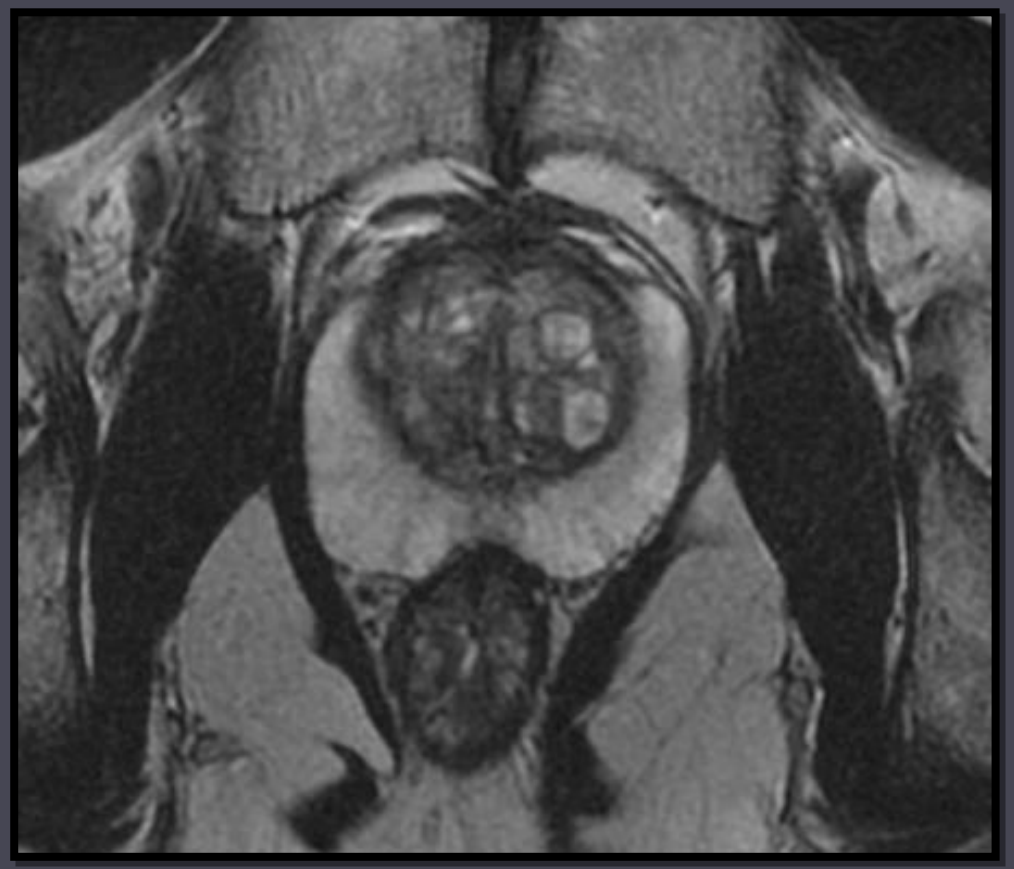
Società Medico Chirurgica di Ferrara dal 1846

IL TUMORE DELLA PROSTATA A FERRARA
Incontro con il Team Multidisciplinare

Venerdì 10 febbraio 2023



RISONANZA MULTI-PARAMETRICA DELLA PROSTATA

Massimo Tilli

AUSL FE

Diagnostica per Immagini *m.tilli@ausl.fe.it*

mpRM

- ***Background***
- ***Metodologia di indagine***
- ***Linee guida PI-RADS v2.1***
- ***Indicazioni***

Obiettivi

mp-MRI: i segreti del successo

Background

Biopsia random

Undersampling

Overdiagnosis

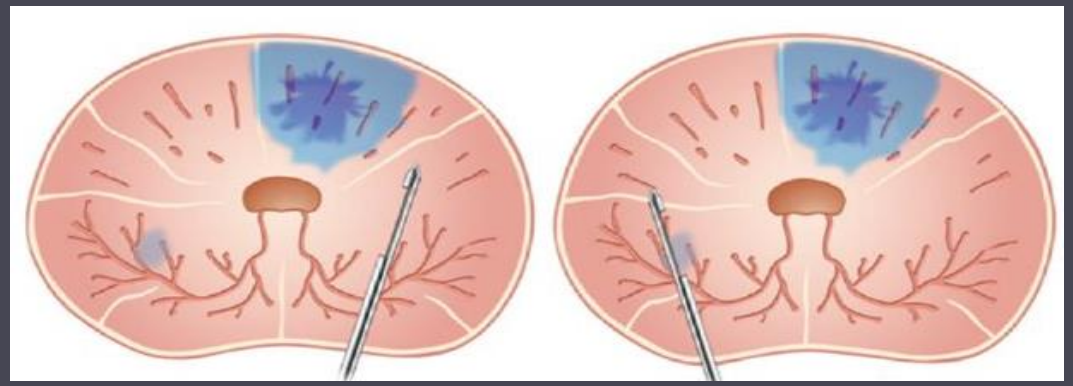
Overtreatment

No imaging pre-operatorio

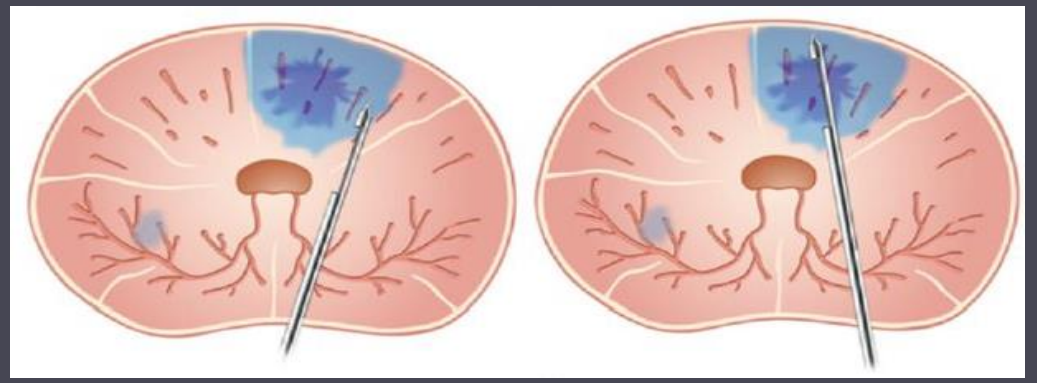
Background

Background

Biopsia sistematica (12-core)



sensibilità limitata (53%) per Ca clinicamente significativi



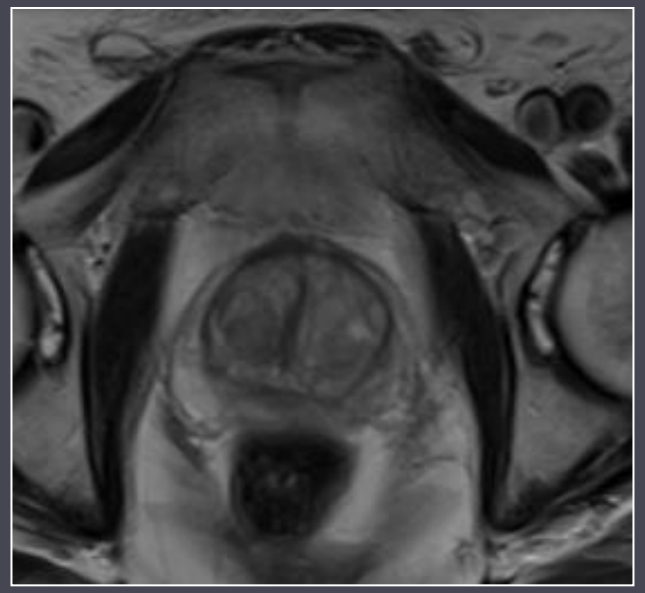
elevata possibilità di overdiagnosi (Ca non clinicamente significativi)

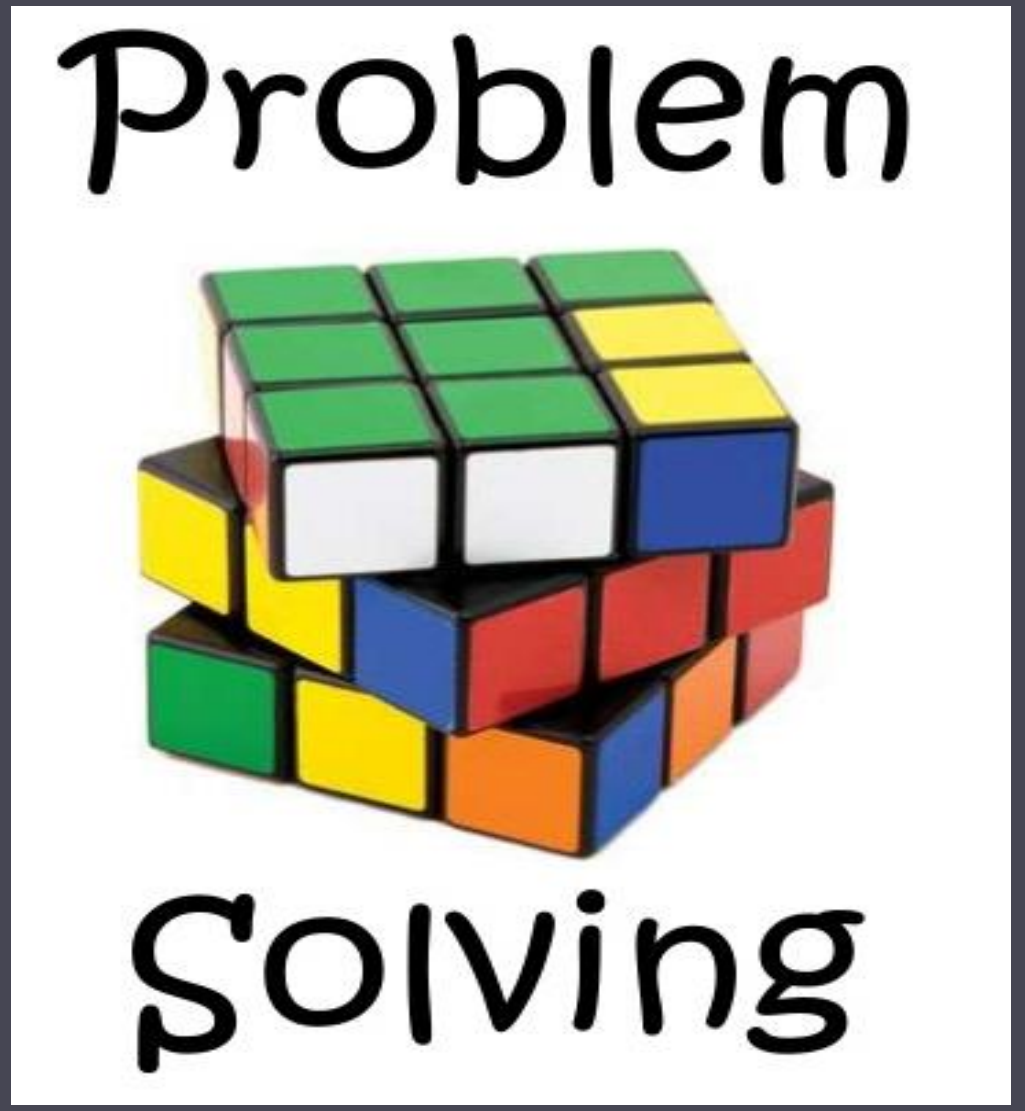
Re-Biopsia TRUS : **Positive solo nel 20-37 % dei casi**

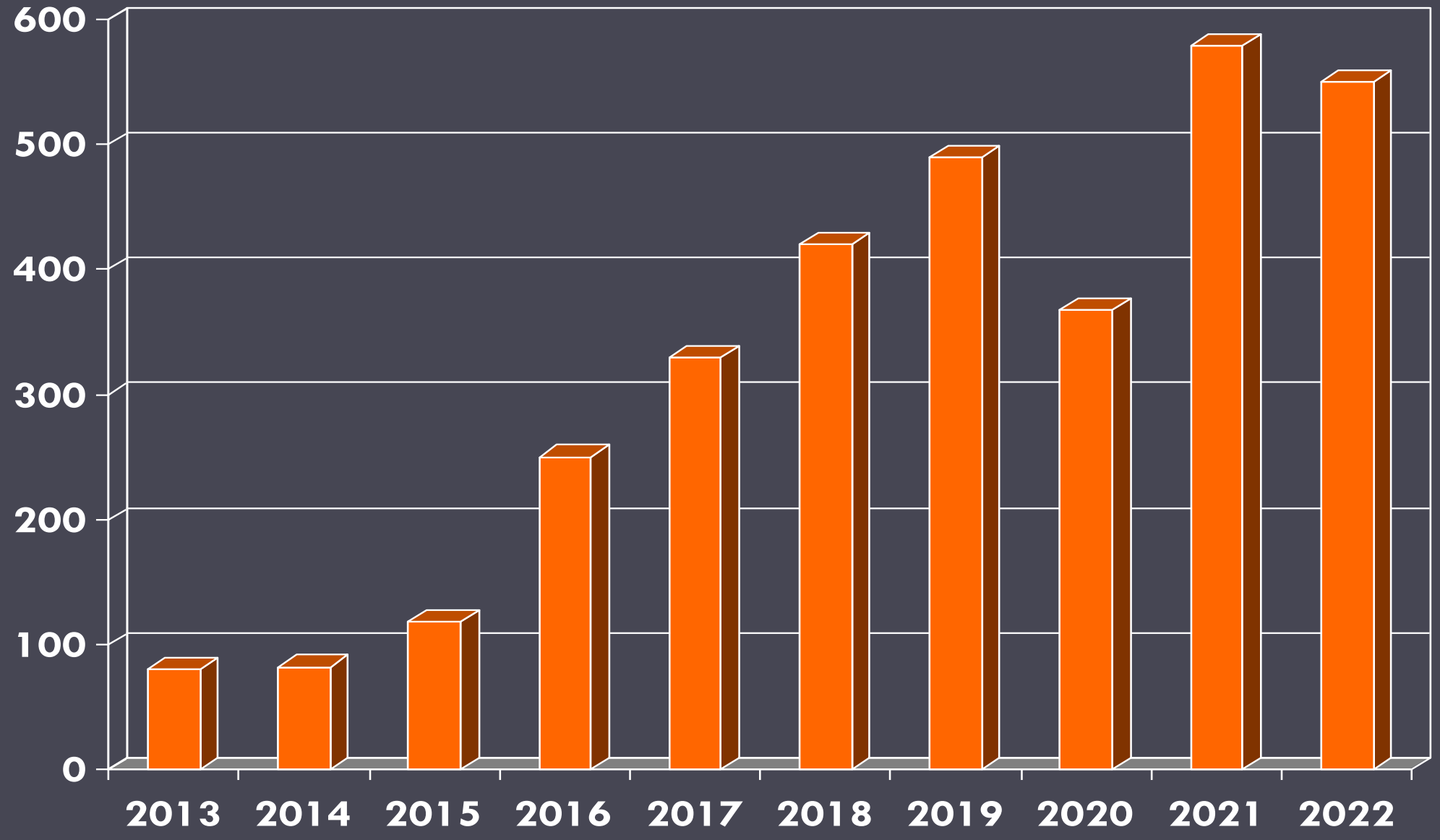
Cooperberg et Al. J Urol 2007
Siddiqui et Al. JAMA 2015

mpRM:

solo moda…??



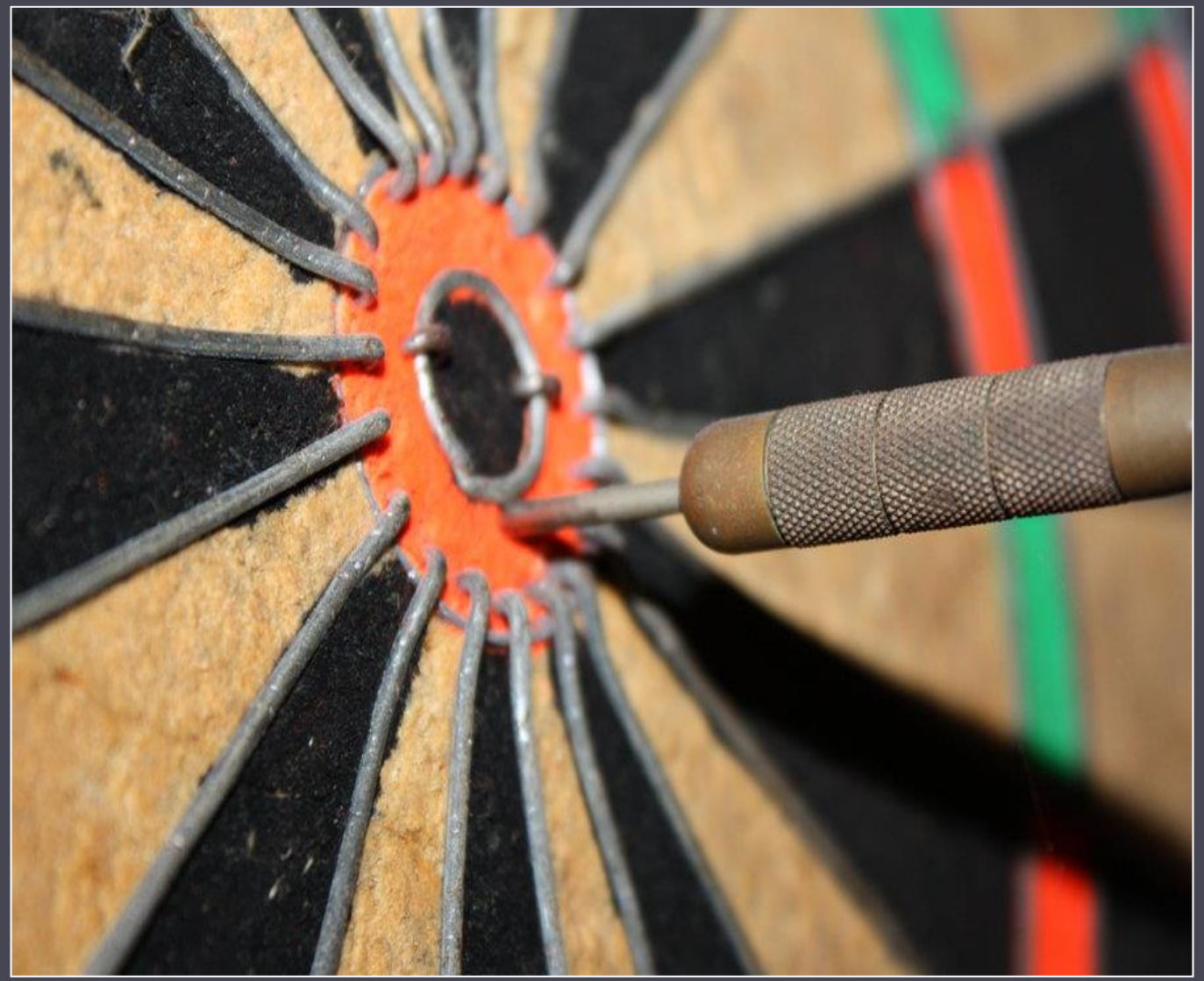




mp-RM

Statistica Radiologia AUSL Ferrara

La macchina (quasi) perfetta?



Background

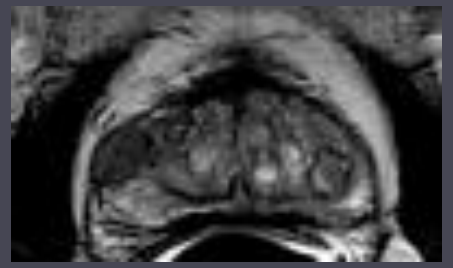
Ca clinicamente significativo ???

Stratificazione del rischio

mp-RM : aiuta a stratificare il rischio?

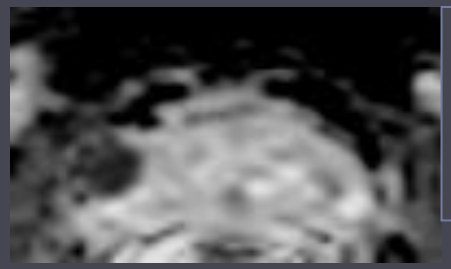
Parametri

Sequenze morfologiche (T2W)



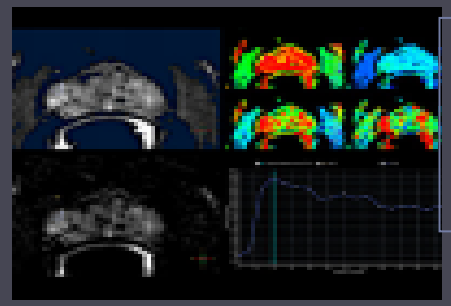
Valutazione anatomia multiplanare
Lesioni della Tz
Stadiazione

Sequenze in Diffusione (DWI)



Caratterizzazione tissutale (densità cellulare)
Lesioni Pz

Sequenze in Perfusione (DCE)

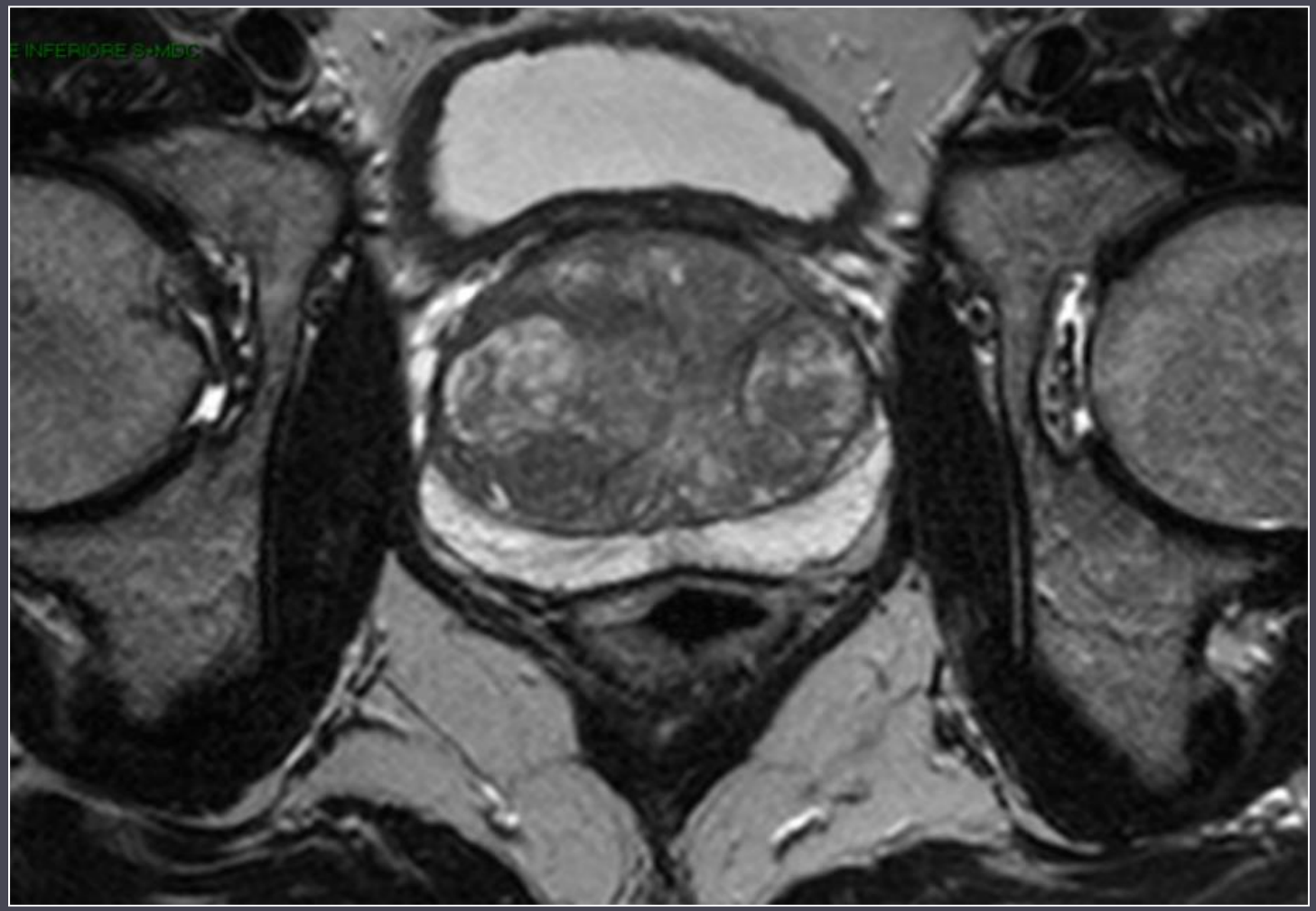


Caratterizzazione perfusione (mdc)
Valutazione lesioni dubbie

mp-RM

Metodologia d'indagine

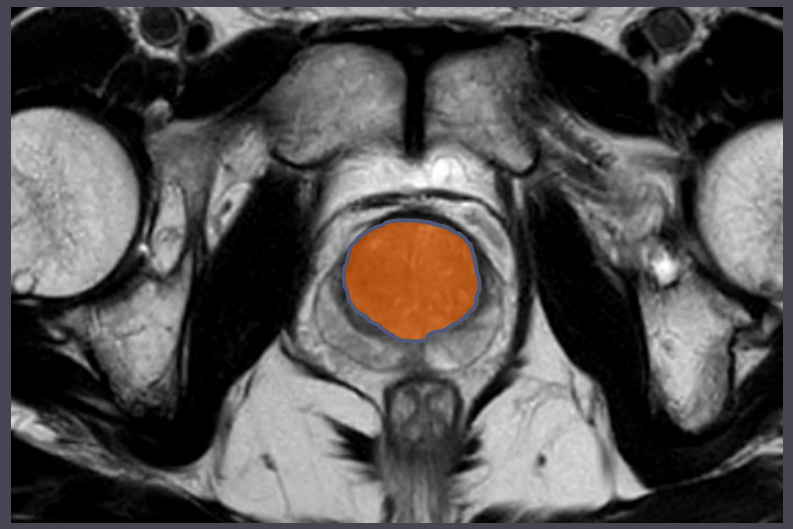
Seq. Morfologiche T2



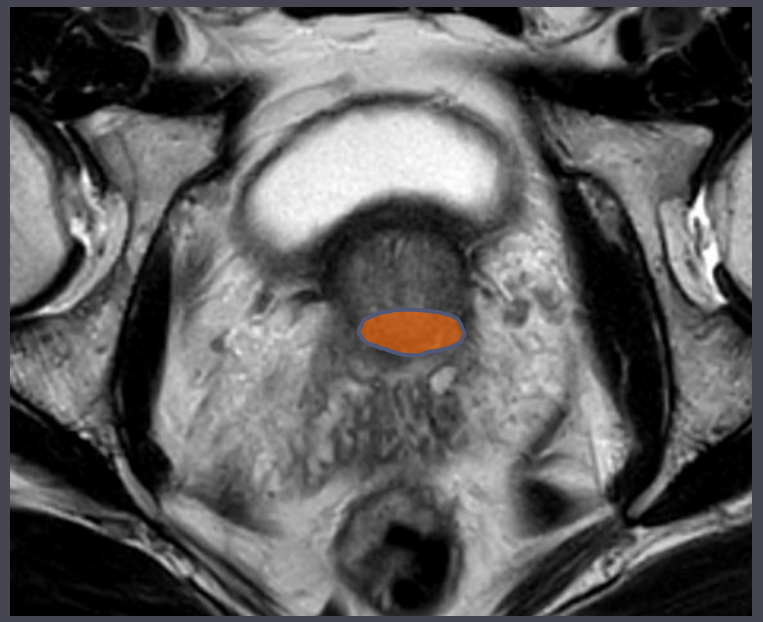
mp-RM

Parametro MORFOLOGICO

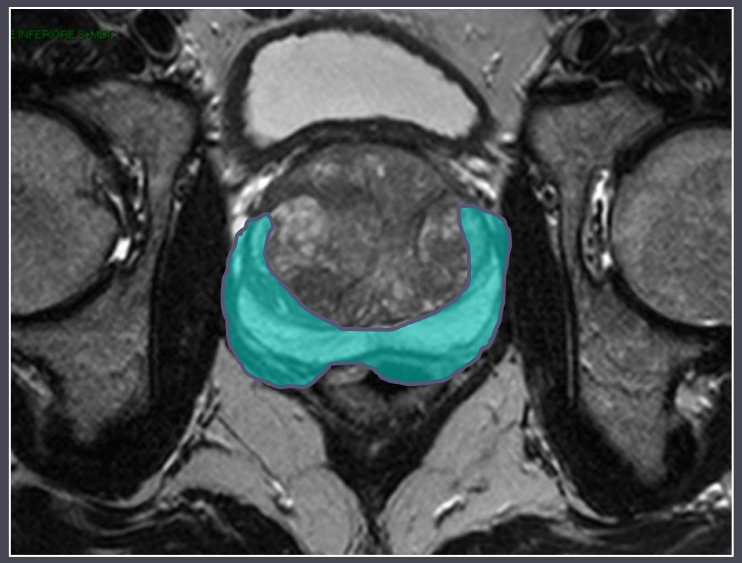
ZONA DI TRANSIZIONE



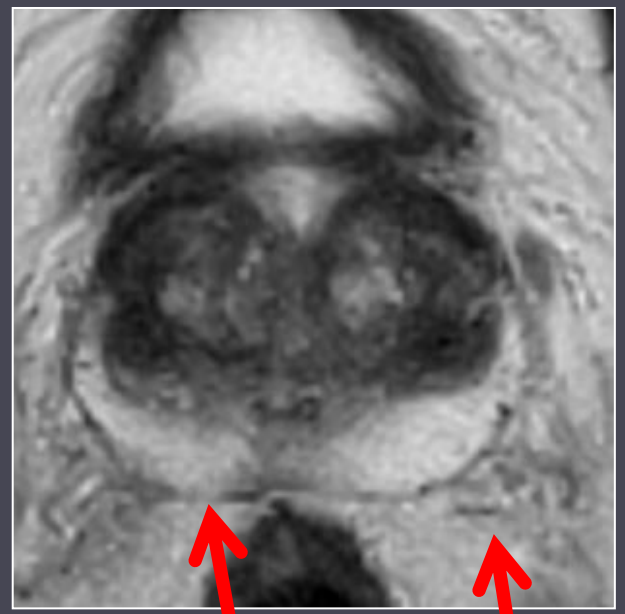
ZONA CENTRALE



ZONA PERIFERICA

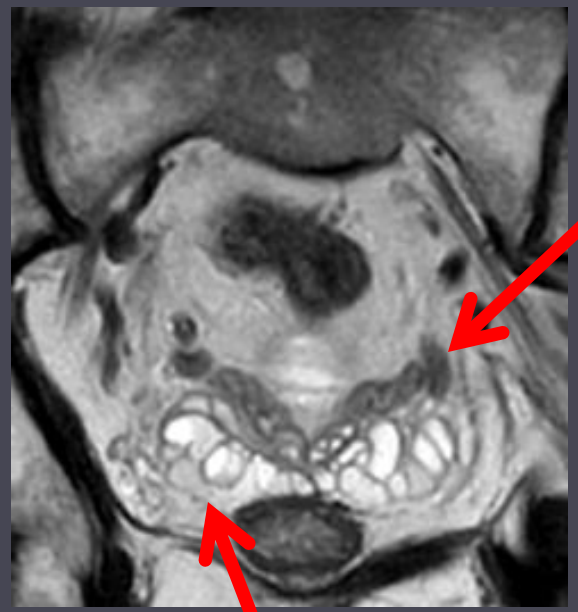


Seq. Morfologiche T2



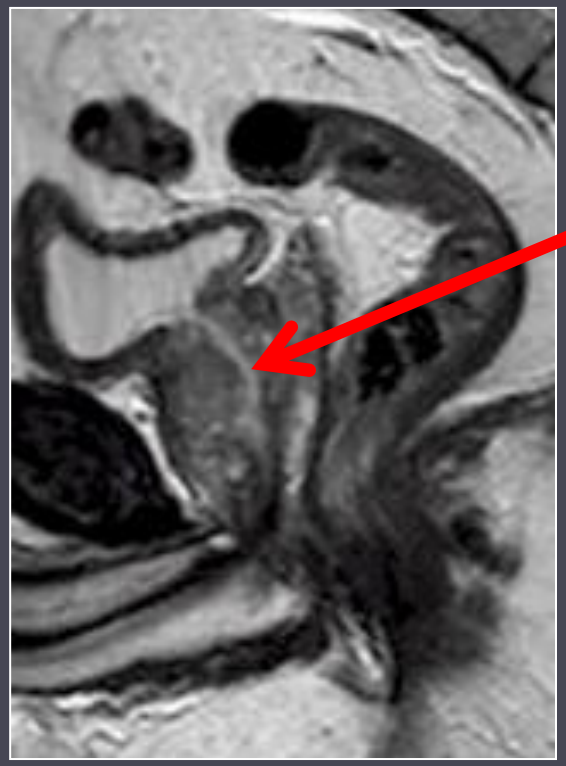
Capsula

Fasci vasculo-nervosi



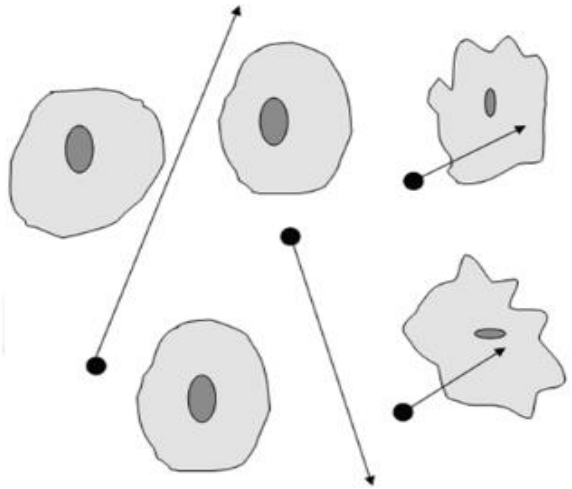
Vescichette Seminali

Dotti Deferenti

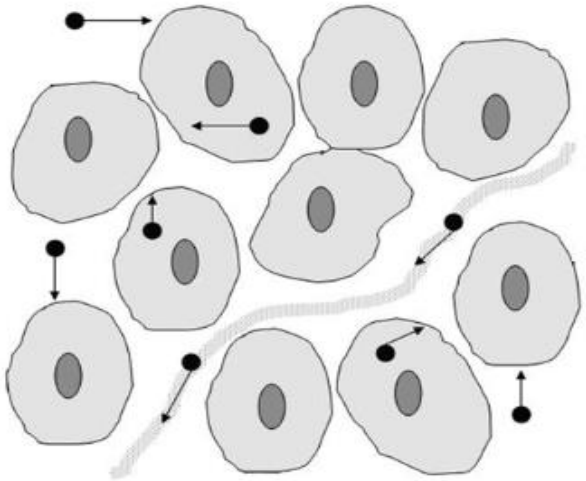


Uretra prostatica

Sequenze in Diffusione (DWI)



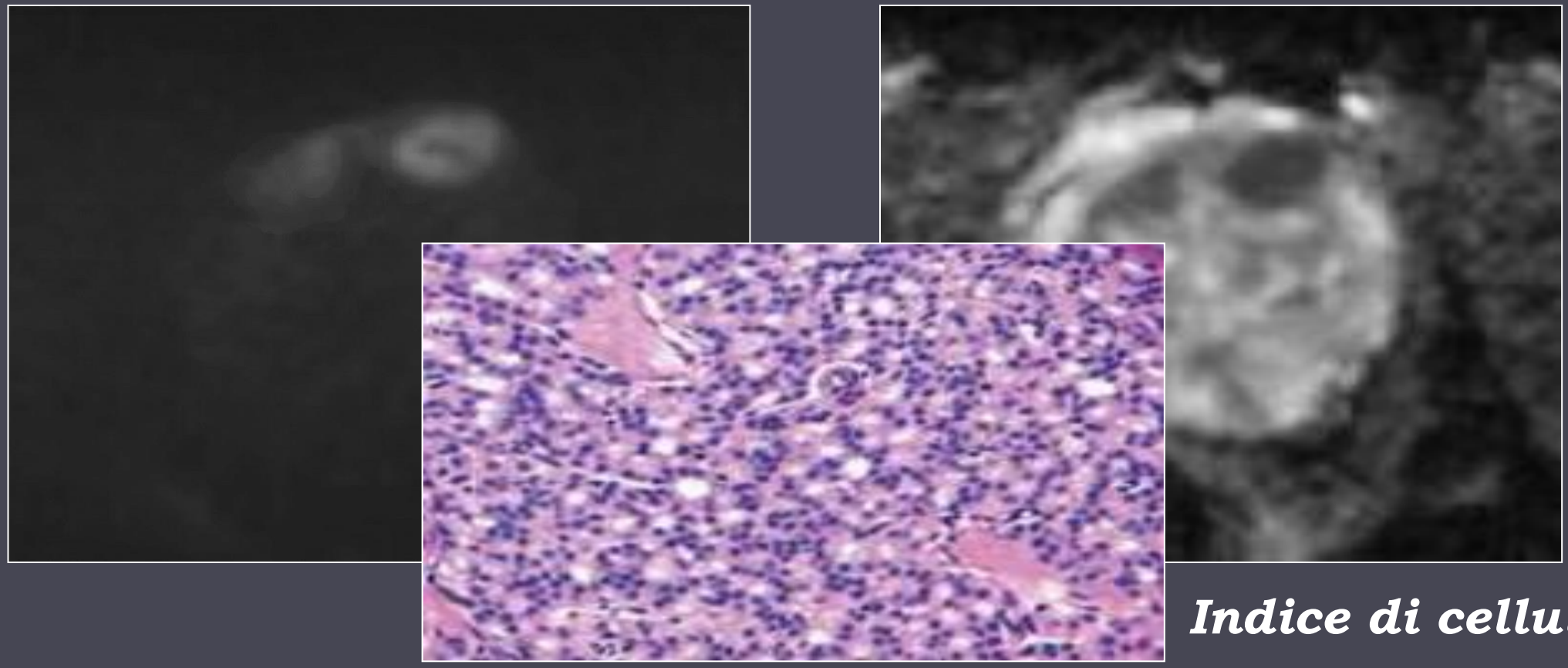
Diffusione
LIBERA delle
molecole
d'acqua.



Diffusione
RISTRETTA
delle molecole
d'acqua.

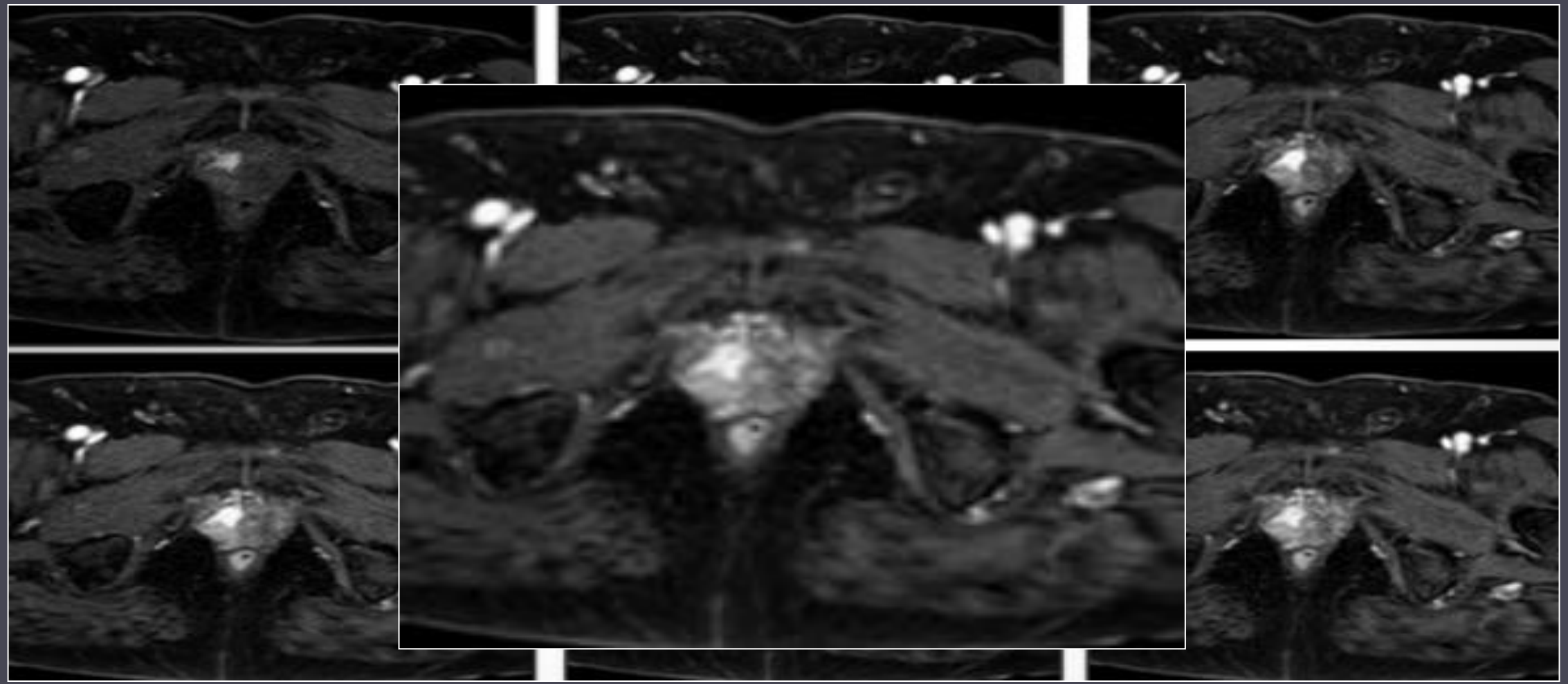
Parametro DIFFUSIONE

Seq. DWI e Mappa ADC

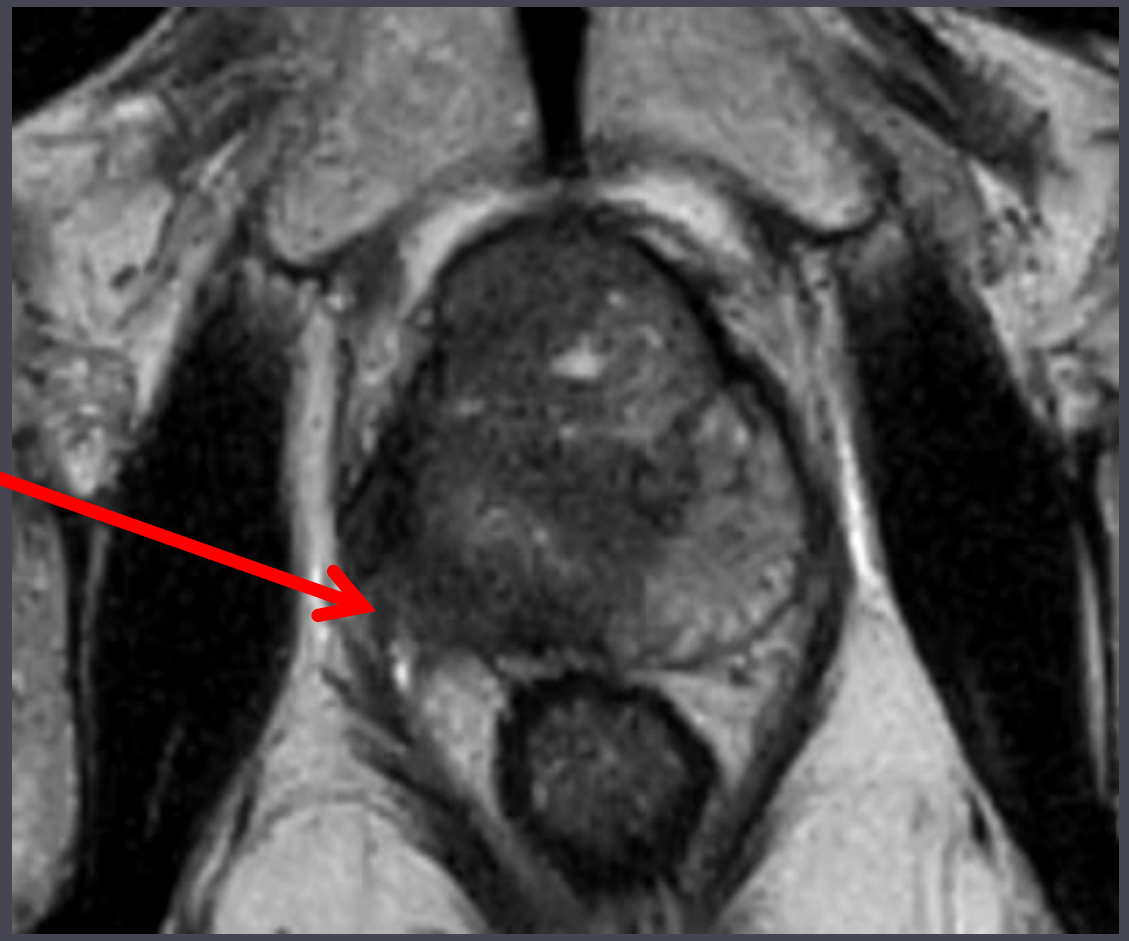


Indice di cellularità !!!

Seq. Perfusionali con mdc



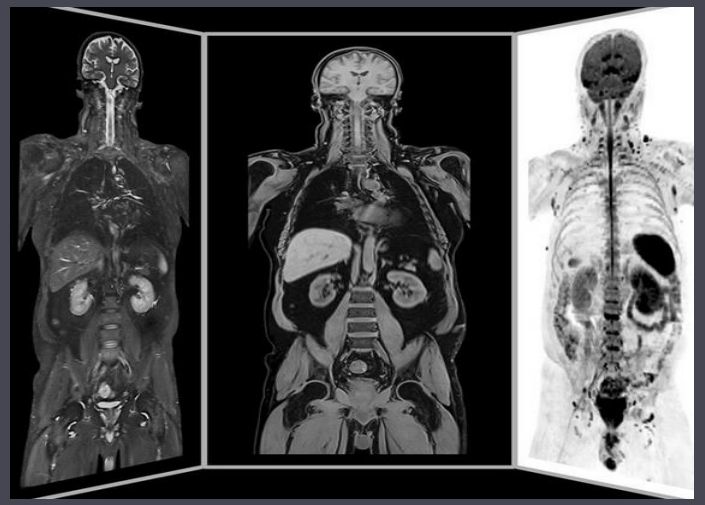
CaP che infiltra capsula e fascio vasculo-nervoso

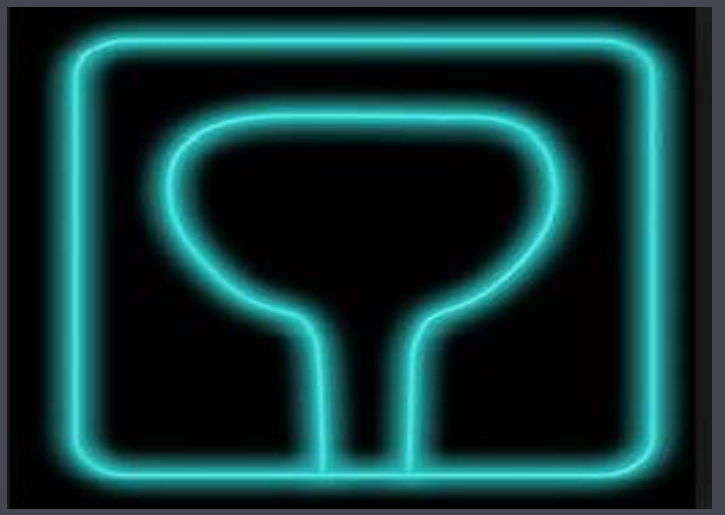


No nerve-sparing

mpRM: work in progress

Standardizzazione





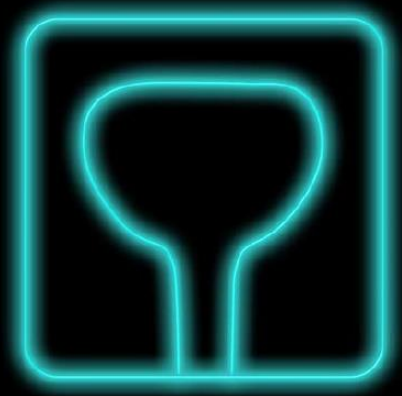
Tecnologia

Interpretazione e refertazione

PI-RADS™

Prostate Imaging – Reporting and Data System

2015
version 2



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

European Association of Urology

Platinum Priority – Review – Prostate Cancer

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

Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2

Baris Turkbey[a,†,], Andrew B. Rosenkrantz[b,†,*], Masoom A. Haider[c], Anwar R. Padhani[d], Geert Villeirs[e], Katarzyna J. Macura[f], Clare M. Tempany[g], Peter L. Choyke[a], Francois Cornud[h], Daniel J. Margolis[i], Harriet C. Thoeny[j], Sadhna Verma[k], Jelle Barentsz[l,†], Jeffrey C. Weinreb[m]*

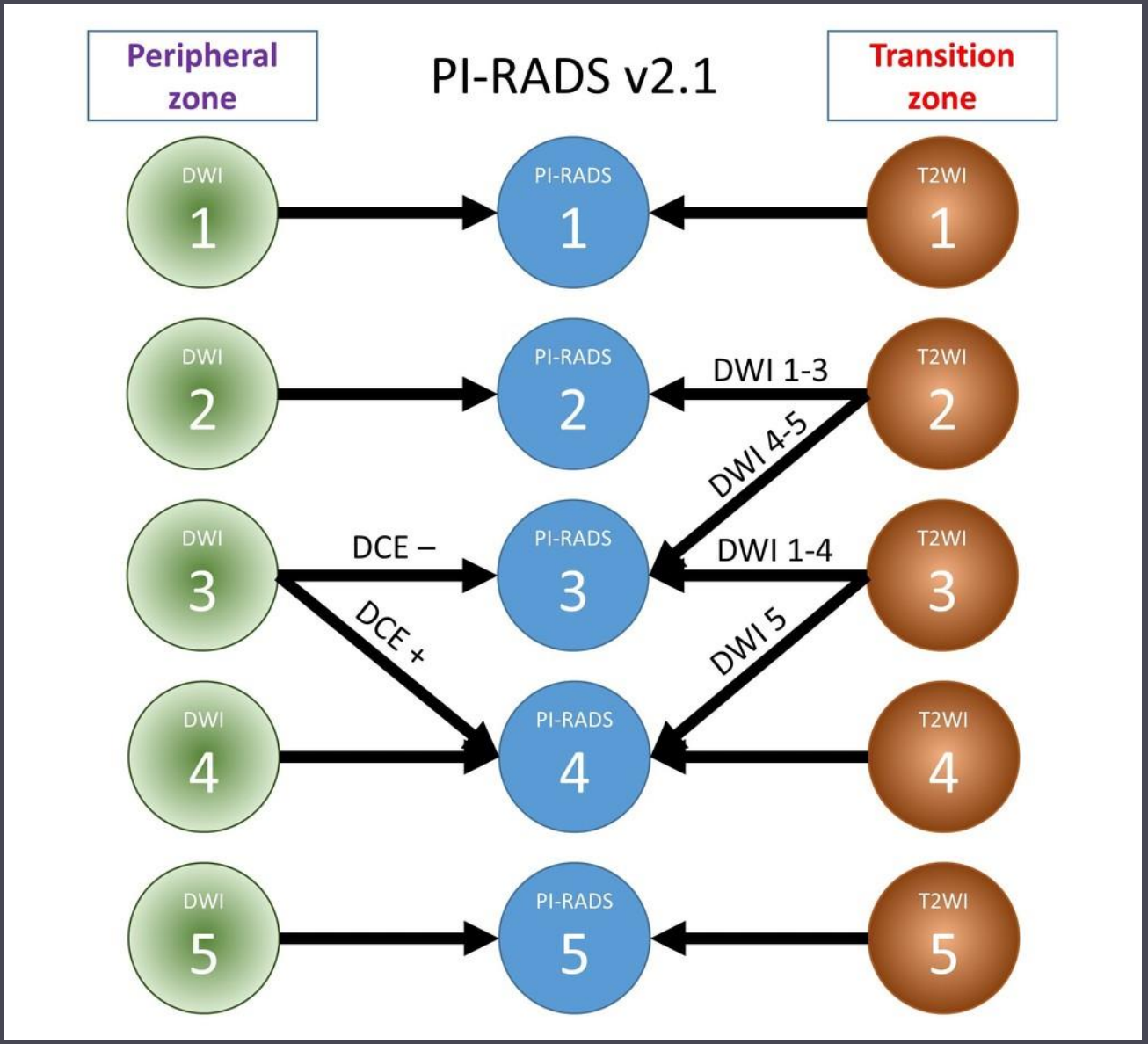
mp-RM

Linee Guida

PI-RADS v2.1
Categorie di valutazione

***Scala a 5 punti** basata su Mp-MRI (combinazione di tutte le sequenze) per valutare la probabilità della presenza di **Ca clinicamente significativo** in una particolare zona*

P1	***Altamente improbabile che ci sia cancro clinicamente significativo***	***Rischio molto basso***
P2	***Improbabile che ci sia cancro clinicamente significativo***	***Rischio basso***
P3	***Incerta e/o equivoca la presenza di cancro clinicamente significativo)***	***Rischio incerto***
P4	***Probabile che ci sia cancro clinicamente significativo***	***Rischio medio-elevato***
P5	***Molto probabile che ci sia cancro clinicamente significativo***	***Rischio elevato***


Peripheral zone
PI-RADS v2.1
Transition zone
DWI 1
PI-RADS 1
T2WI 1
DWI 2
PI-RADS 2
T2WI 2
DWI 1-3
DWI 4-5
DWI 3
DCE –
PI-RADS 3
DWI 1-4
T2WI 3
DCE +
DWI 5
DWI 4
PI-RADS 4
T2WI 4
DWI 5
PI-RADS 5
T2WI 5

› Cochrane Database Syst Rev. 2019 Apr 25;4(4):CD012663. doi: 10.1002/14651858.CD012663.pub2.

Prostate MRI, with or without MRI–targeted biopsy, and systematic biopsy for detecting prostate cancer

Frank-Jan H Drost [1], Daniël F Osses, Daan Nieboer, Ewout W Steyerberg, Chris H Bangma, Monique J Roobol, Ivo G Schoots

Cochrane meta-analysis: compared MRI to template biopsies (≥ 20 cores) in biopsy-naive and repeat-biopsy settings

ISUP grade ≥ 2 cancers: pooled sensitivity of **0.91** (95% CI: 0.83–0.95) and a pooled specificity of 0.37 (95% CI: 0.29–0.46)

ISUP grade ≥ 3 cancers: pooled sensitivity and specificity of **0.95** (95% CI: 0.87–0.99) and 0.35 (95% CI: 0.26–0.46), respectively.

ISUP grade 1 cancers: pooled sensitivity of 0.70 (95% CI: 0.59–0.80) and a pooled specificity of 0.27 (95% CI: 0.19–0.37)

mp-RM

SCORE PIRADS

Analisi delle lesioni

Sequenza dominante

- **DWI per PZ**
- **T2W per TZ**

Sequenze complementari

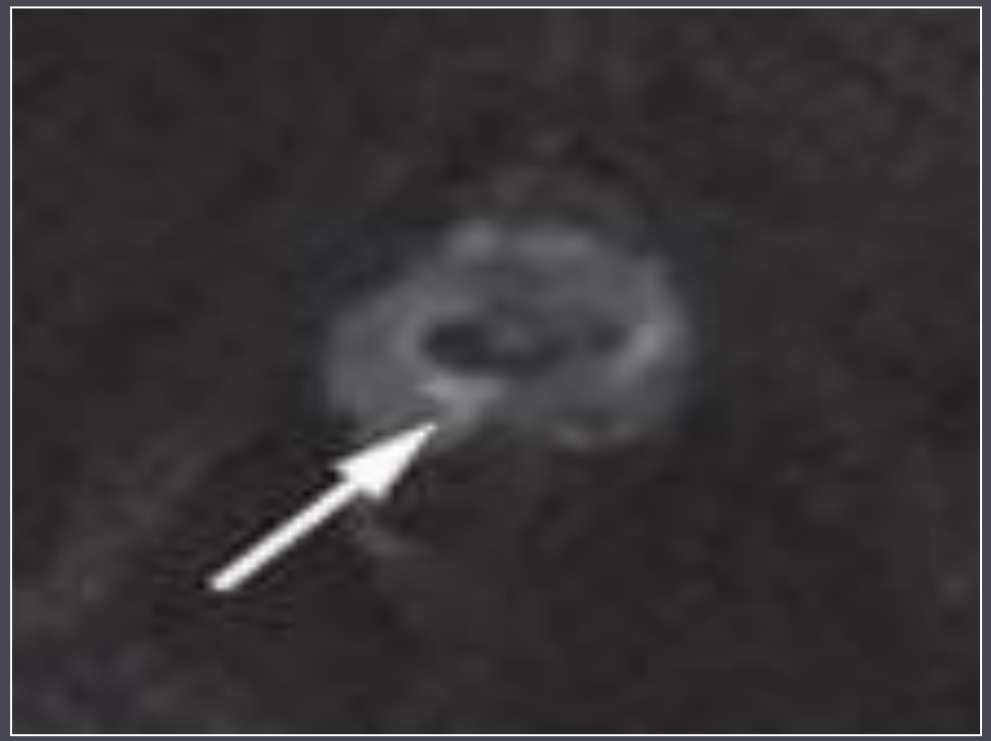
↓

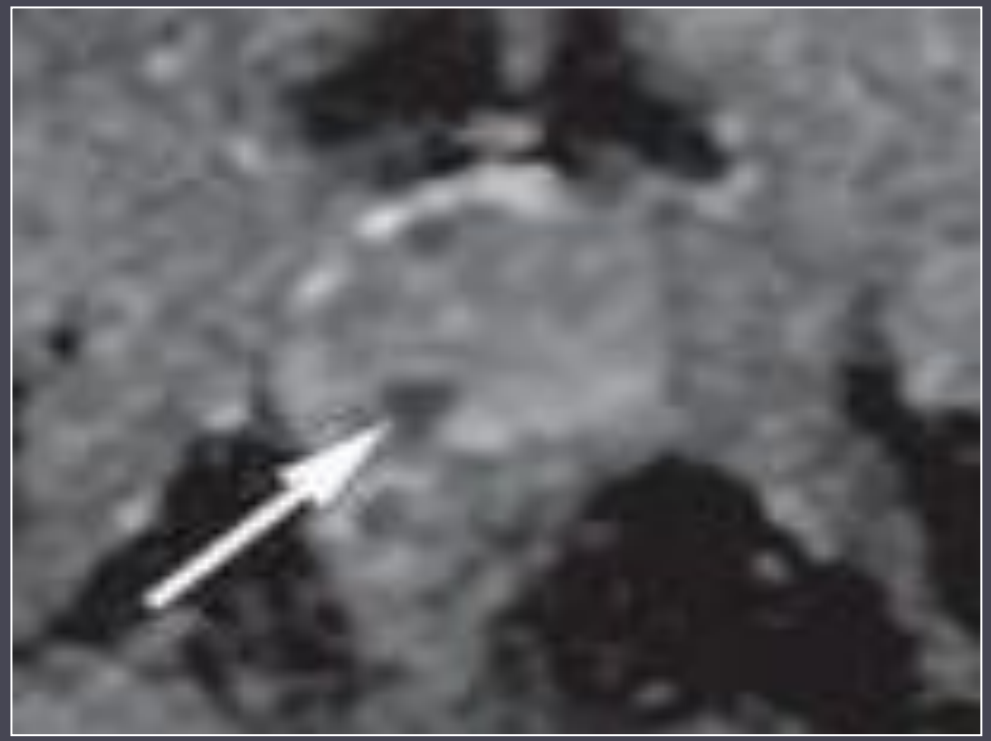
Score PI-RADS

Analisi delle lesioni

Zona Periferica

Sequenza dominante :DWI e Mappe ADC





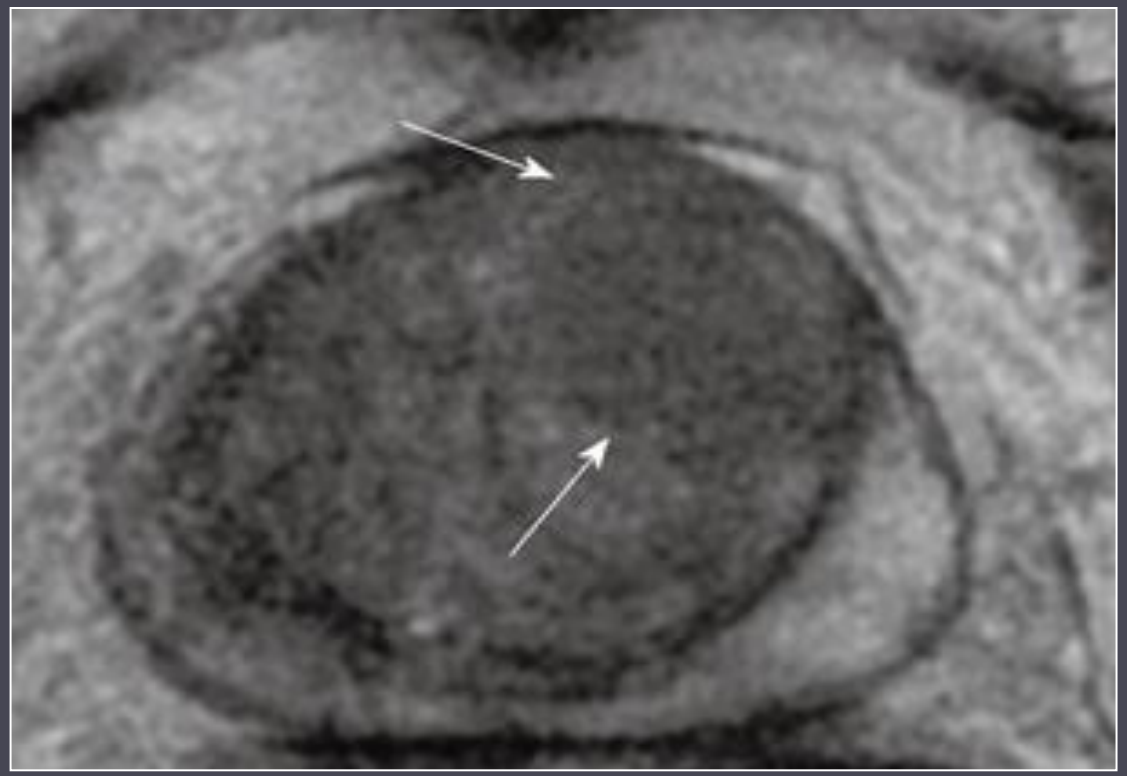
mp-RM

Score PIRADS

Analisi delle lesioni

Zona di Transizione

Sequenza dominante : T2W



mp-RM

SCORE PIRADS

Questioni “under debate”

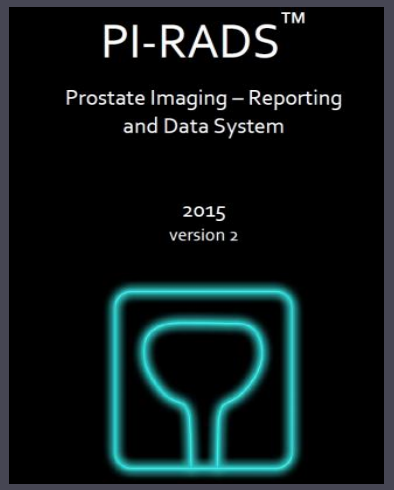
3T vs 1,5 T

Bobina endorettale vs phased array

Criticità Pi-RADS

Rm biparametrica (NO mdc) vs mp-RM

Gestione Pi-RADS 3



3T vs 1,5 T... quale bobina ??

1,5 T

16-32 canali

cancer. At 3T without use of an ERC, image quality can be comparable with that obtained at 1.5T with an ERC, although direct comparison of both strategies for cancer detection and/or staging is lacking. Importantly, there are many technical factors other than the use of an ERC that influence SNR (e.g., receiver bandwidth, coil design, efficiency of the RF chain), and some contemporary 1.5T scanners that employ a relatively high number of external phased array coil elements and RF channels (e.g., 16 or more) may be capable of achieving adequate SNR in many patients without an ERC.

Credible satisfactory results have been obtained at both 1.5T and 3T without the use of an ERC. Taking these factors into consideration as well as the variability of MRI equipment available in clinical use, the PI-RADS Steering Committee recommends that supervising radiologists strive to optimize imaging protocols in order to obtain the best and most consistent image quality possible with the MRI scanner used. However, cost, availability, patient preference, and other considerations cannot be ignored.

RMN biparametrica vs multiparametrica

PI-RADS v2
1–5 point dominant score:
• For peripheral zone, DWI is dominant
• For transition zone, T2W is dominant
Secondary role for DCE (positive or negative)
For DWI: ADC and high b-value images (b value >1400) are mandatory
39-Sector map
MRSI is not included
Size (>15 mm) is used for T2W + DWI to separate PI-RADS scores 4 and 5

Accuratezza diagnostica:

- *542 pts, 89.1% bpMRI vs 87.2% mpMRI*

  Kuhl CK et al, Radiology 2017

- *82 pts biopsy-naïve, AUC bpMRI 0.91-0.93*

  Stanzione A et al, Eur J Radiol, 2016

- *41 pts, sensibilità 97.6% bp=mp MRI*

  Scialpi M et al, Anticancer Res, 2017

Vantaggi della DCE

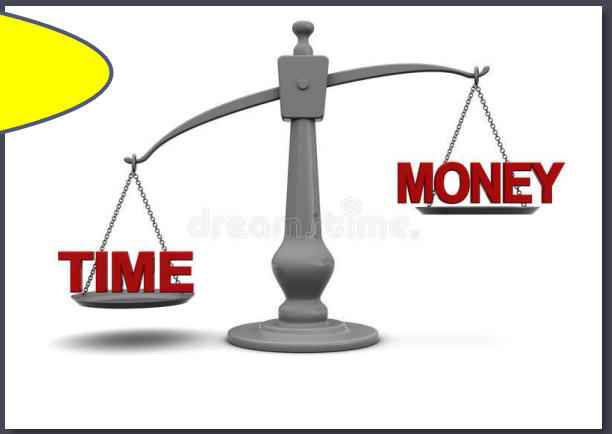
- ***Aumento della proba***
  - ***15,7% (PIRADS 2)***
  - ***16% (PIRADS 3)***
  - ***9,2% (PIRADS 4)***

Rosenkrantz AB et al. Radiology, 2017

- ***Upgrade di lesioni della zona periferica***
  - ***PIRADS 3 → 4 con DCE+ (~ 30%)***

Greer MD et al. Radiology, 2017

Valore aggiunto nel limitare i PI-RADS3



MDC ??

Criticità PIRADS

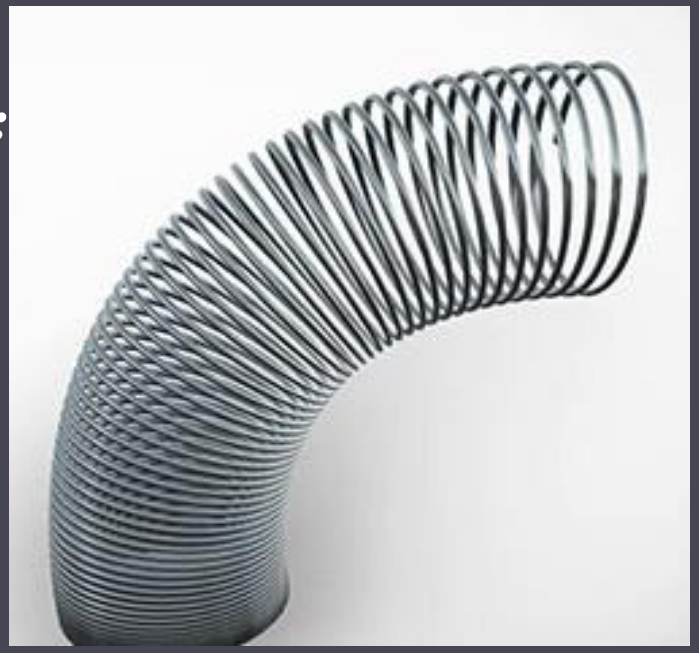
Pi-RADS v2: rigidità vs flessibilità

Utilizzando il PI-RADS v2 in maniera matematica si incorre spesso in errori:

- ***falsi positivi:*** *BPH*, ***prostatite,*** *esiti*
- ***falsi negativi***

Correlazione con:

- ***dati clinico-laboratoristici (es. PSA Density..)***
- ***Possibilità di pitfalls***



Gestione PI-RADS 3

biopsia o no???

- Prevalenza cancro ISUP ≥ 2 nella categoria PI-RADS 3 = 20%
- Prevalenza di cancro ISUP ≥ 3 nei PI-RADS 3 da bpMRI = 0%
- Prevalenza di assegnazioni PI-RADS 3 ideale < 10% (per prevalenza di malattia di circa il 40%)

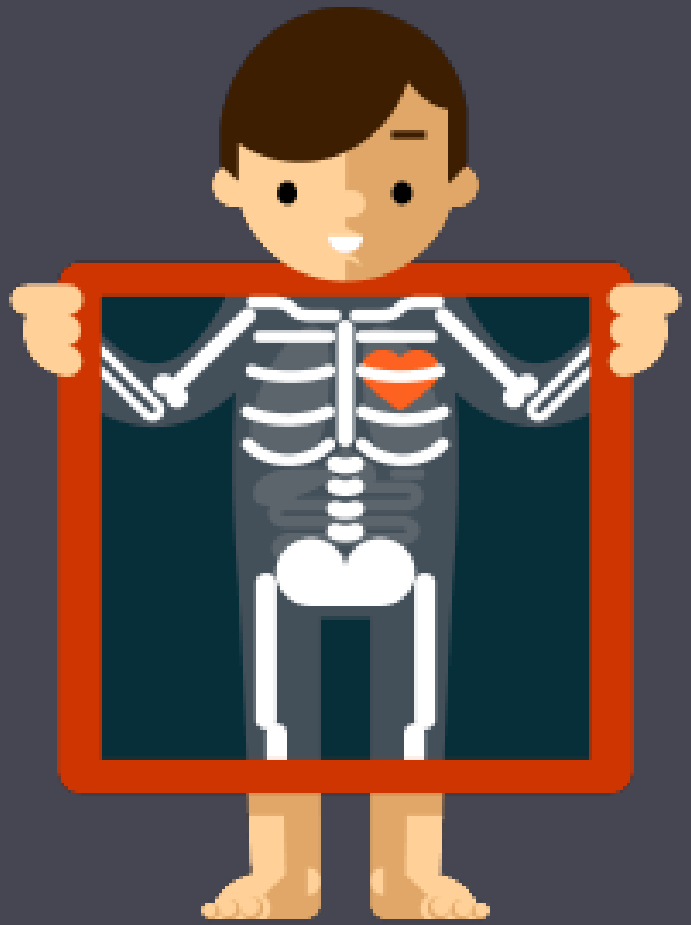
Schoots IG et al., Transl Androl Urol 2018;7:70-82
Junker D et al., World J Radiol 2019;37:691-699
Schoots IG et al., AJR 2021;216:1-17

*Alcuni autori suggeriscono che il **PSA Density** ed altre analisi PSA-correlate (tipo la callicreina 4 [4K] score ed il Prostate Health Index [PHI]) possono essere utili nel **decision making***

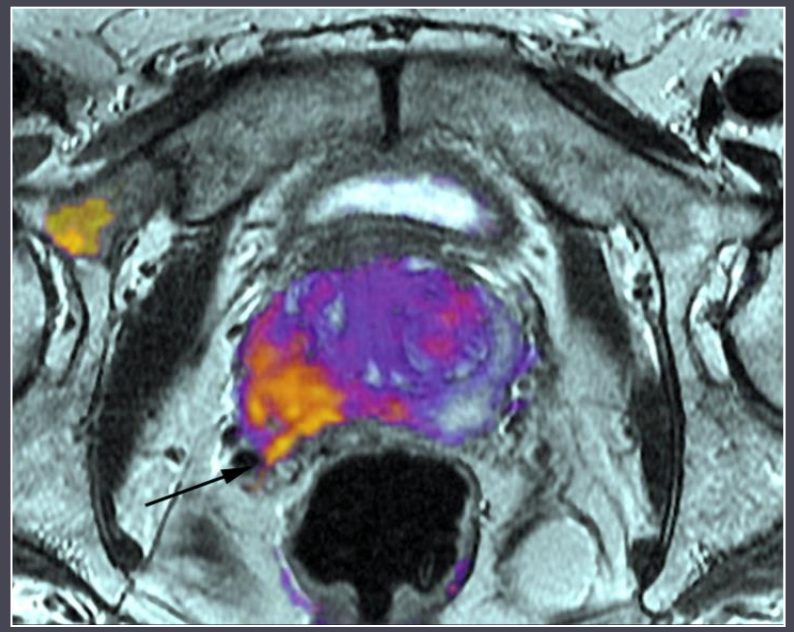
*Alcuni evitano la biopsia in caso di pz **anziani** con **co-morbidità**, specie con basso PSA density, continuando il semplice monitoraggio del PSA*

Esperienza Radiologo ⟷ ***Fiducia Urologo***

Indicazioni mp-RM



Prostate cancer DETECTION



mp-MRI vs TRUS biopsy

THE LANCET

Volume 389, No. 10071, p815–822, 25 February 2017

PROMIS
Prostate MRI Imaging Study

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

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

Test attribute	TRUS-biopsy	MP-MRI	Odds ratio* [95% CI]	*p-value*
Sensitivity	**48%**	**93%**	0.06 [0.02-0.12]	*p<0.0001*
Specificity	**96%**	**41%**	0.02 [0.003-0.05]	*p<0.0001*
PPV	**90%**	**51%**	8.2 [4.7-14.3]	*p<0.0001*
NPV	**74%**	**89%**	0.34 [0.21-0.55]	*p<0.0001*

*For **clinically significant cancer:***

→ *MP-MRI was more sensitive (93%, 95% CI 88–96%) than TRUS-biopsy (48%, 42–55%; p<0·0001)*

TRUS-biopsies directed by MP-MRI findings:

→ *up to 18% more cases of clinically significant cancer might be detected*

The NEW ENGLAND JOURNAL of MEDICINE

2018

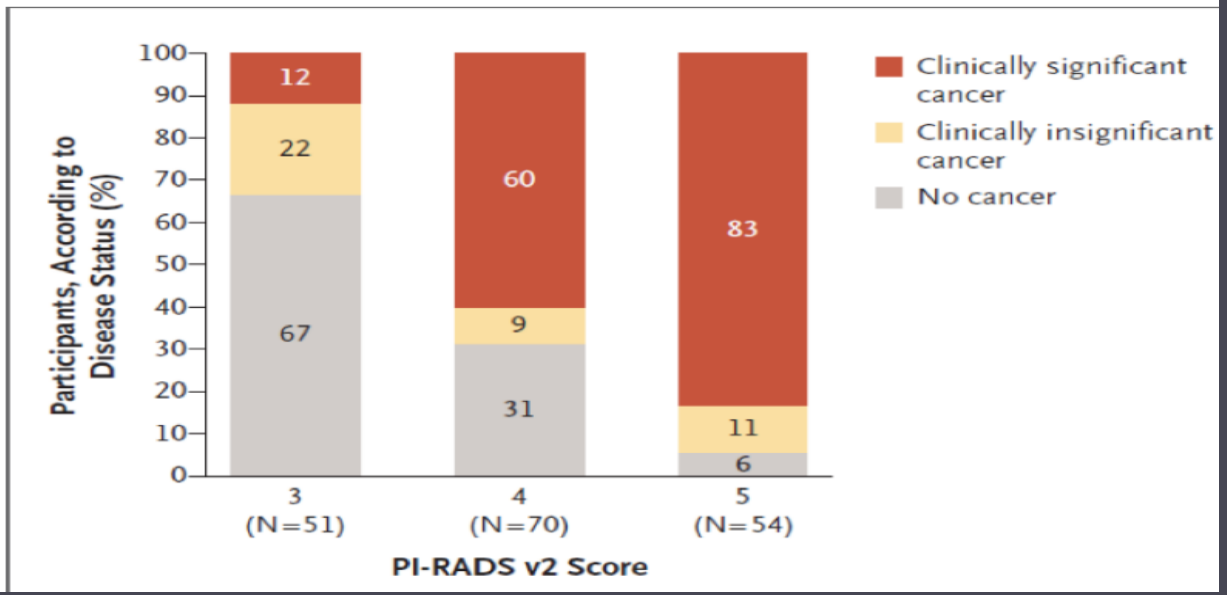
MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

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,

PRECISION trial

Biopsy-naïve men with elevated PSA randomized to:
- *MR-targeted biopsy (if 'negative', no biopsy)*
- *TRUS-biopsy*

Figure 1: Percentages of Men with Clinically Significant, Clinically Insignificant, and No Cancer



mp-RM prima della biopsia e biopsia target RM-guidata

Risultati superiori rispetto al protocollo standard (TRUS-Biopsy)

AIOM

Linee guida

CARCINOMA DELLA PROSTATA

European Association of Urology

Guidelines on Prostate Cancer

NCCN National Comprehensive Cancer Network®

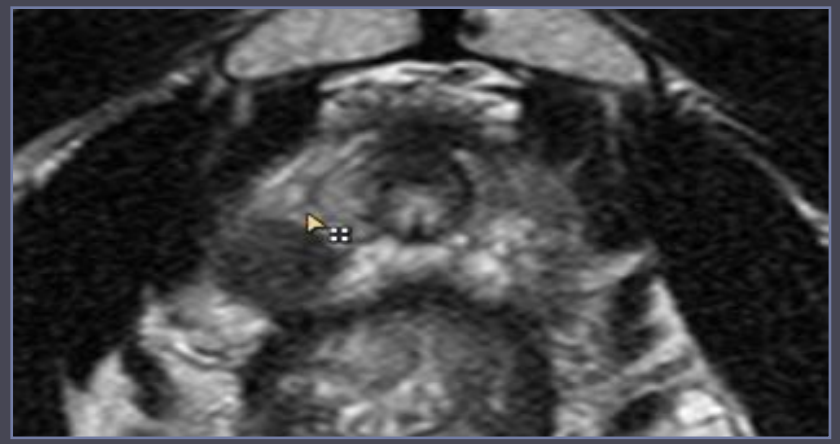
NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®)

Prostate Cancer

Linee Guida

DETECTION - MRI

LINEE GUIDA
ESUR- EAU 2022
NCCN 2022



Recommendations for all patients	Strength rating
Do not use magnetic resonance imaging (MRI) as an initial screening tool.	Strong
Adhere to PI-RADS guidelines for MRI acquisition and interpretation and evaluate MRI results in multidisciplinary meetings with pathological feedback.	Strong

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

Recommendations for biopsy-naïve patients	Strength rating
Perform MRI before prostate biopsy.	Strong
When MRI is positive (i.e. PI-RADS ≥ 3), combine targeted and systematic biopsy.	Strong
When MRI is negative (i.e., PI-RADS ≤ 2), and clinical suspicion of PCa is low (e.g. PSA density < 0.15 ng/mL), omit biopsy based on shared decision-making with the patient.	Weak

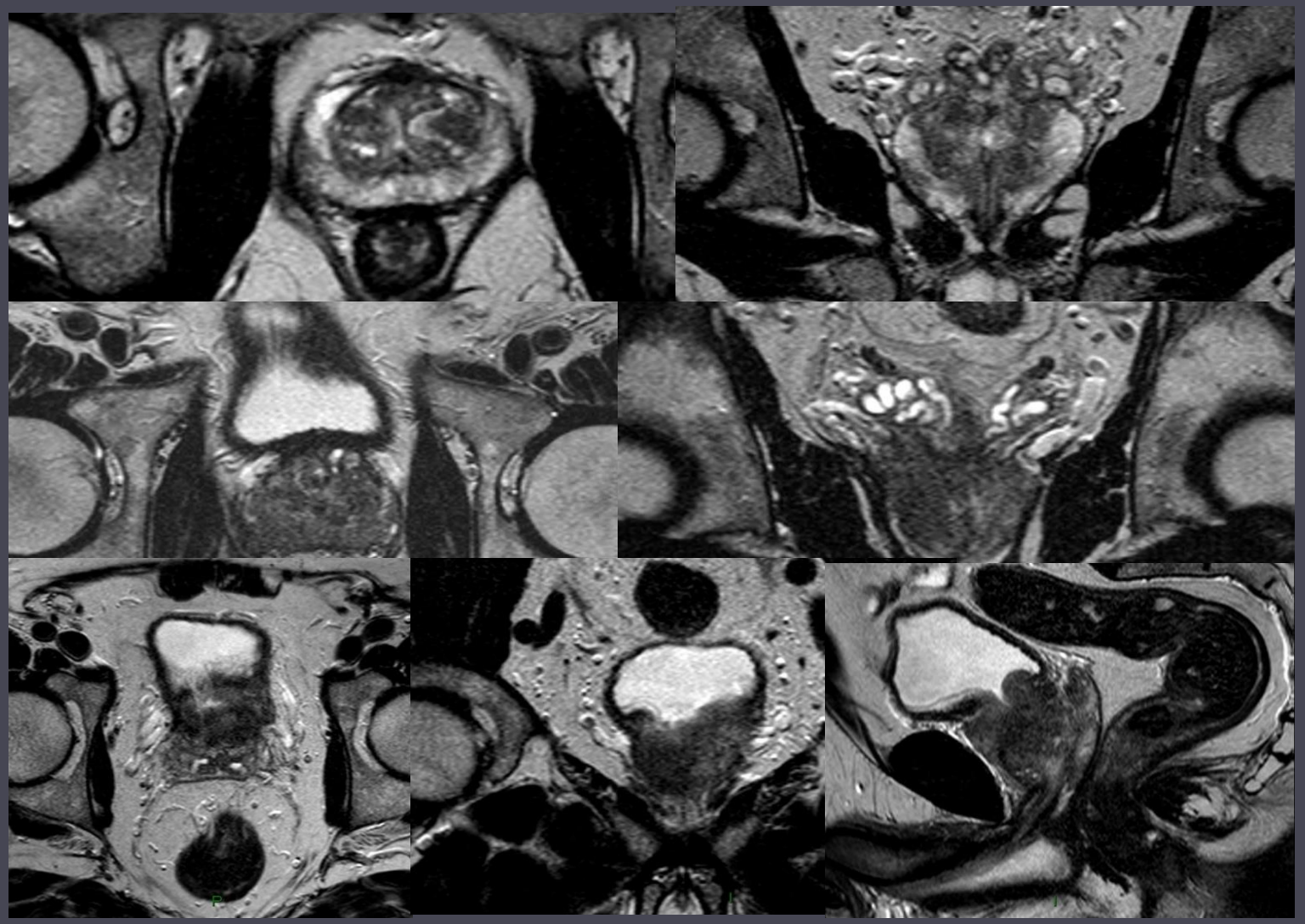
Upgrade rispetto alle linee guida 2019 (Weak)

Indicazioni : STAGING LOCOREGIONALE

Infiltrazione capsulare

Infiltrazione delle vescicole seminali

Estensione agli organi adiacenti



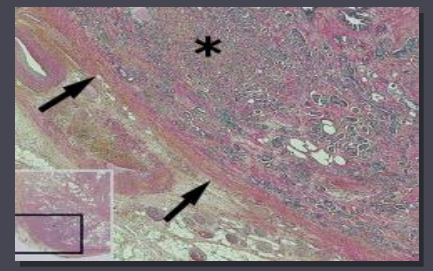
Infiltrazione capsulare ??

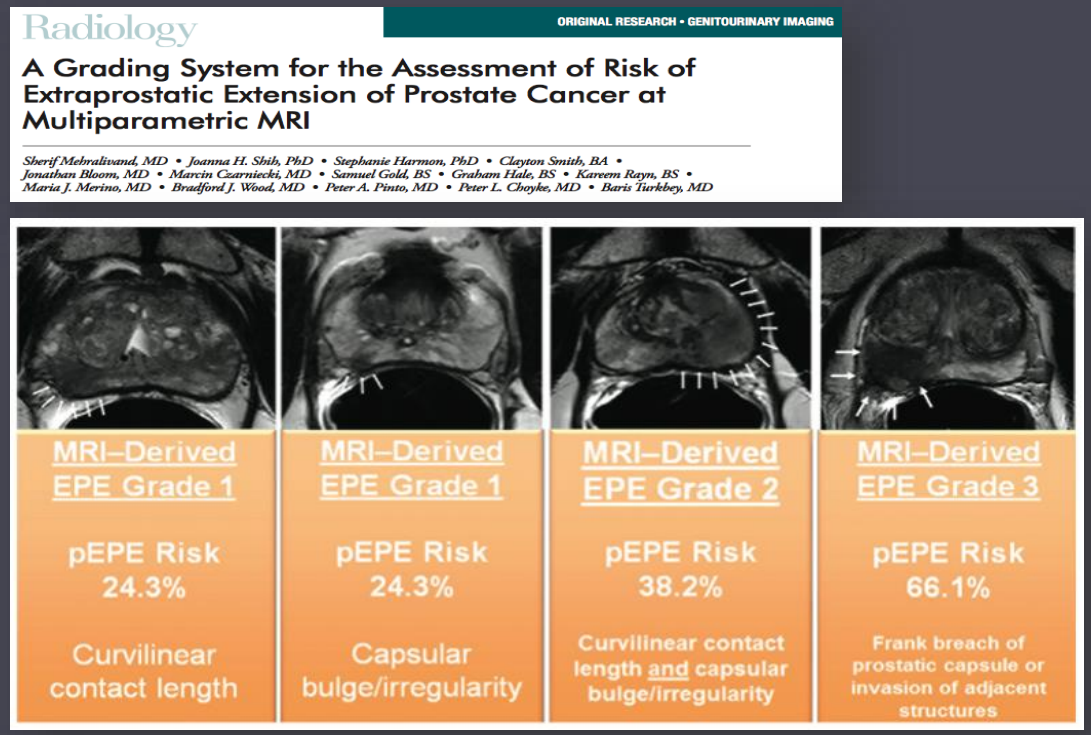
Accuratezza ECE (T3a)

Sensitivity 0.57 (95% CI 0.49-0.65)

Specificity 0.91 (95% CI 0.88-0.93)

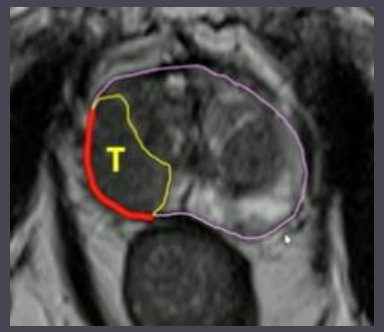
- **Limite nella valutazione dello sconfinamento extra-capsulare microscopico**



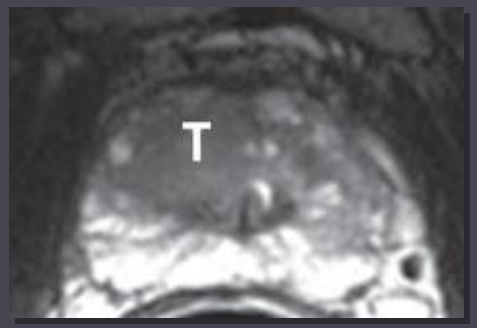


- **Segni secondari**

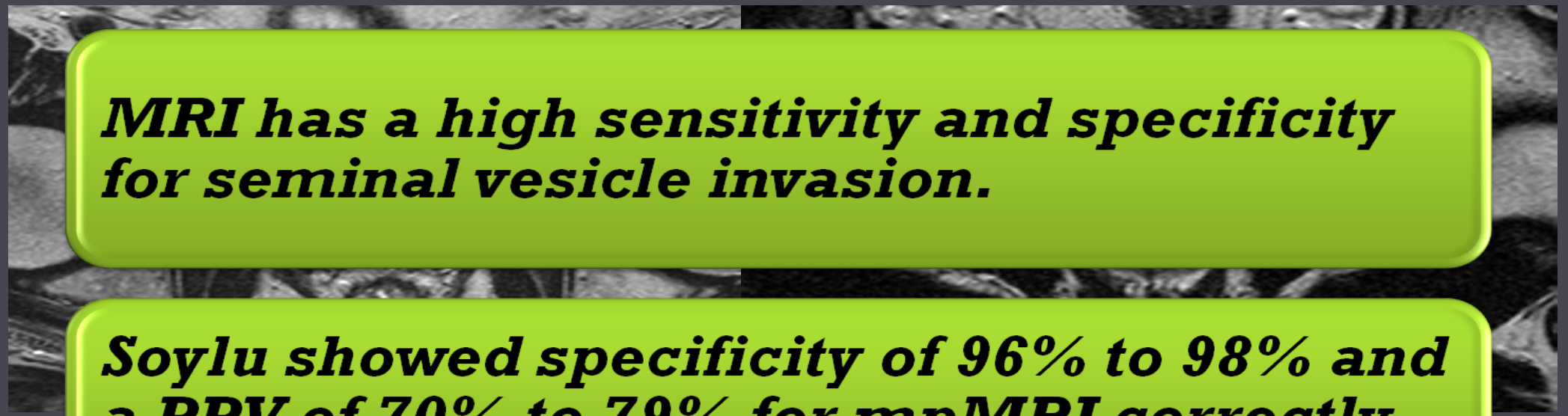
Ampio contatto con la capsula (>1 cm)



Nessun contatto con la capsula



Infiltrazione Vescichette seminali ??



MRI has a high sensitivity and specificity for seminal vesicle invasion.

Soylu showed specificity of 96% to 98% and a PPV of 70% to 79% for mpMRI correctly identified seminal vesicle invasion

- Soylu FN, et al: Seminal vesicle invasion in prostate cancer: evaluation by using multiparametric endorectal MR imaging. Radiology 2013; 267: 797

La RNM può cambiare I piani del chirurgo?

*The surgical plan was **changed in 26%** of the patients, to either a more aggressive nerve sparing approach (57%) or a wider margin of resection (43%). In patients with intermediate and high risk features, a change was made in 83% and 89%, respectively*

5.3.5 ***Guidelines for staging of prostate cancer***

Any risk group staging	**LE**	**Strength rating**
Use pre-biopsy mpMRI for staging information.	2a	Weak

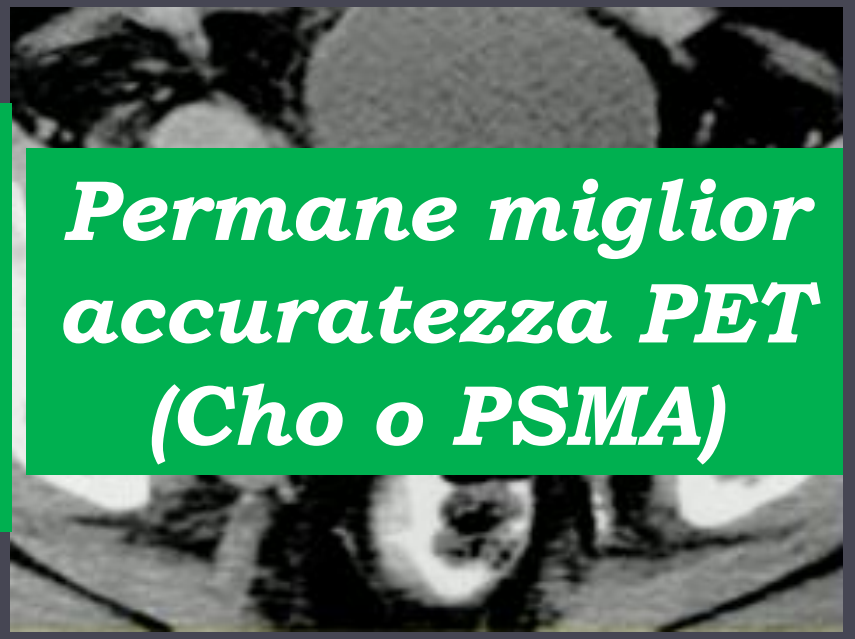
STAGING

– Parametro N -

Dimensioni e morfologia del linfonodo:

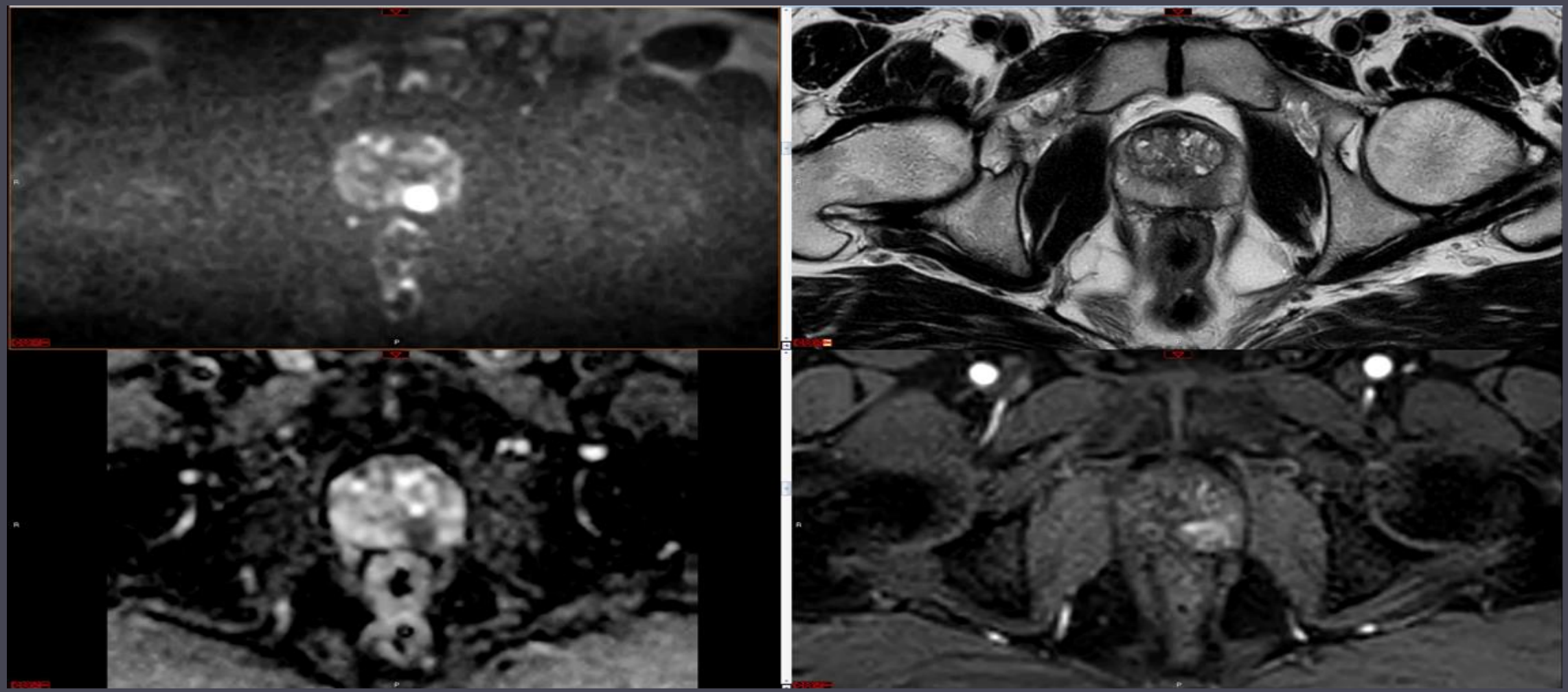
Linfonodo sospetto se:
- Ovale > 10 mm
- Rotondo > 8 mm

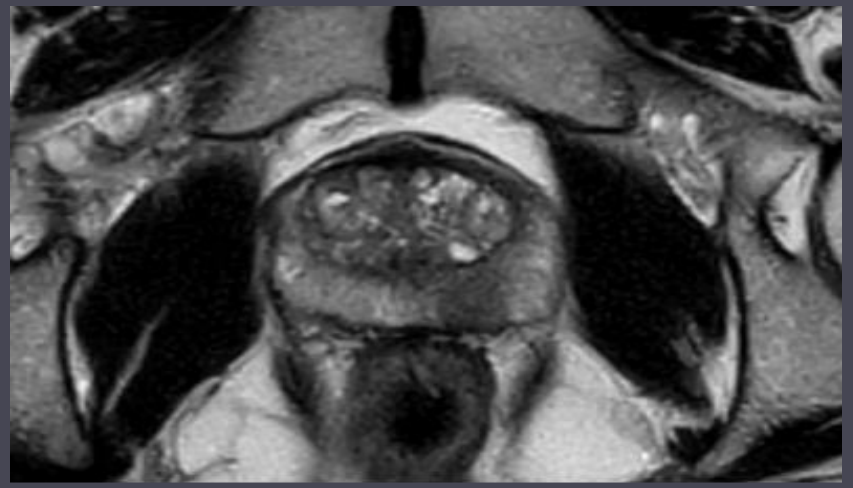
Sensibilità e specificità analoghe alla TC (70-75%)

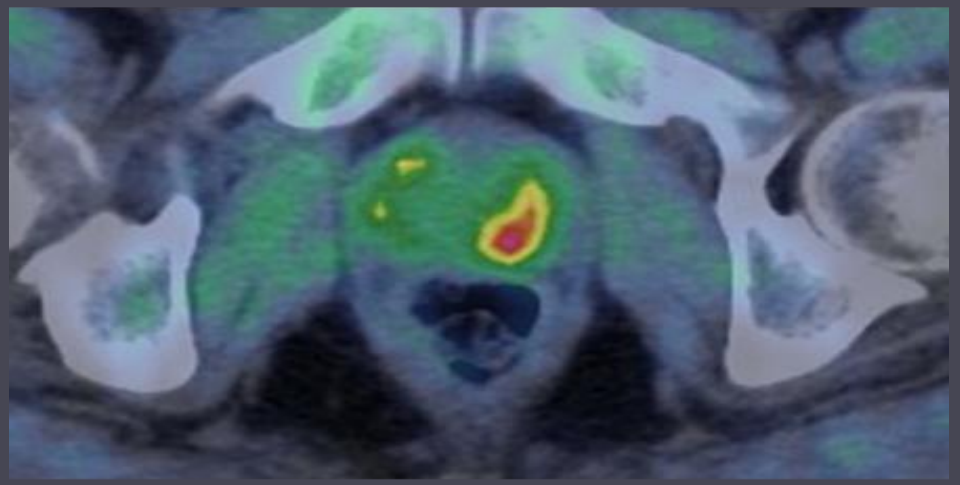


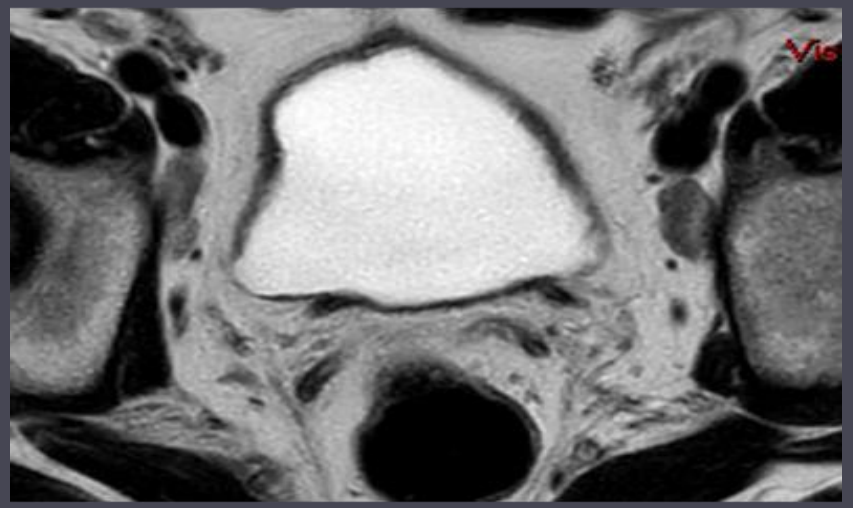
Permane miglior accuratezza PET (Cho o PSMA)

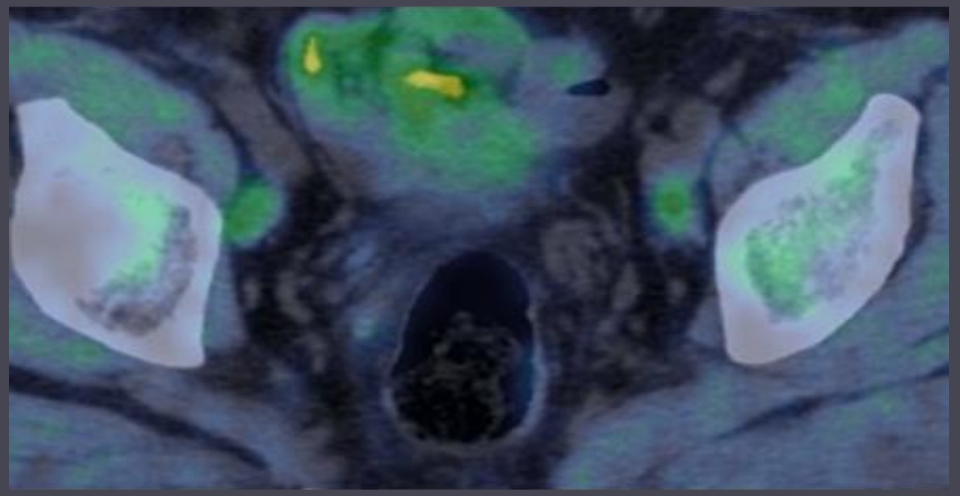
RMmp di stadiazione in pz di 68 anni con lesione della ZP, con PSA di 9ng/ml











PET TC: oltre alla lesione, linfonodi in sede otturatoria, iliaca (interna ed esterna). Ulteriori linfonodi sono presenti in sede presacrale e para-aortica
Pz avviato a radio-ormonoterapia

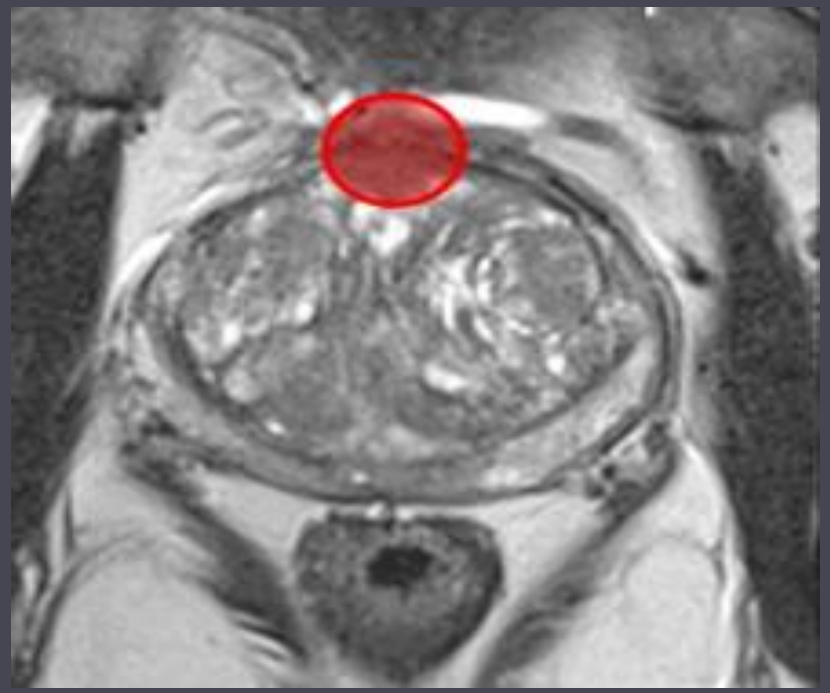
Indicazioni : FOLLOW-UP

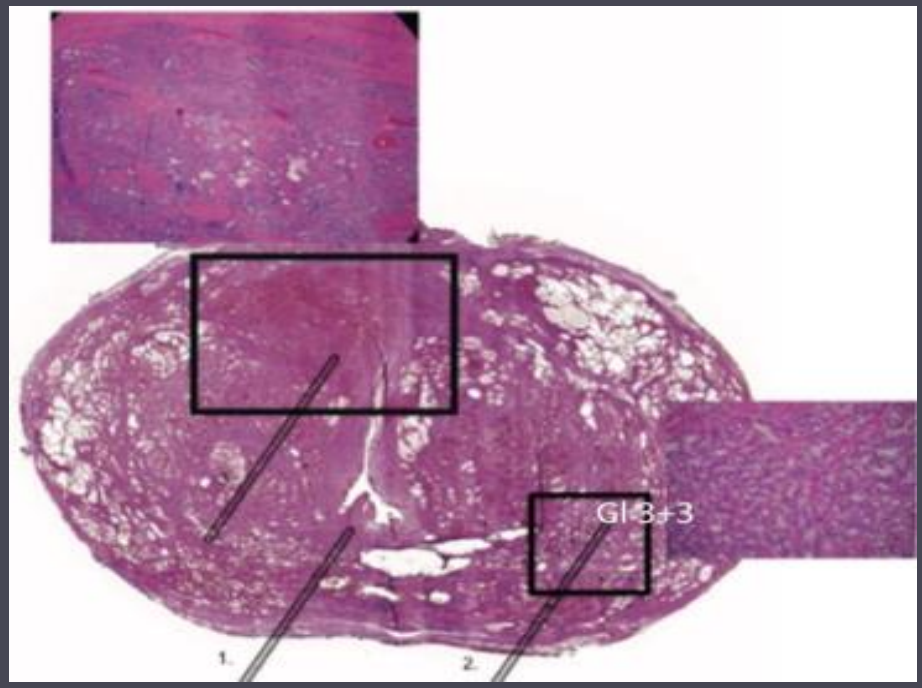
Sorveglianza attiva

Recidiva dopo prostatectomia radicale

Recidiva dopo RT

Sorveglianza attiva



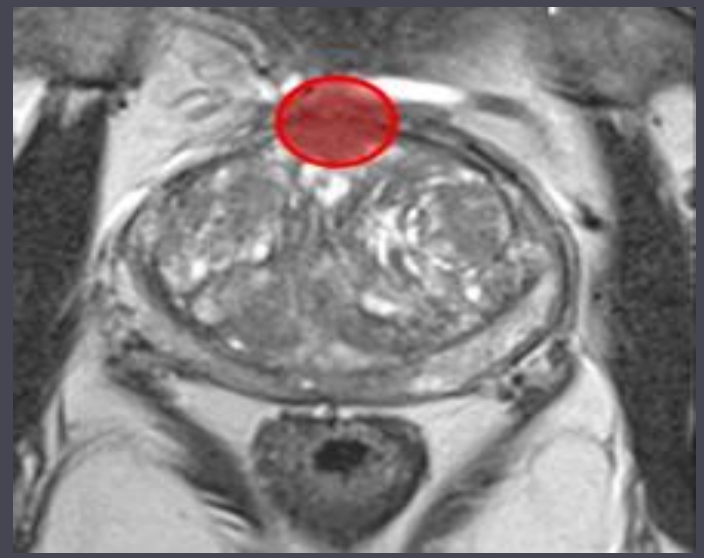


SA: rischio di undersampling !!

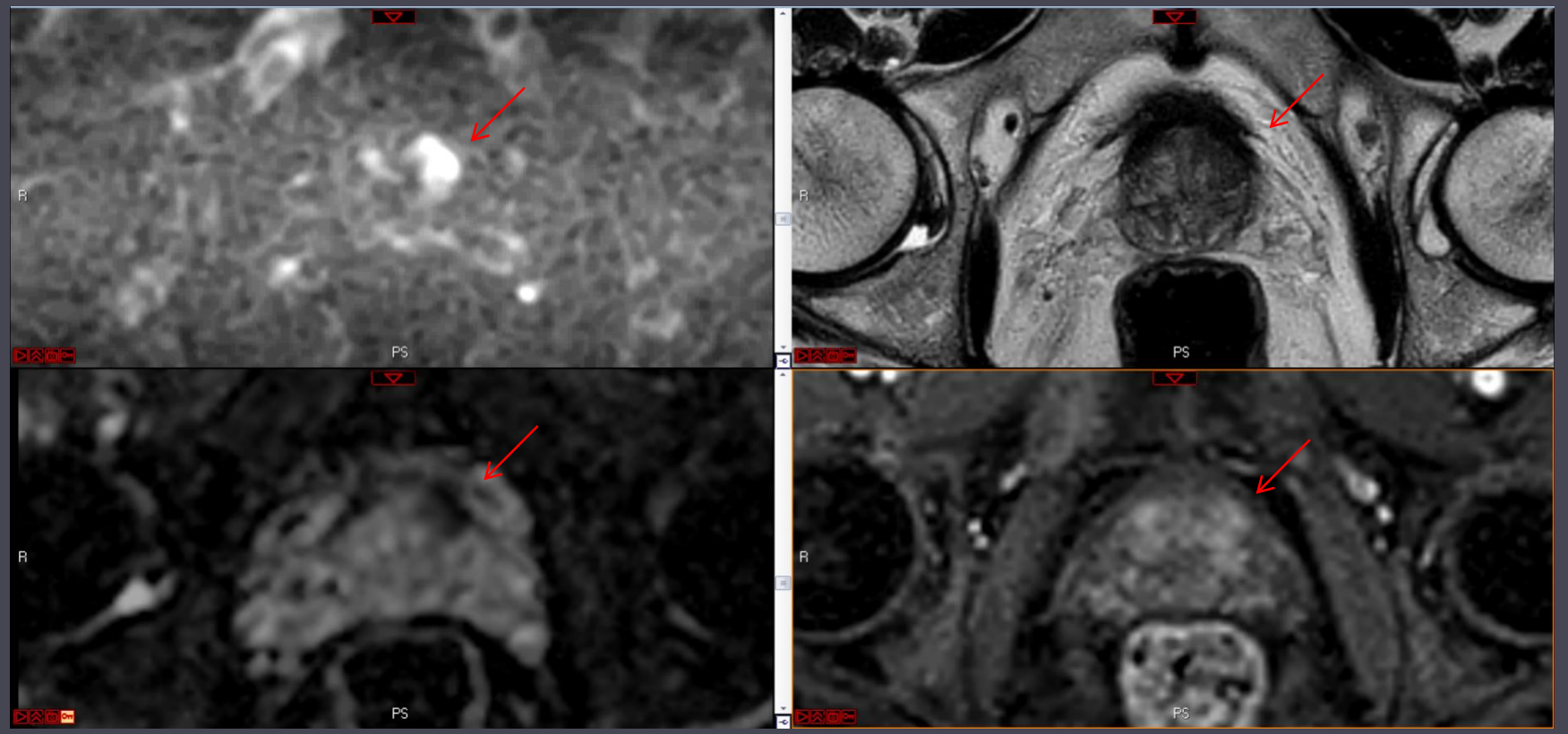
Biopsia random: 1 pos. al 1/3 medio sn (Core 10%) Gleason 3+3
Biospia fusion dopo RM: base anteriore Gleason 4+3

Sorveglianza attiva

mpRM in SA:
IL PROBLEMA DEL MISMATCH !!



- ***di sede: reperto RM positivo in sede diversa dalla positività bioptica***
- ***multiparametrico: lesione con score Pi-RADS elevato***



PAZIENTE IN S.A. PER GLEASON 3+3 DEL LOBO DX IN 1 PRELIEVO BIOPTICO; ALLA RM SI EVIDENZIA LESIONE PI-RADS 5 IN SEDE APICALE ANTERIORE AL LOBO SN CHE DA ZT impegna lo AFS

MISMATCH DI SEDE E DI SCORE MULTIPARAMETRICO

Sorveglianza attiva

	Year	1					2				3		4		5		6		7	
	Month	*0*	*3*	*6*	*9*	*12*	*15*	*18*	*21*	*24*	*30*	*36*	*42*	*48*	*54*	*60*	*66*	*72*	*78*	*84*
	Evaluation	X		X		X		X		X		X		X		X		X		X
Side study	*MRI + targeted biopsies***		*X**			*X*								*X*						*X*

* MR
bio

** If
is t
cur

Ruolo della mpRM prima della biopsia confirmatoria

(p = 0.01, OR 6.53). ***Conclusion:*** A visible lesion on mp-MRI strongly predicts significant PCa in patients eligible for AS according to PRIAS criteria, based on upstaging and unfavorable disease. We believe that mp-MRI is an important tool and should be added to clinical selection criteria for AS.

PRIAS

Studio multicentrico più importante.

Definisce ***upgrade*** *nelle sole lesioni che presentano* ***Gleason Score >6.***

Sorveglianza attiva

European Association of Urology

2022

Recommendations		Strength rating
Low-risk disease		
Active surveillance (AS)	*Selection of patients*	
	Offer AS to patients with a life expectancy > 10 years and low-risk disease.	Strong
	Patients with intraductal and cribriform histology on biopsy should be excluded from AS.	Strong
	Perform an MRI before a confirmatory biopsy if no MRI has been performed before the initial biopsy.	Strong

L'associazione con biopsie mirate risulta di grande interesse nella:

1.Riduzione della mis-classificazione alla prima diagnosi;

2.Riduzione di biopsie non necessarie (target/random);

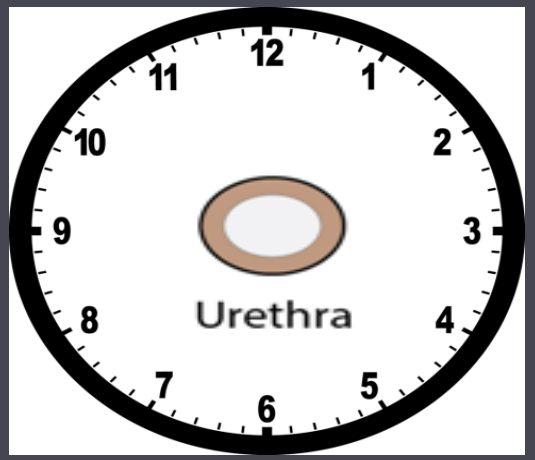
3.Ottimizzare il monitoraggio dei pazienti in SA.

Recidiva dopo prostatectomia radicale

Mp-RM può individuare piccole recidive locali dopo protatectomia (+/-RT) in pz con lieve rialzo del PSA

***DCE**: sequenza dominante*

Mapping anatomico (clock uretrale) e volumetria recidiva pre-RT



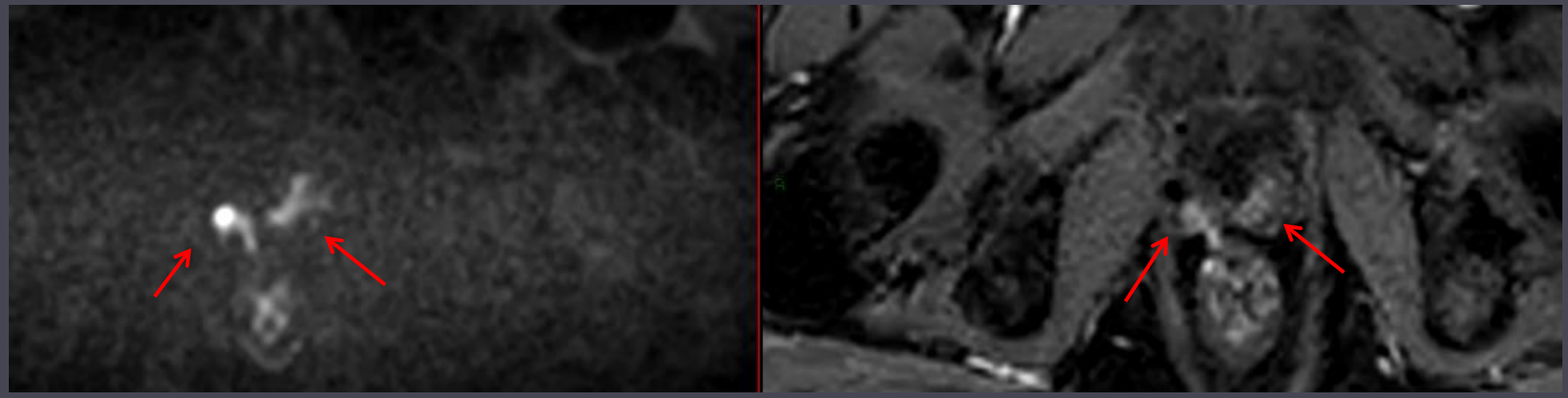
Recidiva dopo prostatectomia radicale

For lesion of about 1 cm

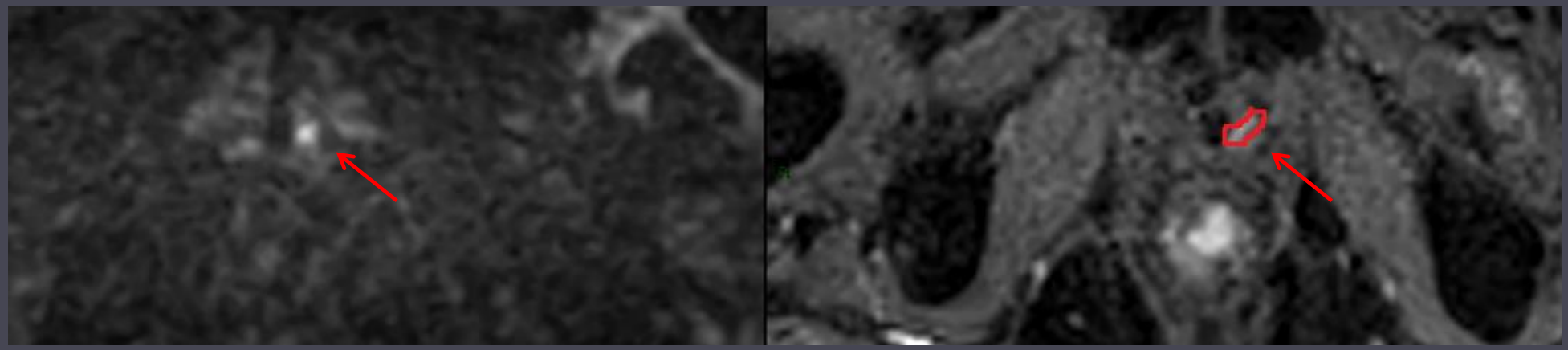
Sensitivity, specificity, PPV and NPV was 91%,45%,85% and 60% *Linder BJ et Al. Can J Urol 2014*

Dopo *prostatectomia radicale**:***

- *PSA non azzerato dopo prostatectomia (possibile residuo ghiandolare)*
- ***PSA tra 0.2 ng/ml e 1.0 ng/ml***
- ***> 2.0 ng/ml*** *c'è sospetto di recidiva a distanza o malattia sistemica* **--> *PET-CT***



PAZIENTE CON RECIDIVA SEMICIRCONFERENZIALE POSTERIORE SOTTOPOSTO A RADIOTERAPIA STEREOTASSICA



AL CONTROLLO POST TERAPIA RIMANE PICCOLO RESIDUO VITALE A SN, A ORE 4 DEL CLOCK URETRALE

Recidiva dopo prostatectomia radicale

Linee Guida AIRO

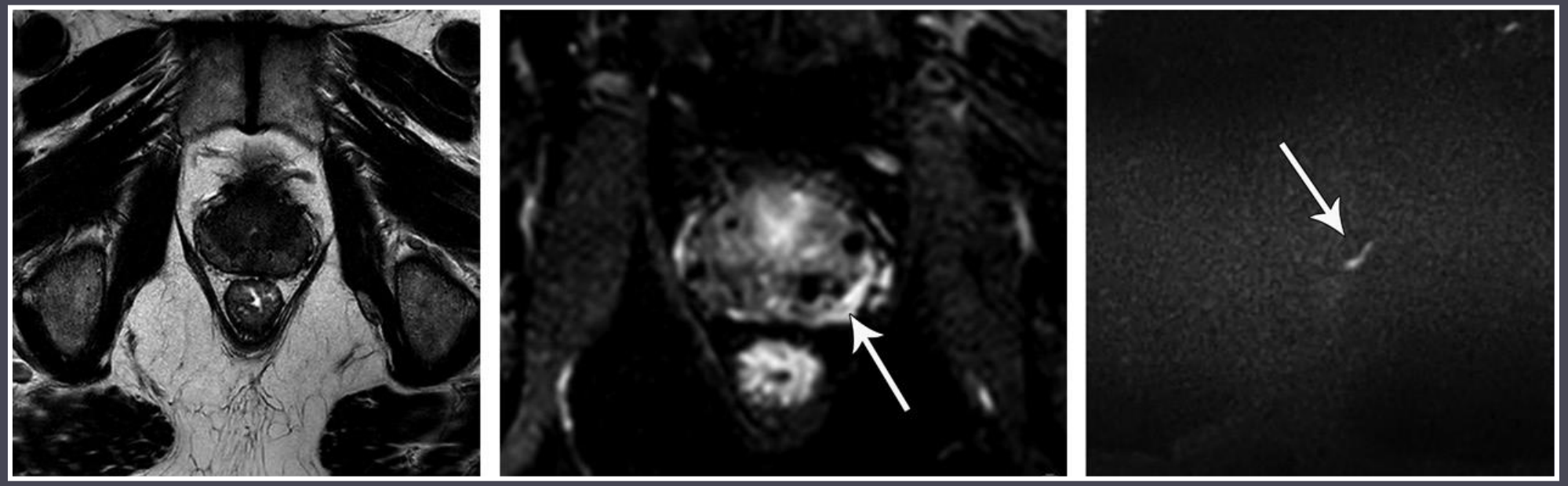
.. la mp-MRI indicata nella ricerca di recidive in loggia prostatica (sens. 88%, spec. 100%, VPP 100%, VPN 88% e accuratezza diagnostica del 94% , senza risentire dei valori del PSA e delle dimensioni delle recidive (diametro 3.5-8 mm)

European Association of Urology

.. la mp-MRI non menzionata a scapito della PET con PSMA anche per valori bassi PSA ***< 2.0 ng/ml***

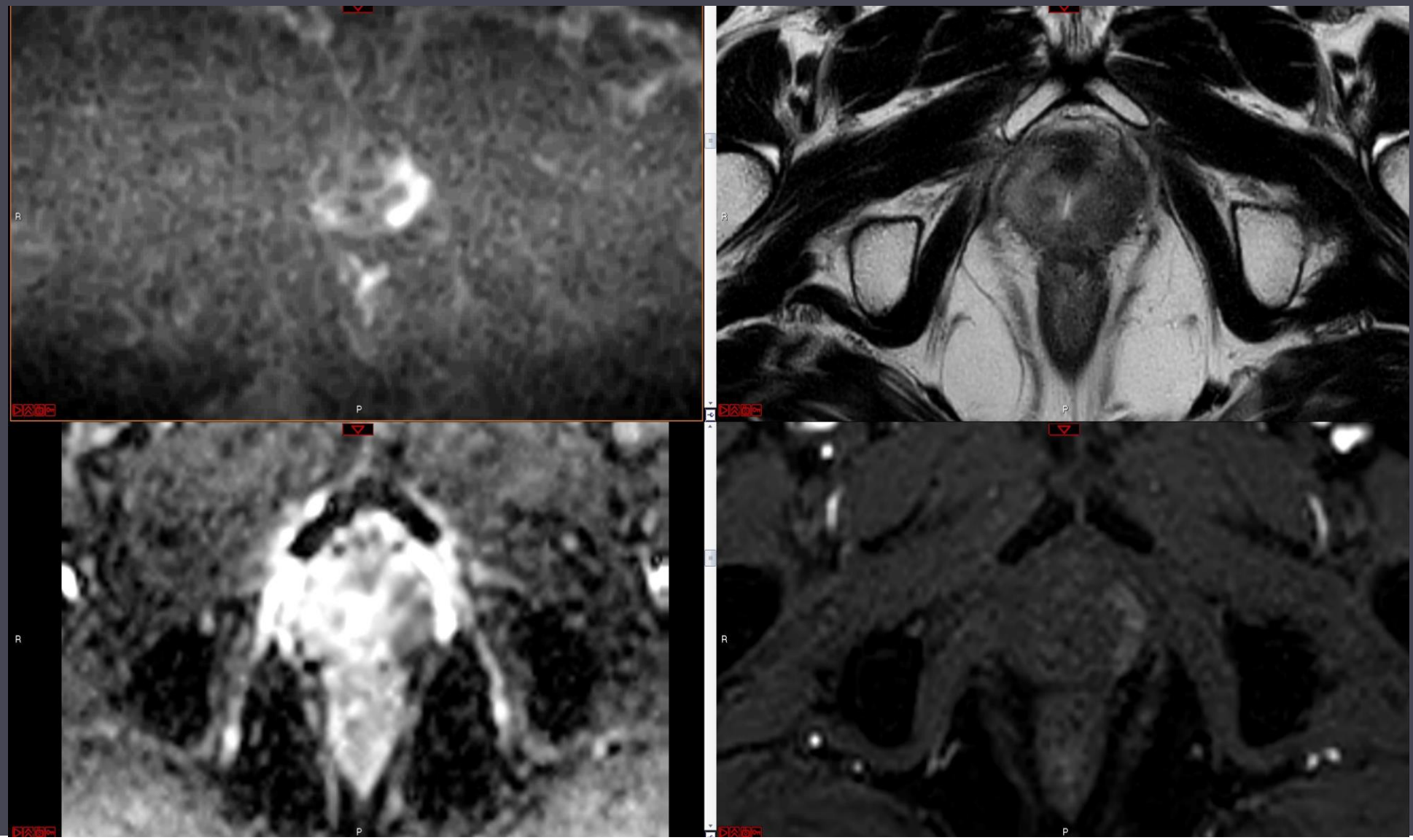
Recidiva dopo RT

- ***DWI e DCE**: sequenze dominanti*
- *Importante conoscere la sede di pregressa malattia*
  - *Più alta frequenza di recidiva*



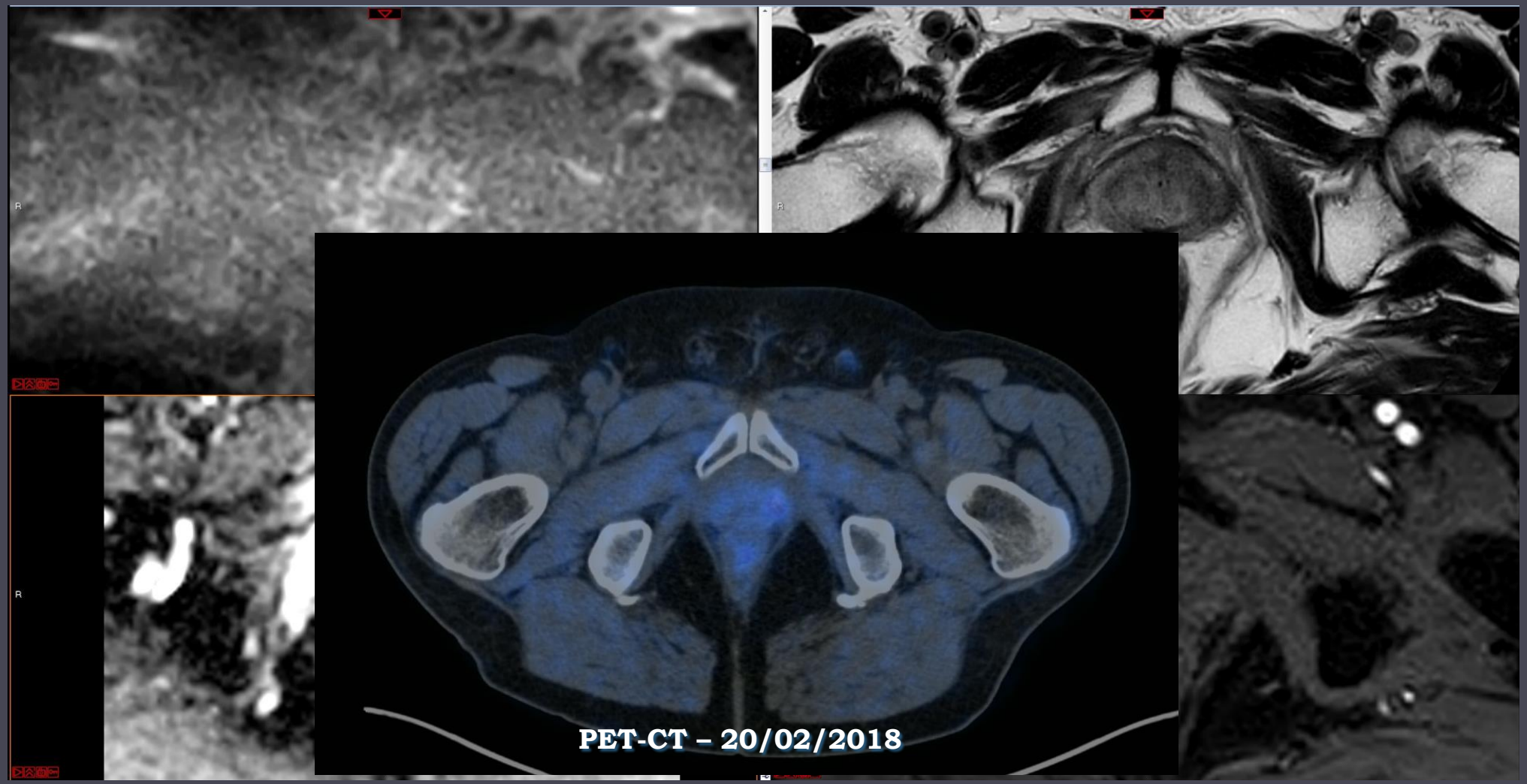
Sospetta recidiva post-RT

03/07/2017



Controllo post-RT stereotassica

12/02/2018



Ruolo mp-RM nel sospetto di RECIDIVA

- ***Dopo prostatectomia radicale***
  - *PSA non azzerato dopo prostatectomia (possibile residuo ghiandolare)*
  - ***PSA tra 0.2 ng/ml e 1.0 ng/ml***
  - ***> 2.0 ng/ml*** *c'è sospetto di recidiva a distanza o malattia sistemica* ***--> PET-CT***
- ***Dopo radioterapia o terapie locoregionali (HIFU, Laser)***
  - *PSA in rialzo progressivo (importante il doubling time)*

Grazie per l’attenzione

Grazie dell’attenzione