRI should be performed in a standardized way (PI-RADS)
  - technical standardization
  - reporting standardization

Take Home Messages

- Level 1 evidence that
  - negative mpMRI virtually excludes aggressive PCa
  - positive mpMRI should get targeted biopsy
- mpMRI has high sensitivity and specificity
  - ranging according to prostate cancer definition
  - ranging according to clinical scenario
  - ranging according to expertise → training and certification

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