RUOLO DELLA RM NELLA DIAGNOSI DI TUMORE PROSTATICO

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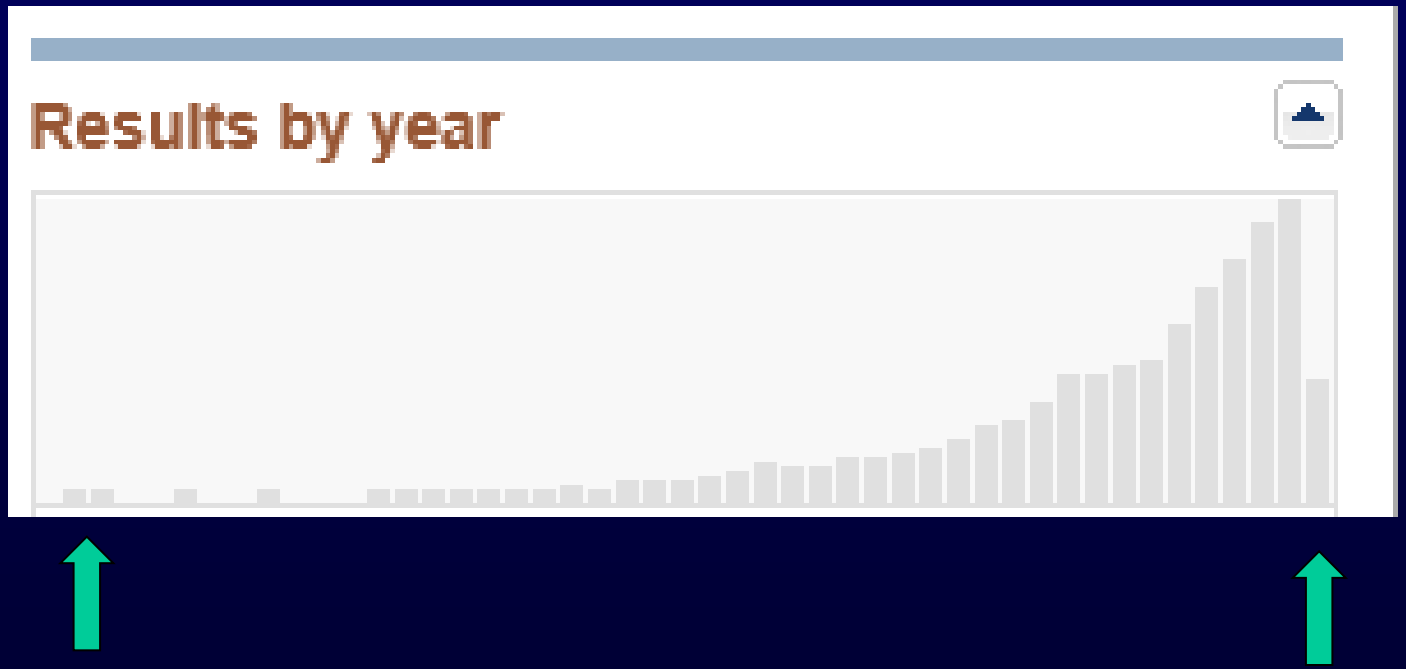
TORINO, 1 GIUGNO 2016

RISONANZA MAGNETICA

TECNICA OTTIMALE PER LO STUDIO DELLA PROSTATA



RISONANZA MAGNETICA

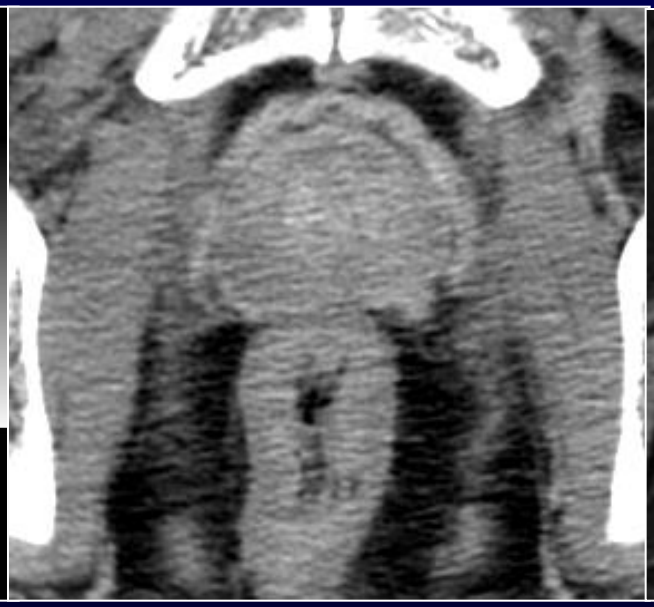
TECNICA OTTIMALE PER LO STUDIO DELLA PROSTATA

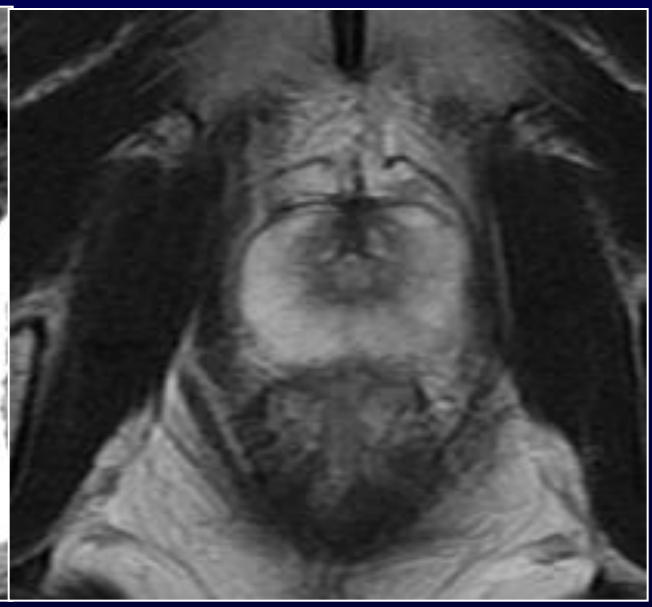
1. **Elevata risoluzione di contrasto**
2. **Multiplanarietà**
3. **Elevata risoluzione spaziale**
4. **Utilizzo di sequenze funzionali**

1

⇧ *RISOLUZIONE DI CONTRASTO*:
LA RM È L'UNICA METODICA DI IMAGING CHE CONSENTE LA VISUALIZZAZIONE DELL'ANATOMIA ZONALE DELLA PROSTATA

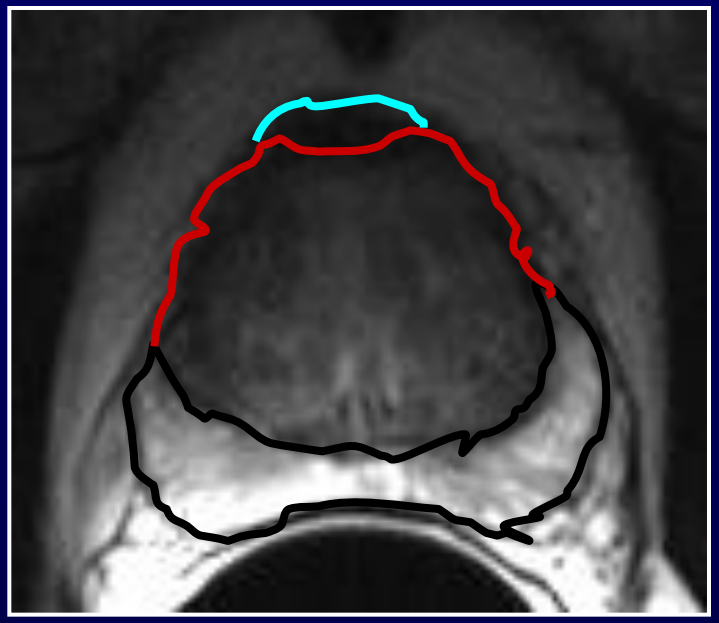
SCANSIONI T2 PESATE

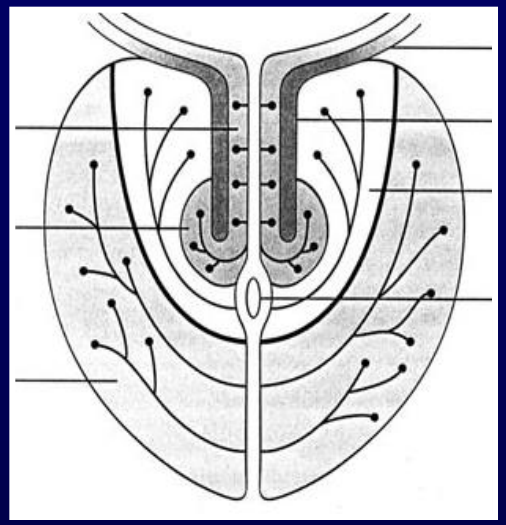


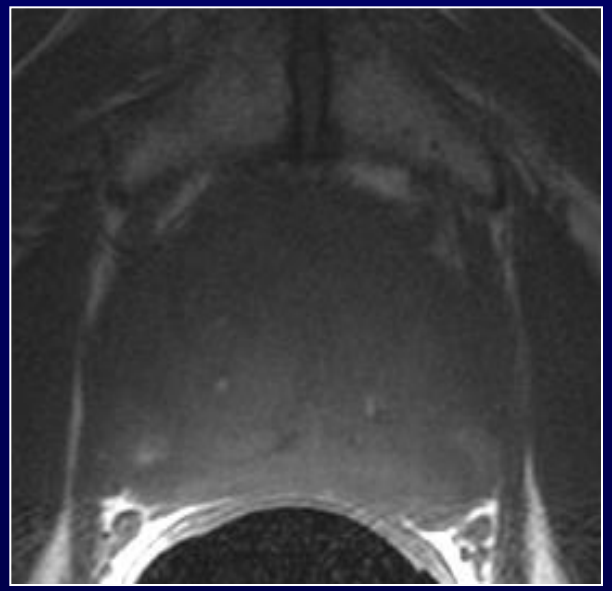


SCANSIONI T2 PESATE

SCANSIONI T1 PESATE



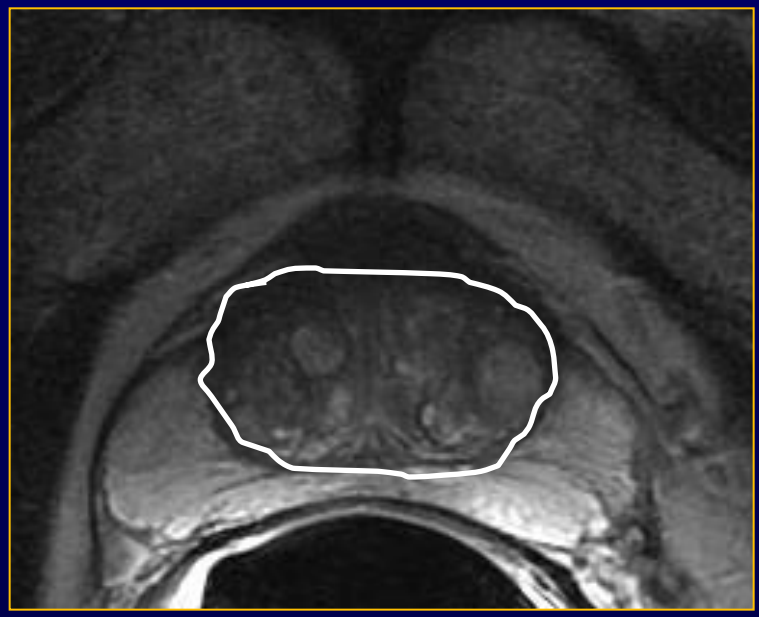




Anatomia zonale radiologica

- **Stroma anteriore fibromuscolare**
- **Ghiandola centrale**
- **Zona periferica**

ANATOMIA ZONALE RADIOLOGICA

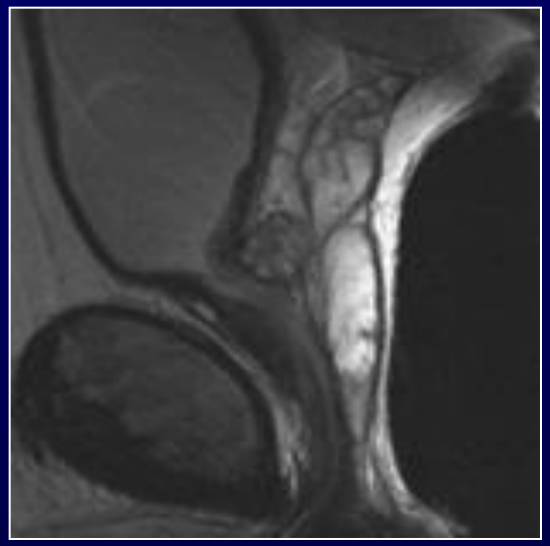


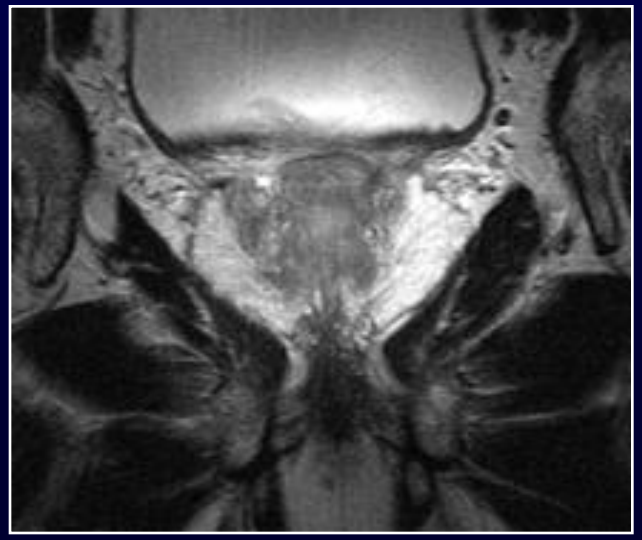
Anatomia zonale radiologica

- **Stroma anteriore fibromuscolare**
- **Ghiandola centrale**
  - Ghiandole periuretrali
  - Zona di transizione
  - Zona centrale
- **Zona periferica**

2

MULTIPLANARIETA': SEQUENZE T2 PESATE NEI TRE PIANI DELLO SPAZIO



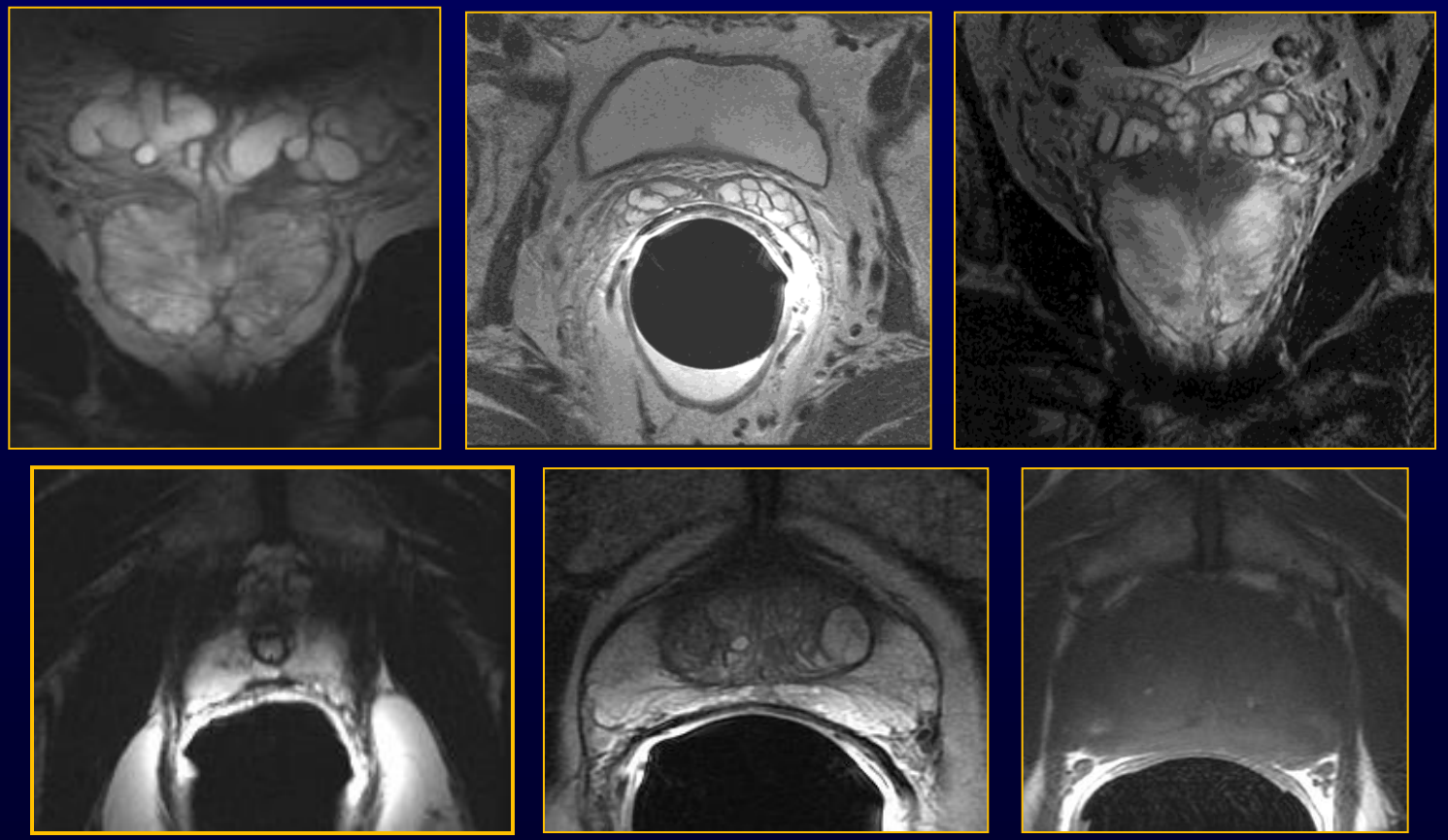


3

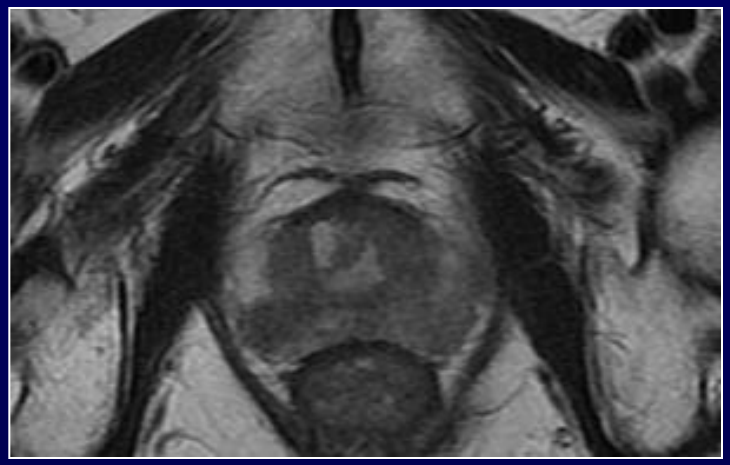
⇧ *RISOLUZIONE SPAZIALE*

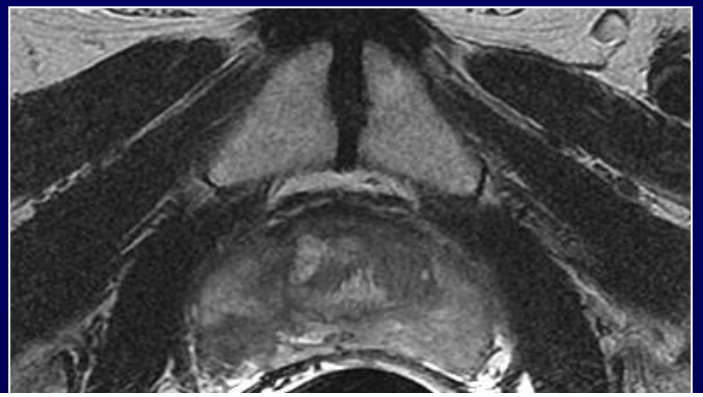
Progresso tecnologico:
NUOVE SEQUENZE
BOBINE ENDORETTALI
GRADIENTI ELEVATI

MIGLIORE VALUTAZIONE DI ALCUNE STRUTTURE ANATOMICHE

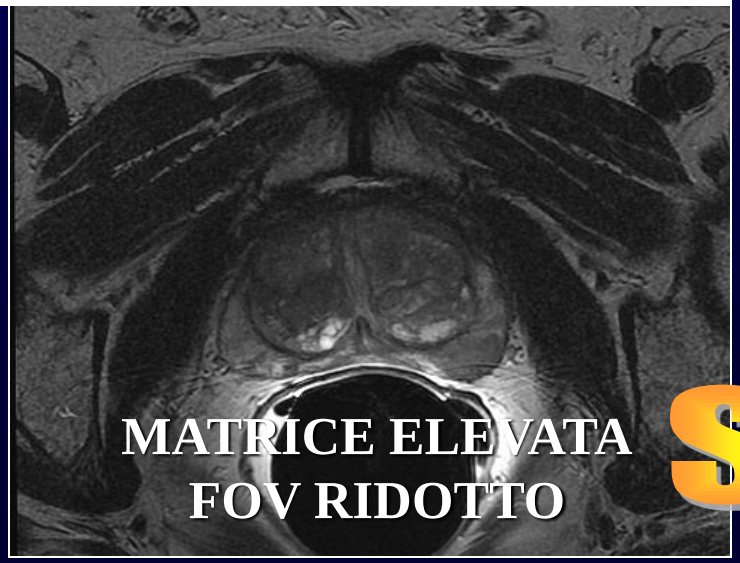


REQUISITI TECNICI





Matrice 384 x 288
FOV 16 x 16



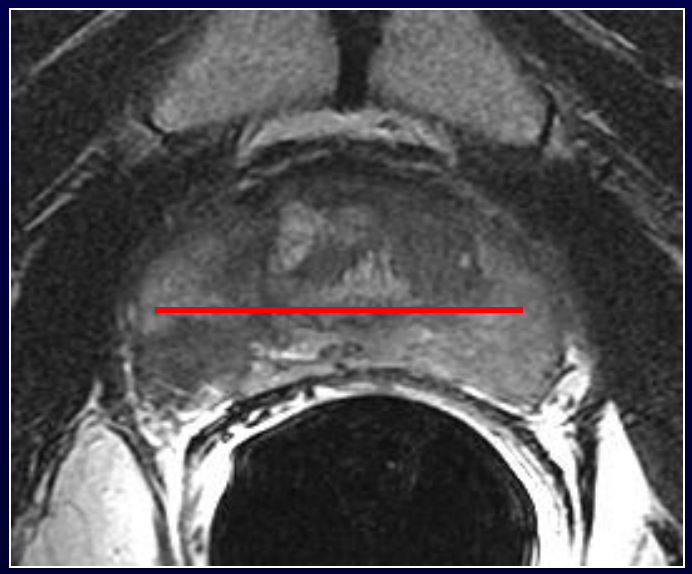
BOBINE ENDORETTALI

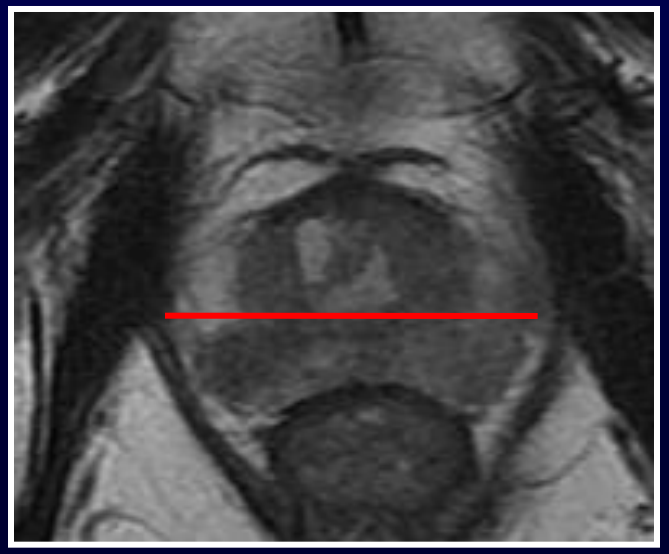
VANTAGGI

- elevata ris.spaziale
- miglior rapporto s/r

SVANTAGGI

- movimenti involontari retto
- diametri prostatici alterati
- perdita di segnale anteriore
- disconfort per il paziente

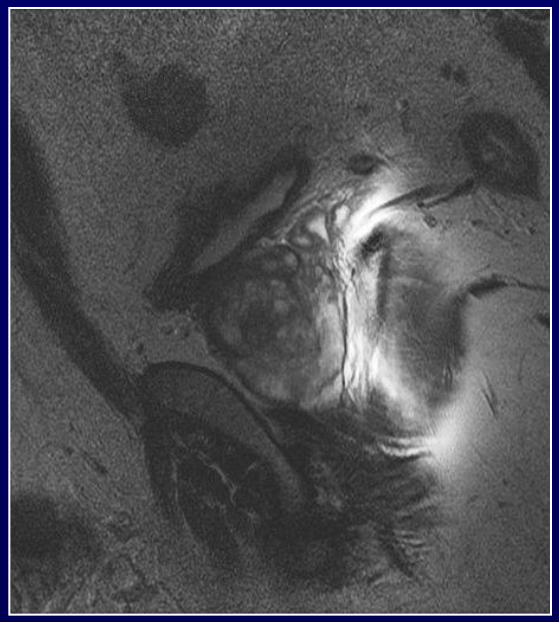


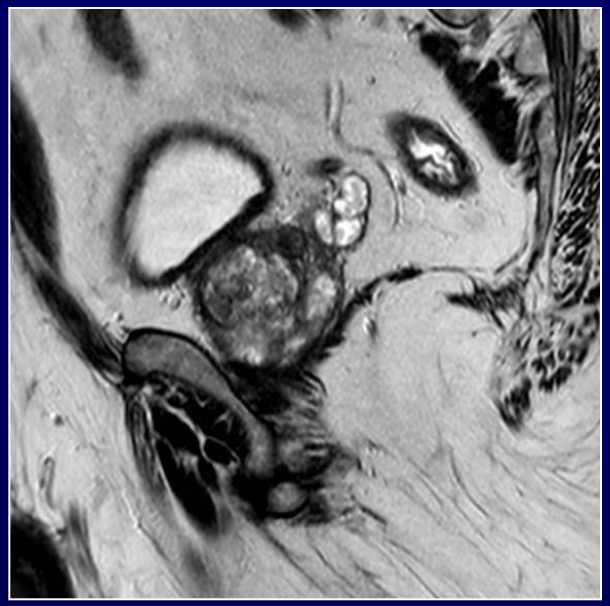


APPARECCHI A 3 TESLA

APPARECCHI A 1.5 TESLA CON GRADIENTI ELEVATI

POSSIBILITA' DI ESEGUIRE GLI ESAMI SENZA BOBINA ENDORETTALE

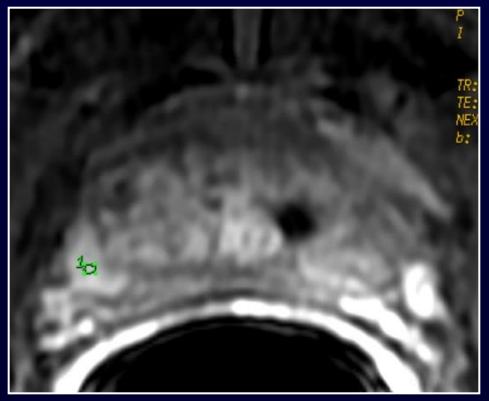


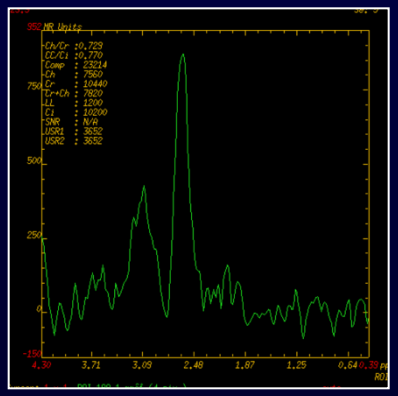


4

POSSIBILITA' DI ESEGUIRE STUDI FUNZIONALI (SPETTROSCOPIA, STUDI DINAMICI, DIFFUSIONE)

↑ ACCURATEZZA NELL'IDENTIFICAZIONE DI NEOPLASIA





RISONANZA MAGNETICA: RUOLO IN AMBITO PROSTATICO

DIAGNOSI

STADIAZIONE

FOLLOW-UP

RISONANZA MAGNETICA: RUOLO IN AMBITO PROSTATICO

STADIAZIONE

FOLLOW-UP

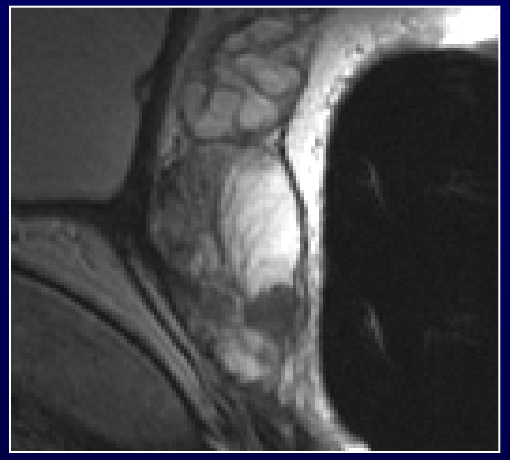
RISONANZA MAGNETICA

DIAGNOSI

COME APPARE IL CARCINOMA PROSTATICO IN RM?

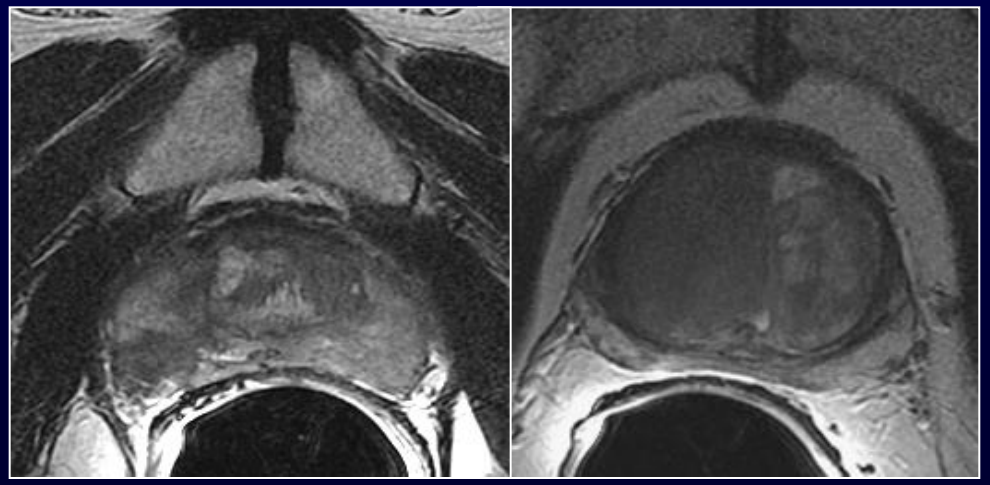
tessuto neoplastico

lesione ipointensa in T2



INDIPENDENTEMENTE

- dimensioni
- sede
- intensità di campo magn.
- bobina utilizzata



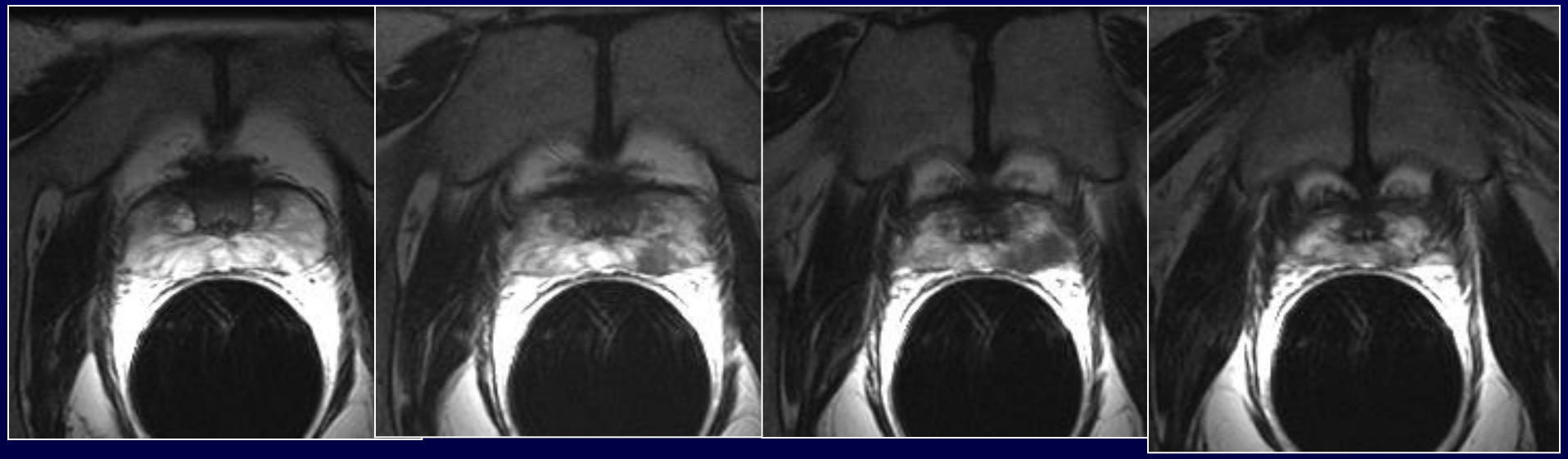
BASSA SPECIFICITÀ

Ipointensità di segnale in T2

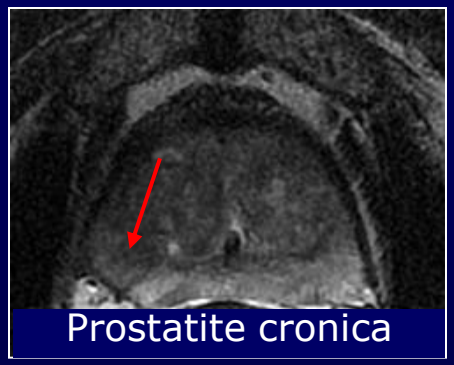
- **prostatite**
- **fibrosi**
- **tumore**
- **emorragia**
- **Iperplasia fibroleiomatosa**

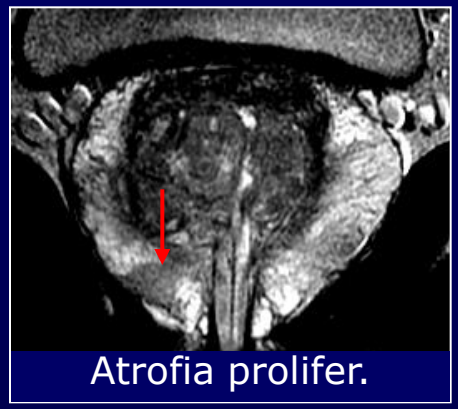
74 PAZIENTI	SPEC	VVP
RM-T2W MORFOLOGICA	64%	56%

Cirillo S; Clin Radiol 2008

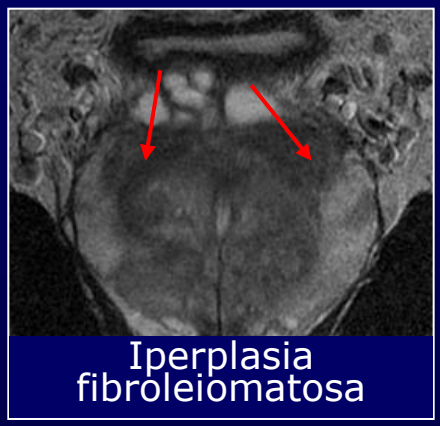


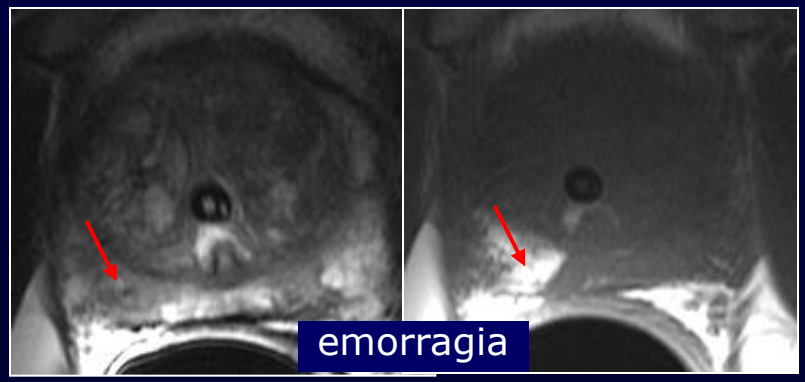
PROBLEMA RM: *bassa specificità*
(altre lesioni con bassa intensità di segnale in T2)


Prostatite cronica


Atrofia prolifer.

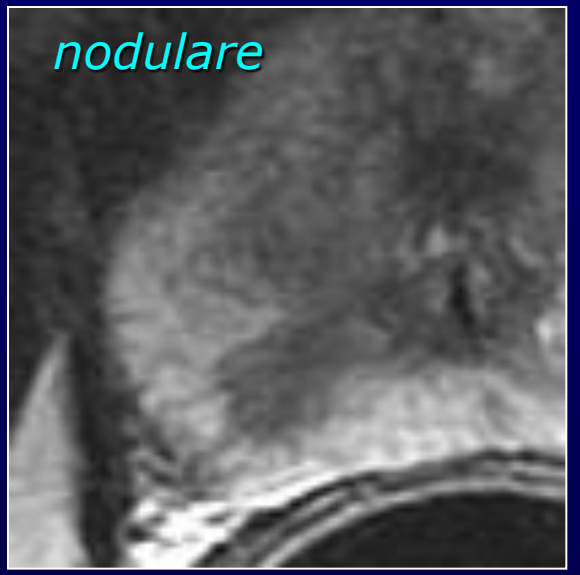

Atrofia fibrosa

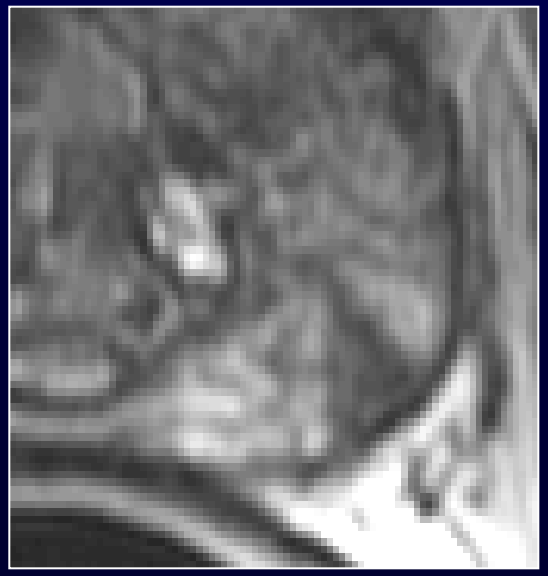

Iperplasia fibroleiomatosa

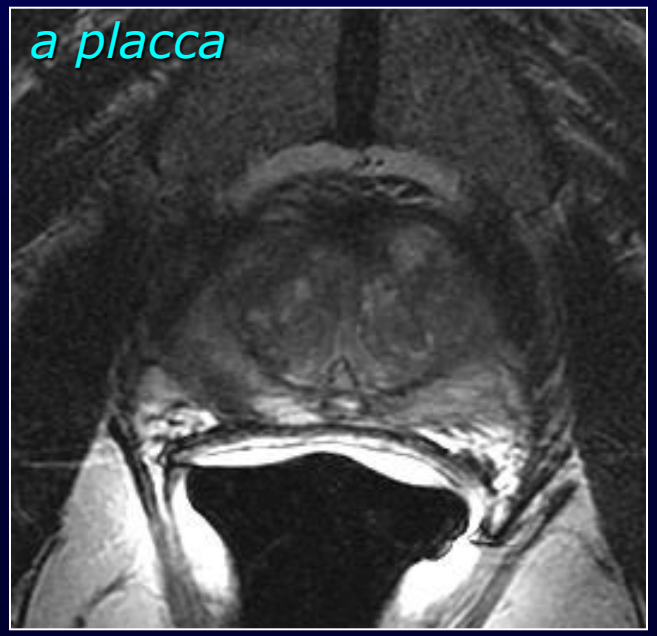

emorragia

POSSIBILI CRITERI DI MALIGNITA’

FORMA





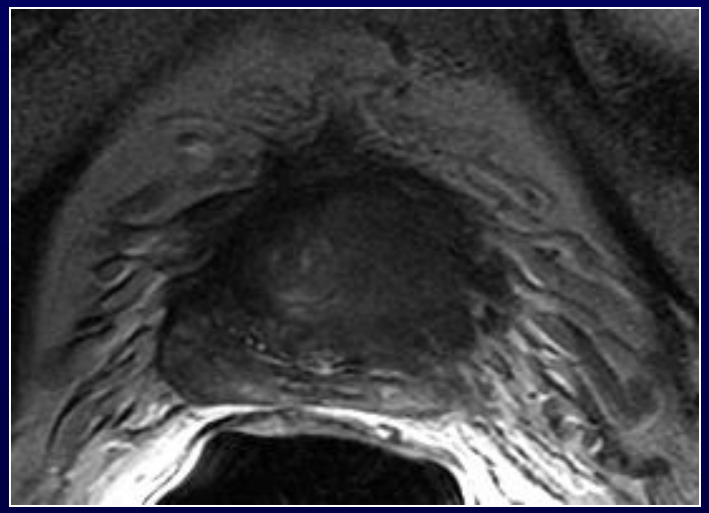


IDENTIFICAZIONE TUMORE ZONA CENTRALE

IDENTIFICAZIONE TUMORE NELLA PORZIONE CENTRALE DELLA GHIANDOLA (30%)

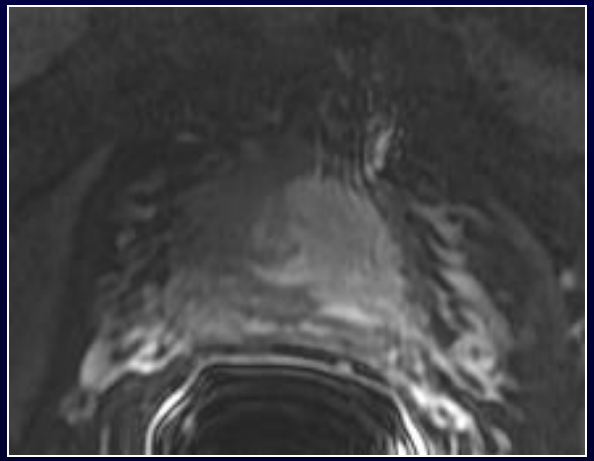
Conventional MRI capabilities in the diagnosis of prostate cancer in the transition zone

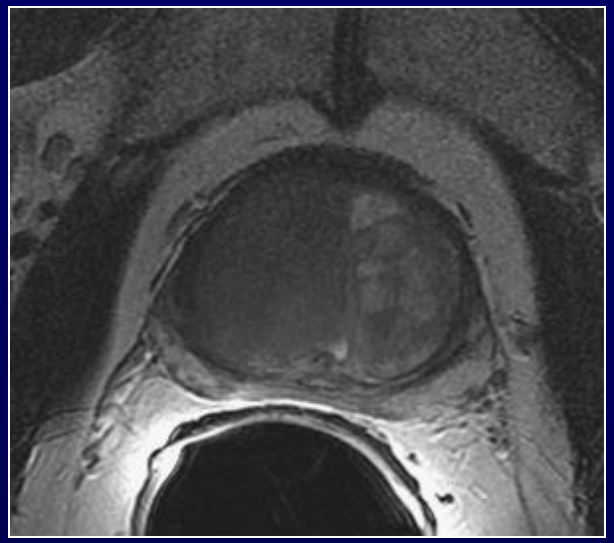
Hong Li, AJR 2006

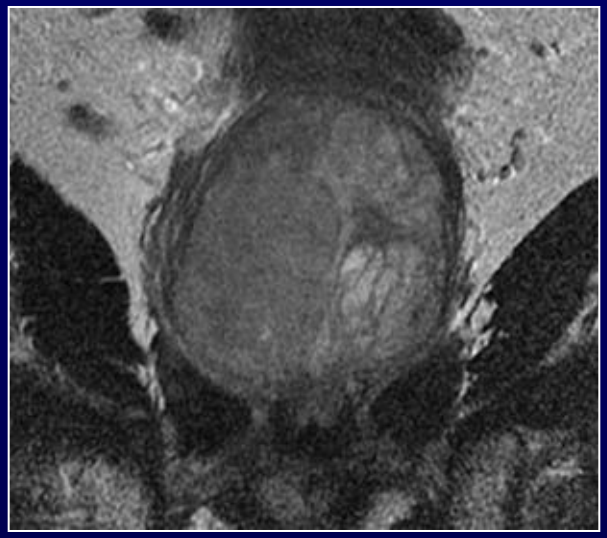


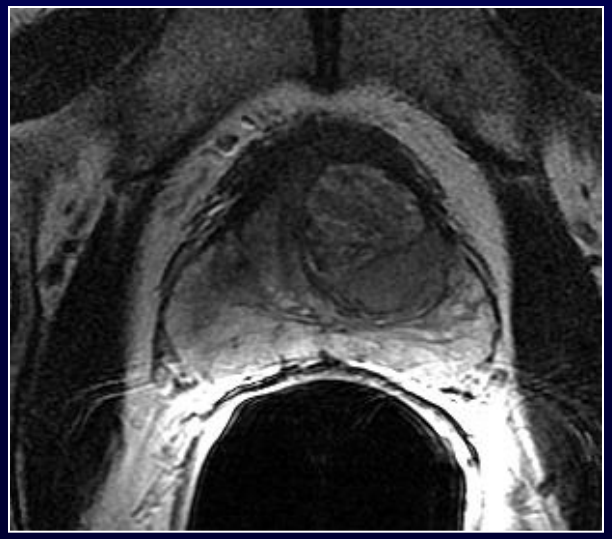
CRITERI PER IDENTIFICARE IL TUMORE NELLA ZONA CENTRALE

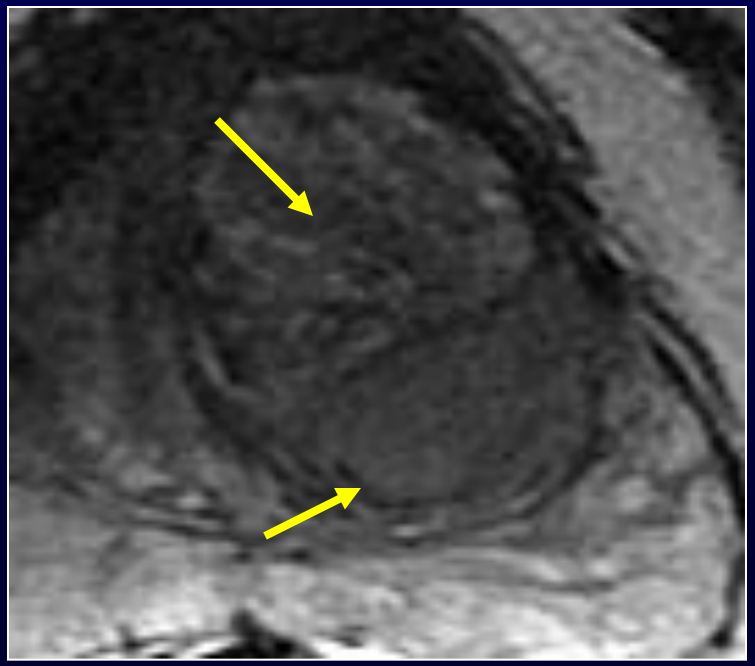
- *Bassa ed uniforme intensità di segnale in T2*
- *omogeneo enhacement*
- *margini irregolari in T2 e dopo contrastro*











PROBLEMA RM → **SCARSA SPECIFICITA'**

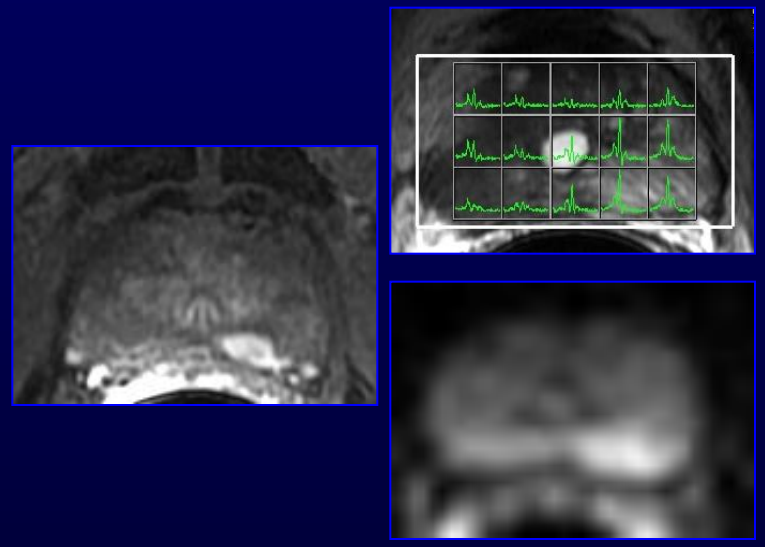
IMAGING RM

MORFOLOGICO + **FUNZIONALE**

DIAGNOSI DIFFERENZIALE TRA TESSUTI

IDENTIFICAZIONE DI AREE SOSPETTE

- Spettroscopia RM (MRS) a H
- Dynamic Contrast Enhanced-MRI (DCE-MRI)
- Diffusion MRI (DWI-MRI)



IMAGING MULTIPARAMETRICO

Megwalu; BJU International, 2008
Scattoni V; Eur Urol. 2009


EDUCATION EXHIBIT 63

RadioGraphics

Functional MR Imaging of Prostate Cancer[1]

TEACHING POINTS

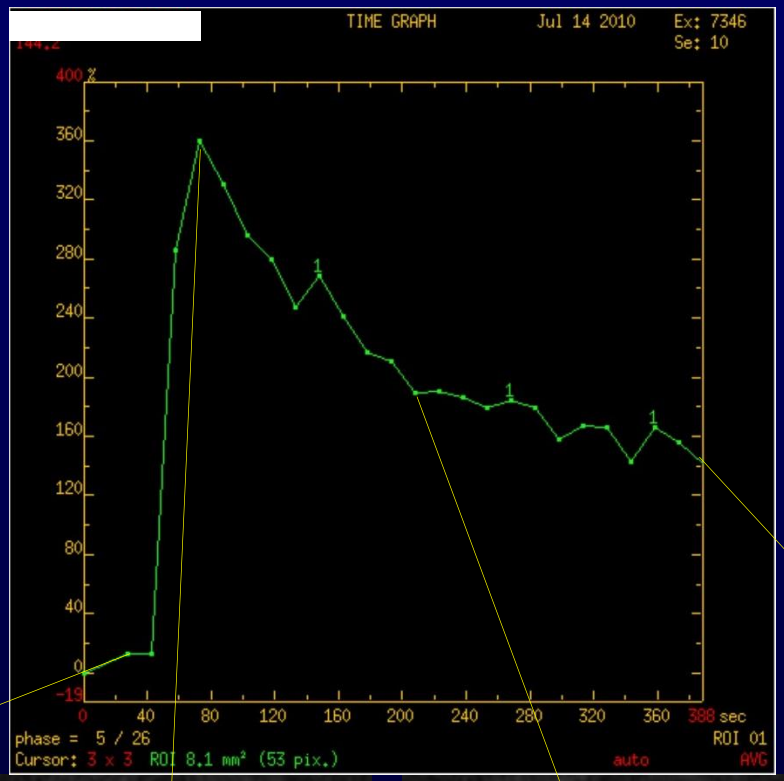
Young Jun Choi, MD • Jeong Kon Kim, MD • Namkug Kim, MS
Kyoung Won Kim, MD • Eugene K. Choi, BA • Kyoung-Sik Cho, MD

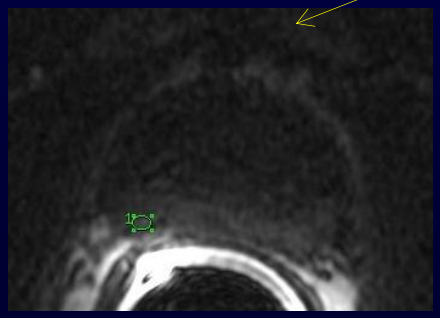
- Spettroscopia RM (MRS) a H → Metabolismo
- Dynamic Contrast Enhanced-MRI (DCE-MRI) → Perfusione e permeabilità
- Diffusion MRI (DWI-MRI) → Cellularità

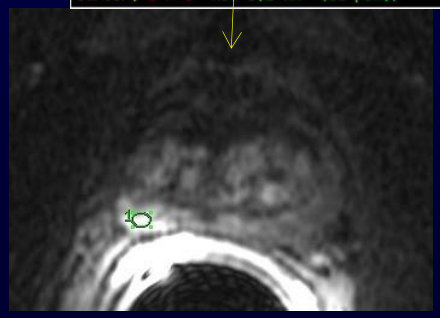
IMAGING MULTIPARAMETRICO

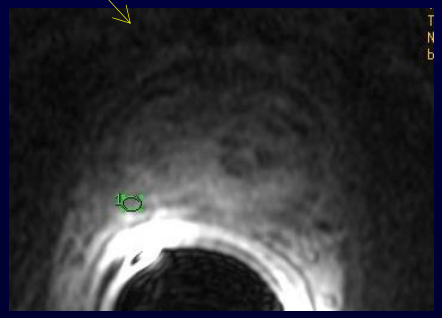
Megwalu; BJU International, 2008
Scattoni V; Eur Urol. 2009

DYNAMIC CONTRAST-ENHANCED MRI (DCE-MRI)





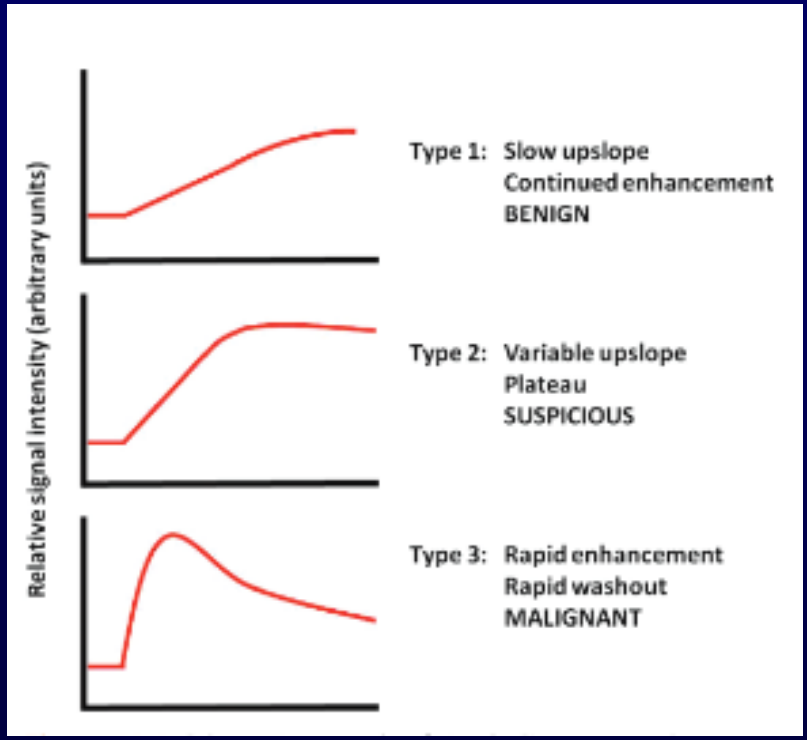




VALUTAZIONE QUALITATIVA

Morfologia della curva:

- **Tipo 1**: crescita lenta e progressiva
- **Tipo 2**: plateau
- **Tipo 3**: rapida crescita con successivo wash-out

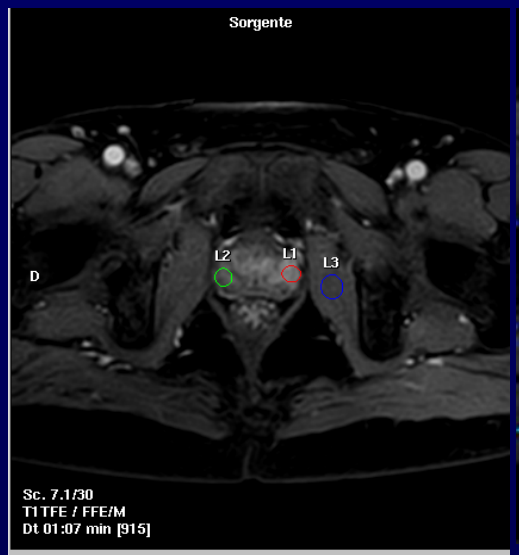


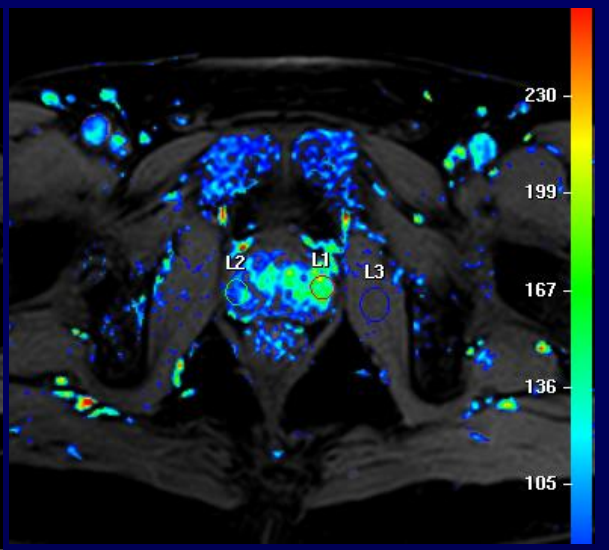
Ito; Br J Radiol 2003

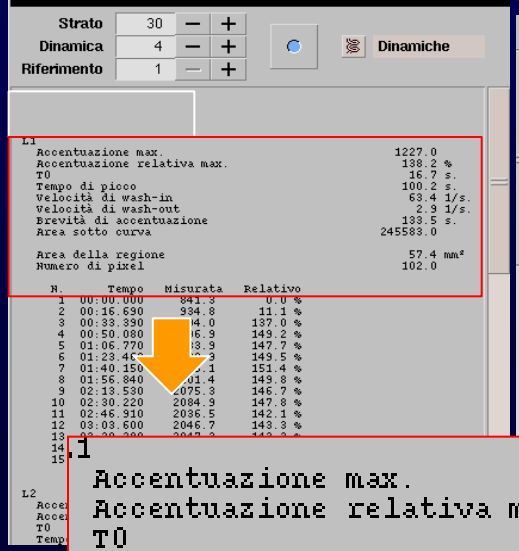
VALUTAZIONE SEMIQUANTITATIVA

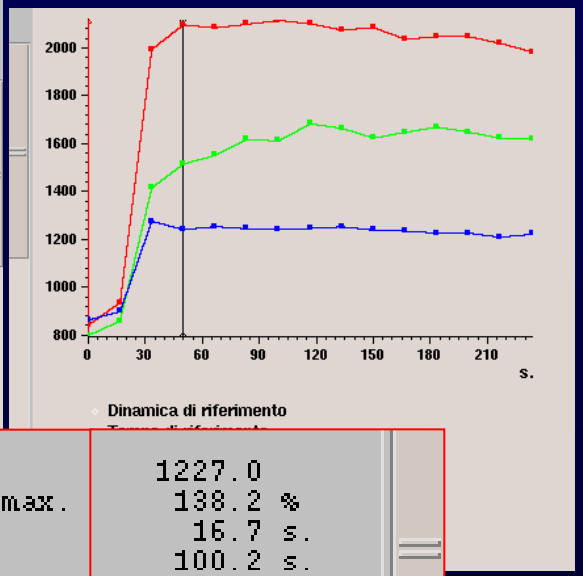
PARAMETRO NUMERICO

VALUTAZIONE QUANTITATIVA









L1

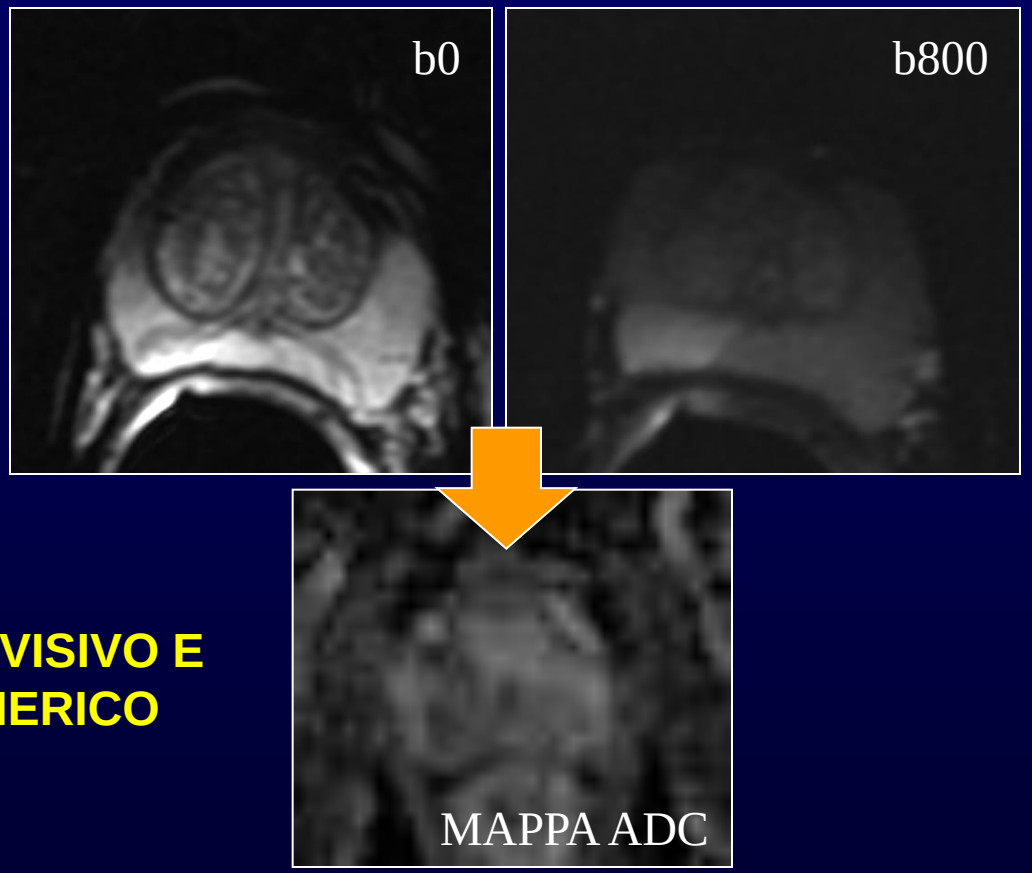
Accentuazione max.	1227.0
Accentuazione relativa max.	138.2 %
T0	16.7 s.
Tempo di picco	100.2 s.
Velocità di wash-in	63.4 1/s.
Velocità di wash-out	2.9 1/s.
Brevità di accentuazione	133.5 s.
Area sotto curva	245583.0

PARAMETRI SEMIQUANTITATIVI

RM DIFFUSIONE DELLA PROSTATA

Lo studio RM della diffusione si basa sulla valutazione dei moti browniani delle molecole di acqua: evidenza di aree con maggiore cellularità

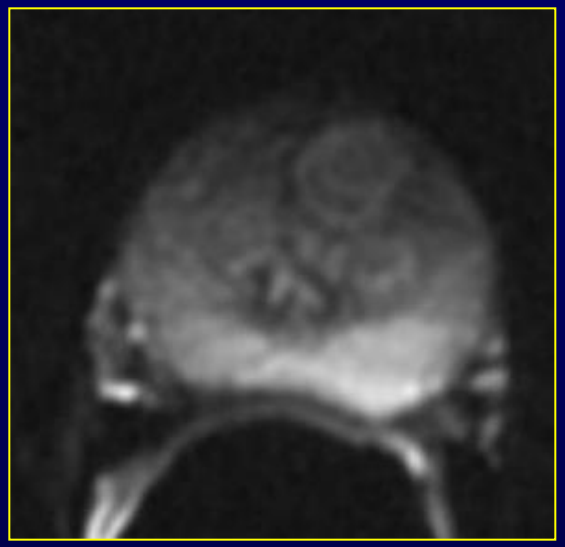
Gradiente bipolare applicato a sequenze Spin Echo eseguite con imaging eco-planare (EPI)



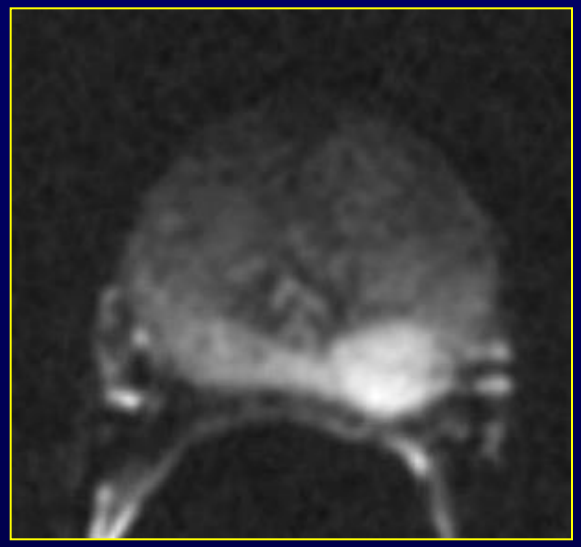
DATO VISIVO E NUMERICO

TECNICA NON STANDARDIZZATA!!!

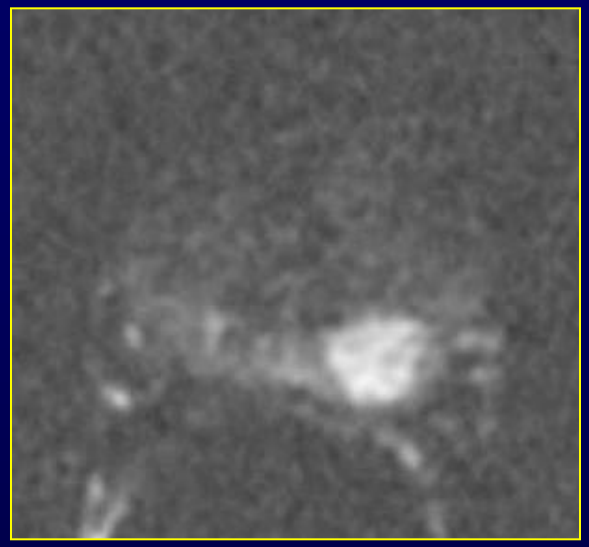
valutazione di tipo *qualitativo*



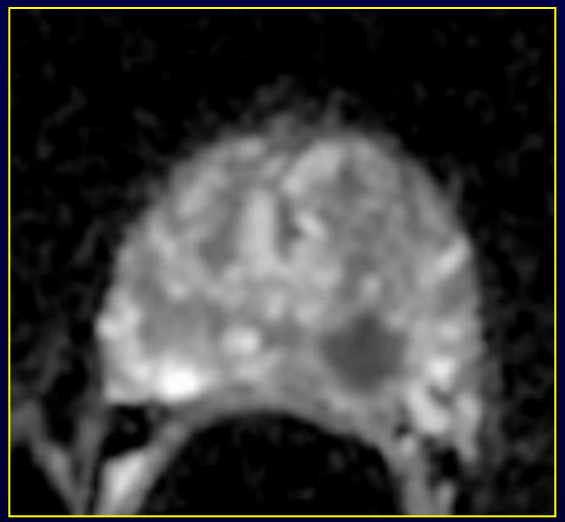
600 s/mm²



1000 s/mm²



2000 s/mm²



DIFFUSIONE RISTRETTA:

- *Area iperintensa in DWI*

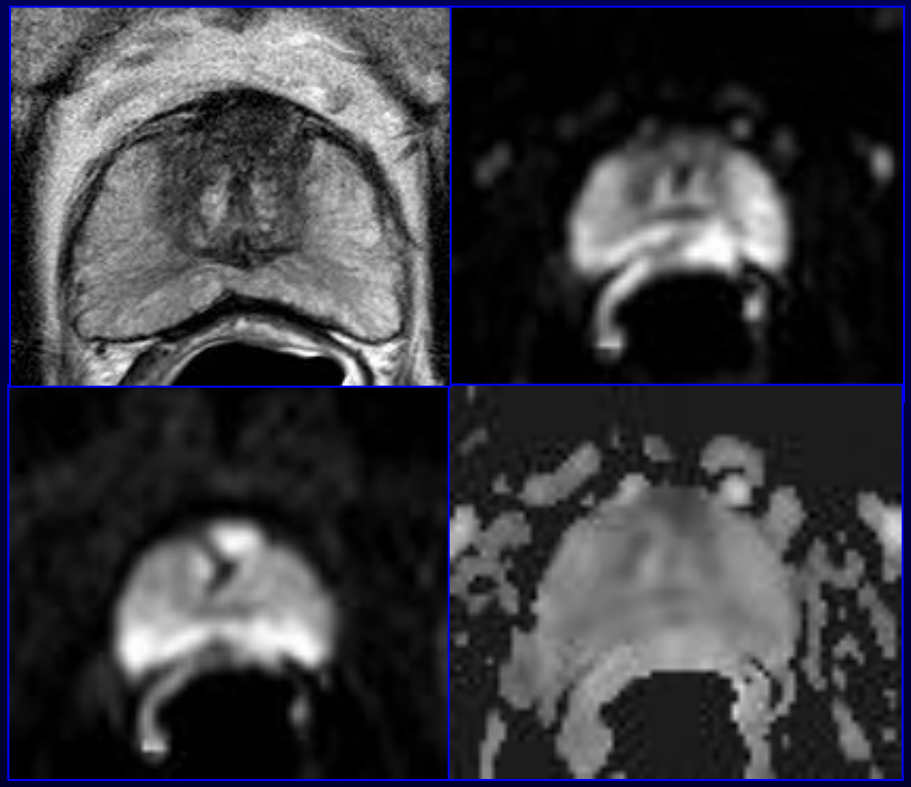
DIFFUSIONE RISTRETTA:

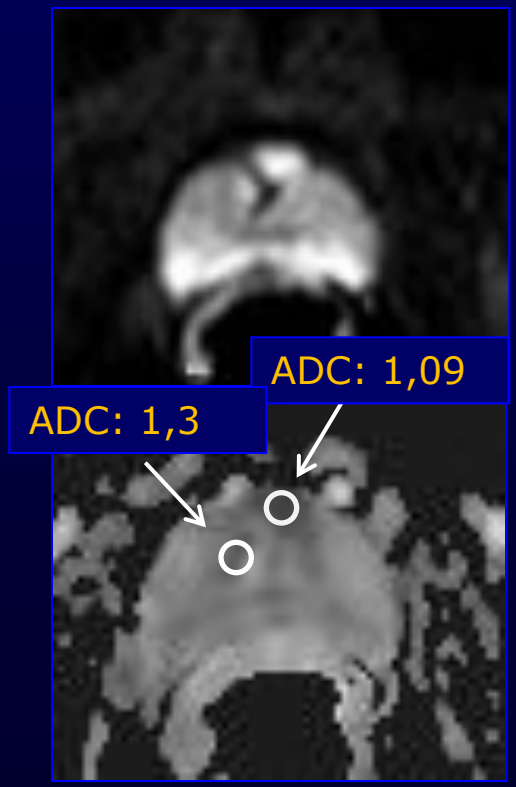
- *Area ipointensa nella mappa ADC*

ANALISI QUANTITATIVA: calcolo ADC

- *molti articoli in letteratura*
- *necessita di post-processing*
- *influenzata da fattori tecnici*
- *influenzata da fattori biologici*

- eta' paziente, temperatura corporea





ANALISI QUANTITATIVA

non possibile identificare CUT OFF di ADC da utilizzare routinariamente per identificazione delle neoplasie prostatiche per la mancanza di standardizzazione protocolli

Studio	CUT OFF ADC	Sens.	Spec
De Souza et al. *Br J Radiol 2007*	1.60	86.7%	72.2%
Reinsberg *AJR 2007*	1.26	93.3%	57,4%
Zelhof et al. *BJU Int 2009*	1.62	81%	78%
Yagci AB et al . *Diagn Interv Radiolo 2011*	1.2	84%	82%
Yamamura et al. *J Comput Assist Tomogr 2011*	1.21	92%	93%
Kazuhiro Ktajima *Journal of Magnetic Resonance Imaging 2012*	1.03	86,8%	91,3%

STUDIO MULTIPARAMETRICO:

- *Variabilità interpretativa*
- *Discordanza fra esami funzionali*
- *Elevato numero di dati da analizzare*

REFERTI

INCONCLUDENTI

NECESSITA' DI STANDARDIZZARE

(linguaggio comune)

grado di sospetto di malattia attraverso score

PIRADS:

PROSTATE IMAGING REPORTING DATA SYSTEM

Barentsz JO et al *Eur Radiol (2012) 22:746-757*

ESUR prostate cancer MR guidelines 2012

RMmp

punteggio 1-5

1: non sospetto

5: molto sospetto

T2W
DWI
DCE
(MRS)

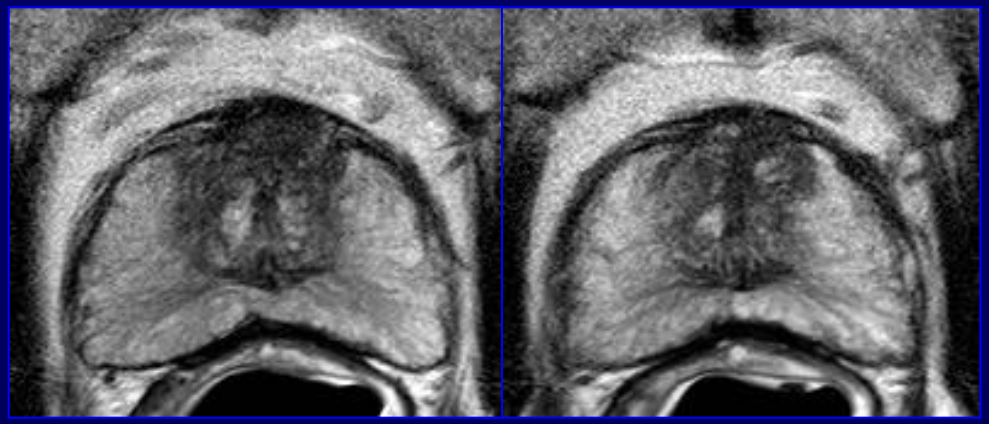
A ogni lesione individuata si sommano i vari punteggi e si attribuisce un punteggio totale

Punteggio PI-RADS: ***indica la probabilità di rischio di tumore***

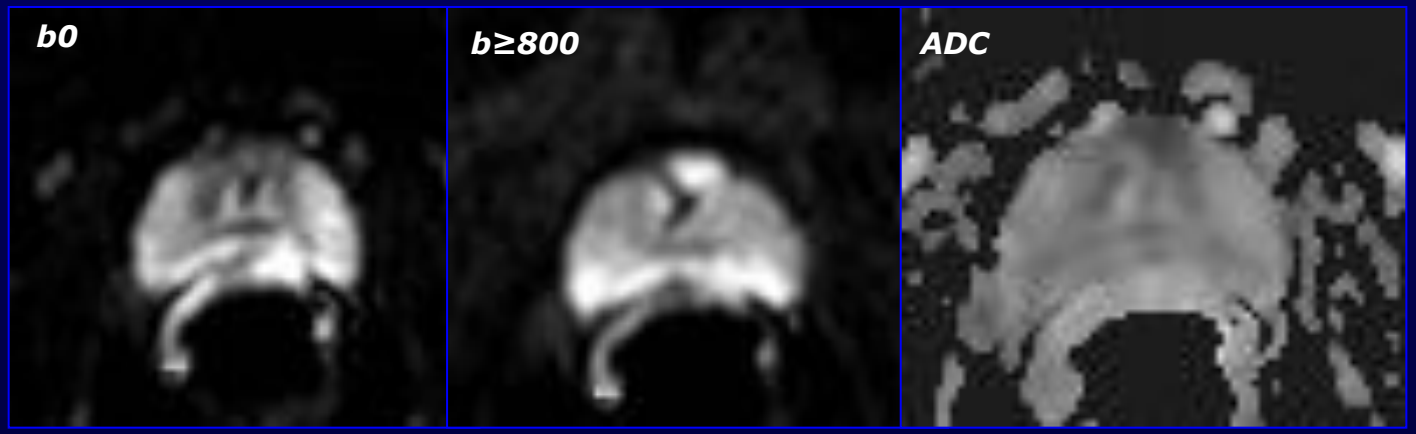
PI-RADS classification	Definition	Total score with T2, DWI, DCE
1	most probably benign	3, 4
2	probably benign	5, 6
3	indeterminate	7 – 9
4	probably malignant	10 – 12
5	highly suspicious of malignancy	13 – 15

Se sono state eseguite 3 sequenze ≥10: alta probabilità di neoplasia

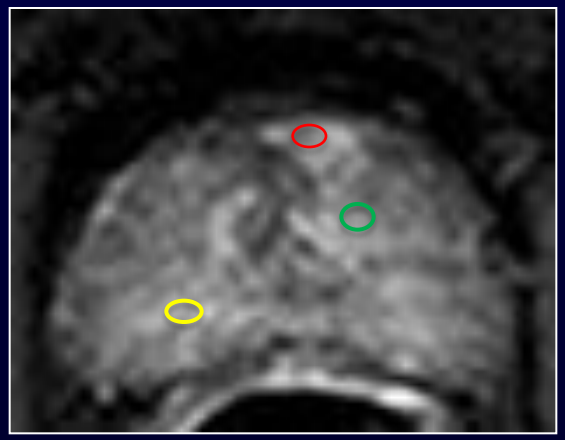
Punteggio PI-RADS:

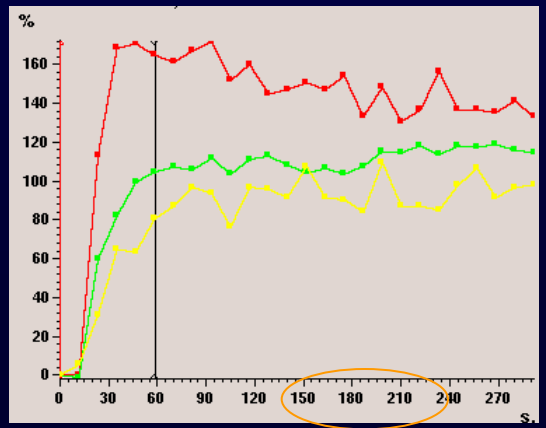


morfologico: score 3



diffusione: score 5





DCE: score 5

TOTALE :13

Barrett T et al *Clinical Radiology 2015*

PI-RADS version 2: what you need to know

PiRADS v2 → Individuazione di sequenze dominanti in base alla localizzazione

Zona periferica → DWI

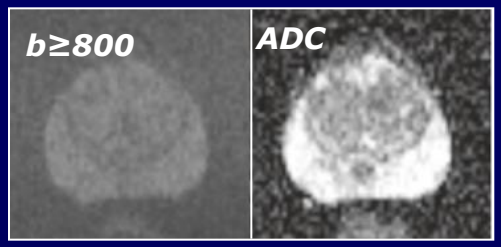
DWI	T2	DCE	PI-RADS
1	any	any	1
2	any	any	2
3	any	neg	3
		pos	4
4	any	any	4
5	any	any	5

- *Steiger and Toeny Cancer imaging 2016*
- *Rothke eta al Clinical Men's Health*

DWI

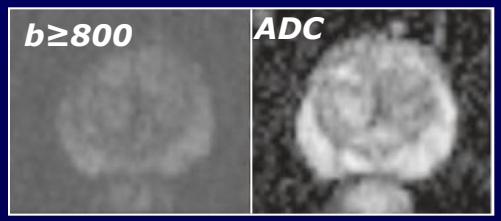
Porzione periferica

Score 1
No alterazioni



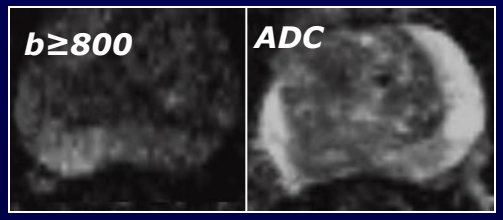
benigno

Score 2
Alterazioni diffuse simmetriche o focalità lineari



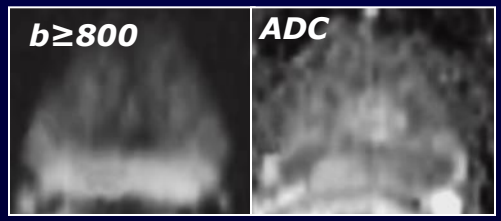
benigno

Score 3
Alterazioni diffuse asimmetriche



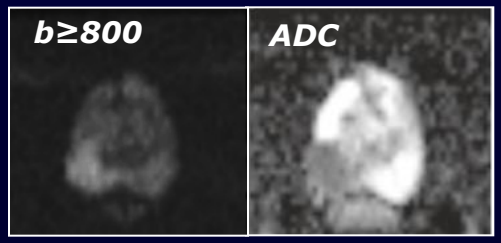
indeterm.

Score 4
Alterazioni focali nodulari < 15 mm



maligno

Score 5
Alterazioni focali nodulari > 15 mm

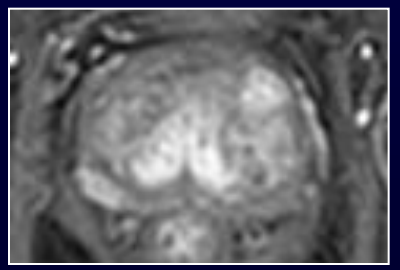


maligno

Morfologico T2: non valutato

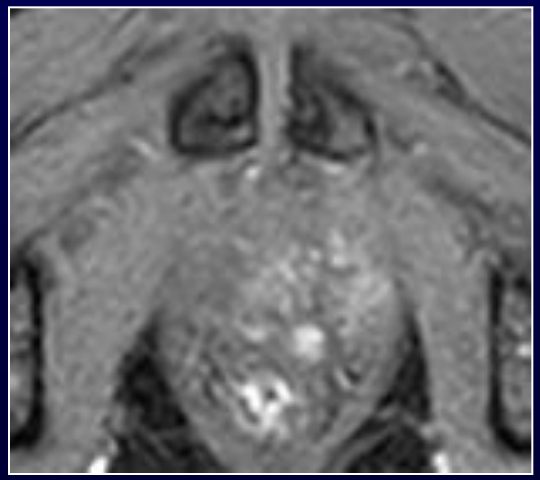
DCE negativa
(no enhancement focale): Score 3

DCE positiva
(enhancement focale): Score 4

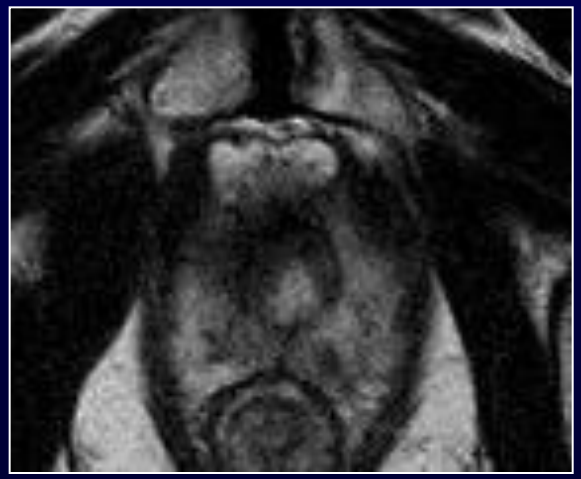


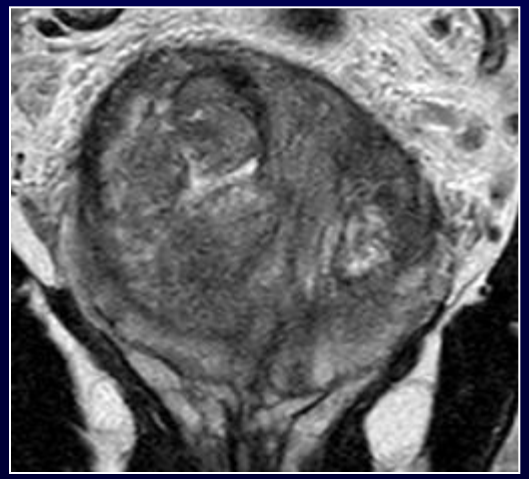
Pi-RADS 4

DWI: score 3

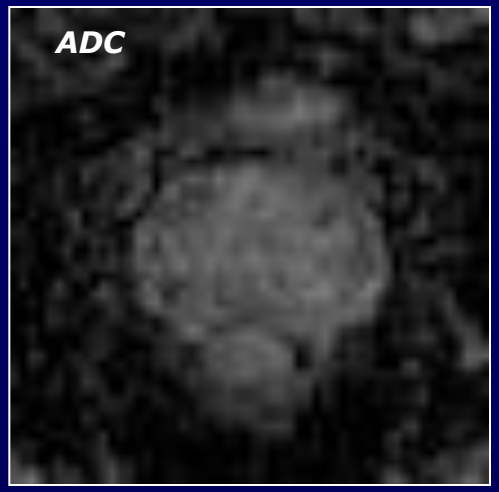


DCE: positiva

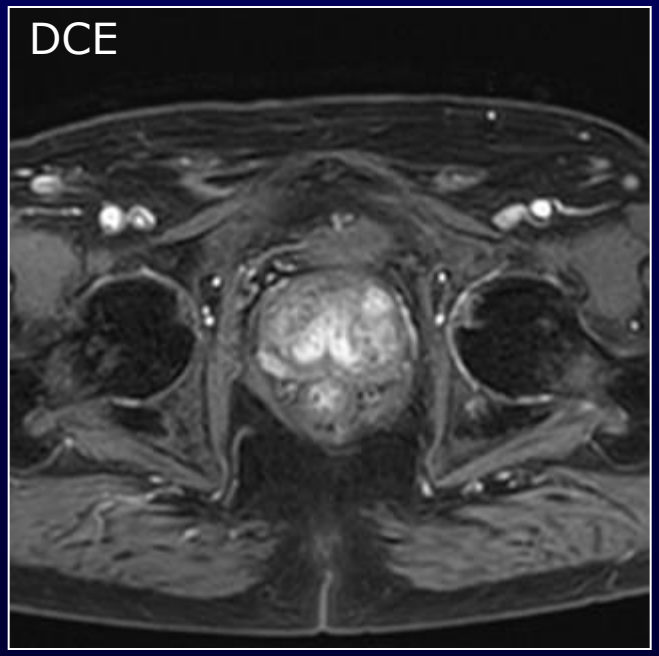


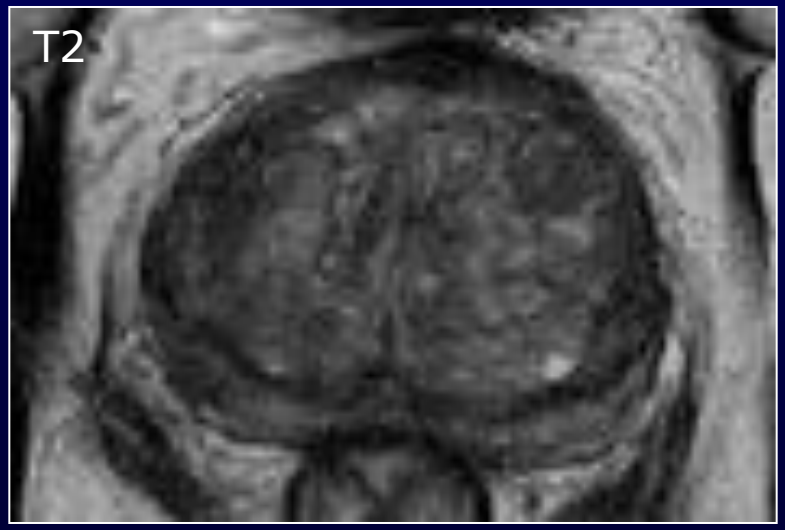


T2w: qualsiasi



DWI: score 4





Pi-RADS 4

Barrett T et al *Clinical Radiology 2015*

PI-RADS version 2: what you need to know

PiRADS v2 ⇒ Individuazione di sequenze dominanti in base alla localizzazione

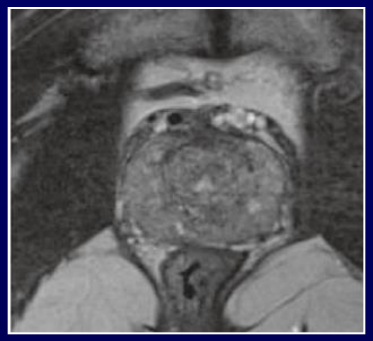
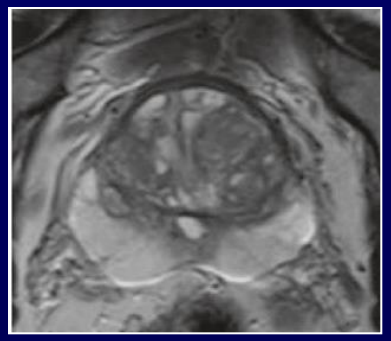
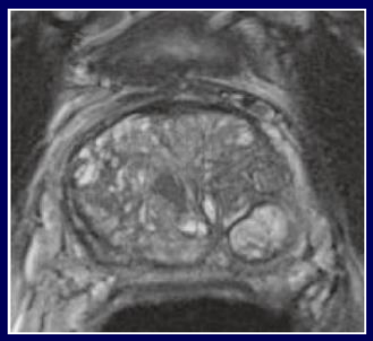
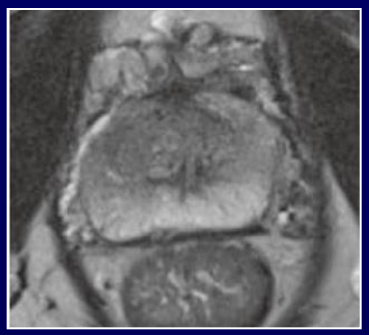
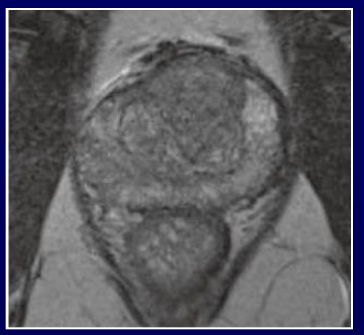
Zona centrale → T2

T2	DWI	DCE	PI-RADS
1	any	any	1
2	any	any	2
3	1-4	any	3
	5		4
4	any	any	4
5	any	any	5

- *Steiger and Toeny Cancer imaging 2016*
- *Rothke eta al Clinical Men's Health*

Porzione centrale

T2

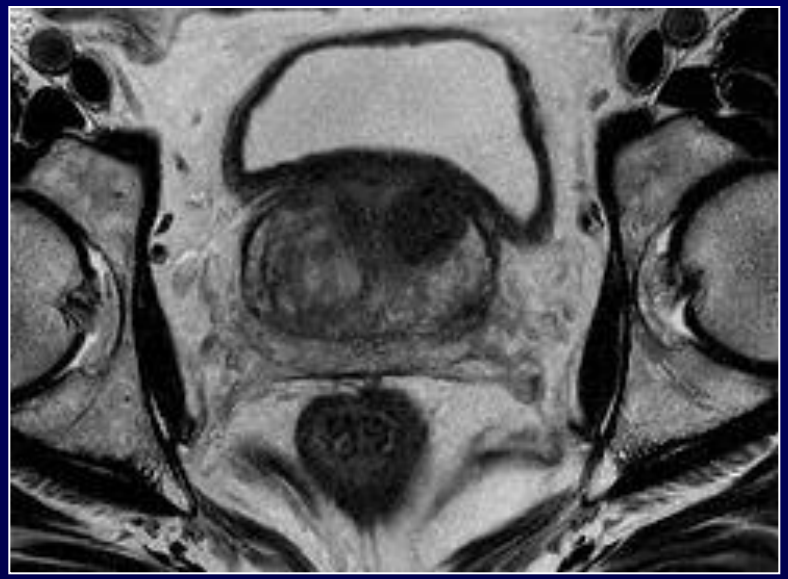
benigno	***benigno***	***indeterm.***	***maligno***	***maligno***
				
Score 1 (no alterazioni focali)	Score 2 (focalità ipontense ben demarcate)	Score 3 (focalità ipointense a margini mal delimitati)	Score 4 (tessuto ipointenso < 15 mm a margini irregolari)	Score 5 (tessuto ipointenso > 15 mm a margini irregolari)

DWI 1-4: Score 3

DWI 5: Score 4

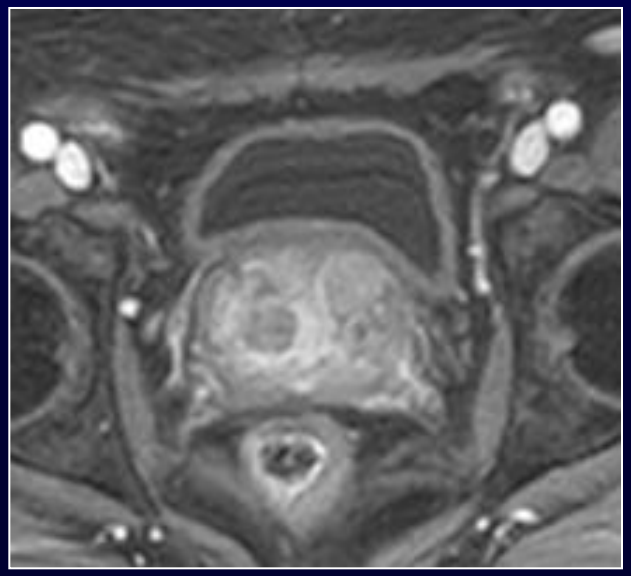
DCE: non valutato

Pi-RADS 4

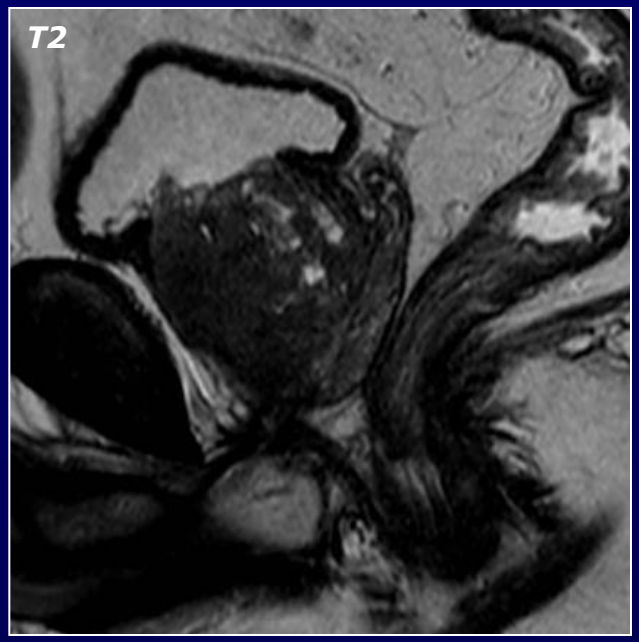


T2w: score 3

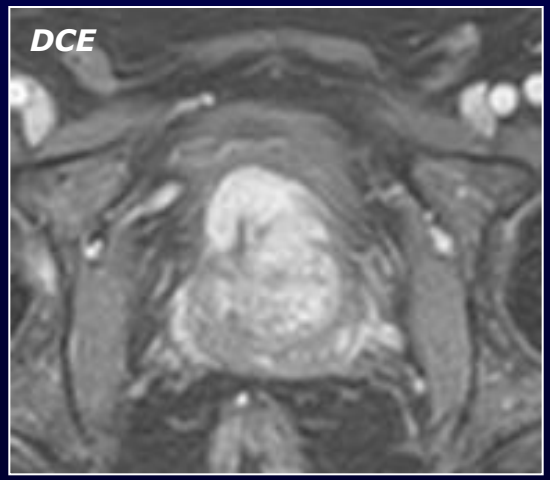
DWI: score 5



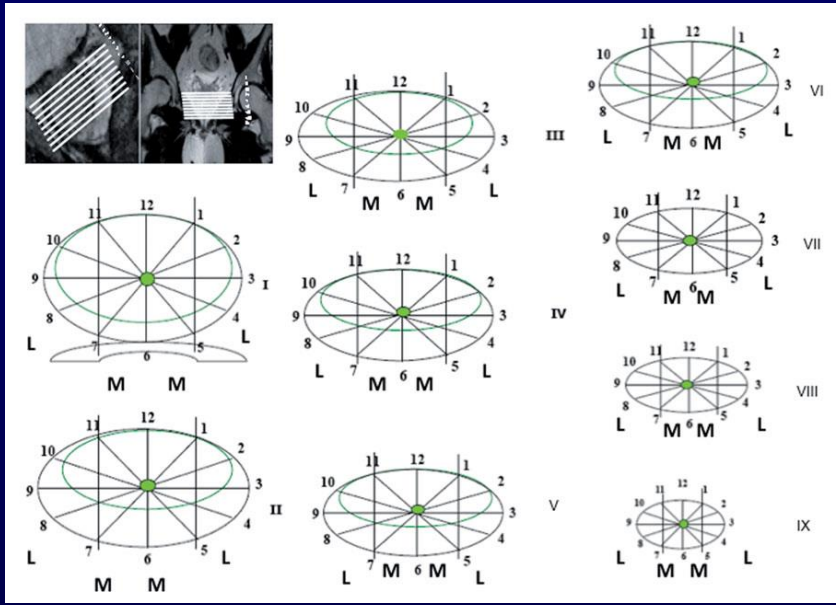
DCE: qualsiasi



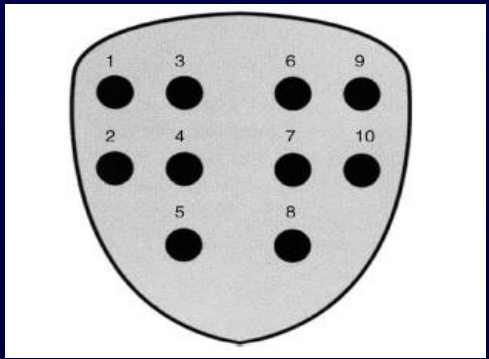
Pi-RADS 5



PROBLEMATICHE: CONFRONTO TRA "MAPPA" DELL'ESAME RM E GUIDA ECOGRAFICA ALLE BIOPSIE

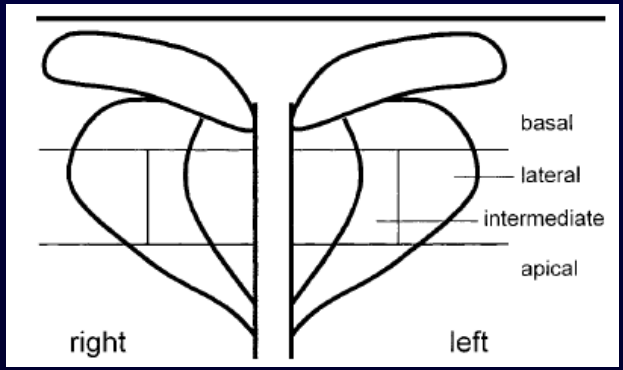


Passariello R et al, Imaging della prostata, Springer Editore

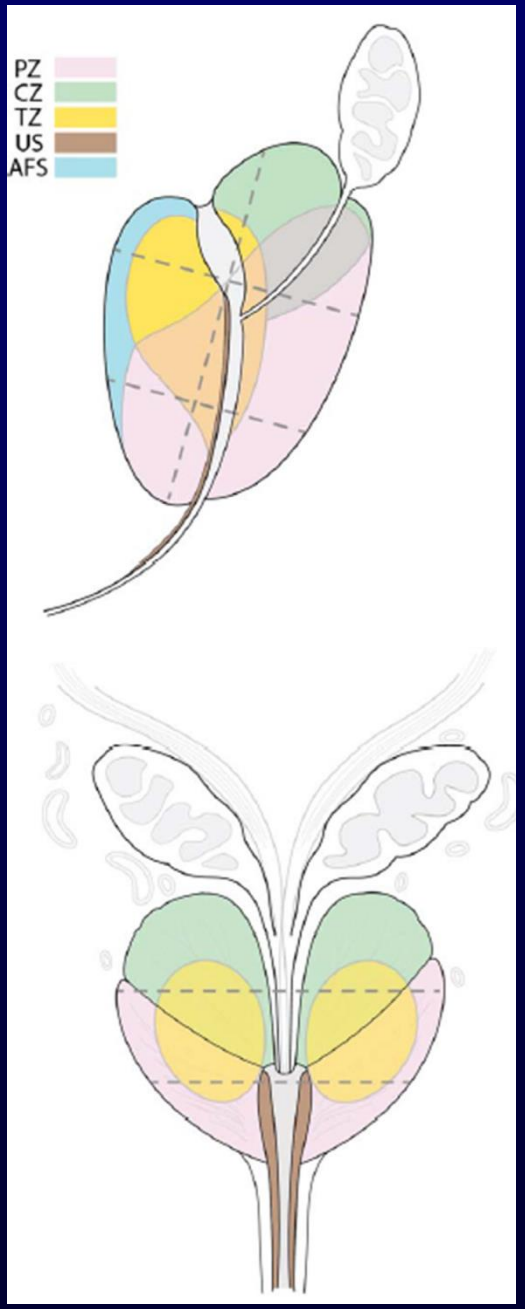


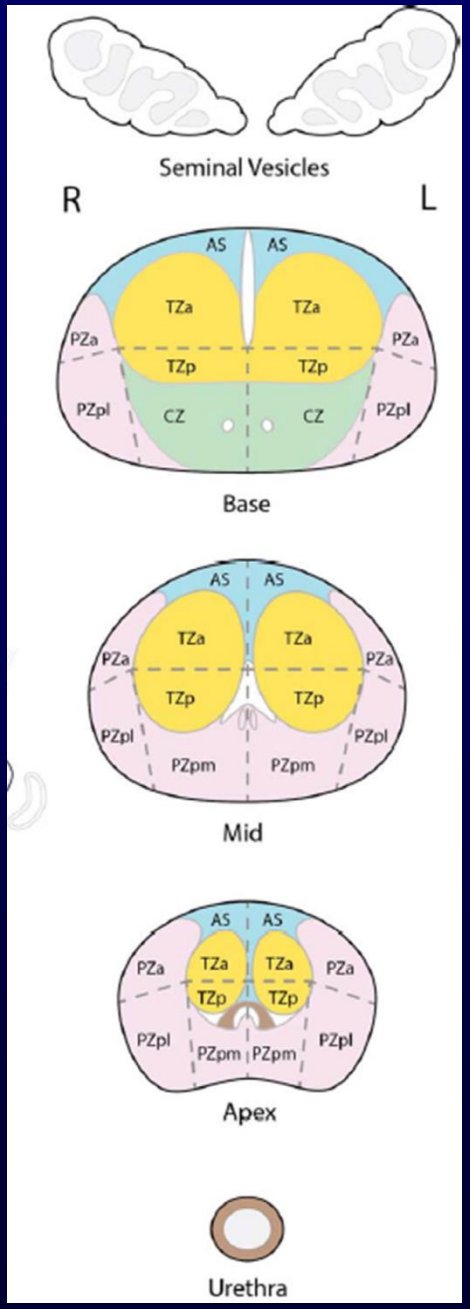
Amsellem-Ouazana, European Urology 2005

Beyersdorff, Radiology 2002



Pi-RADS2:
39 regioni

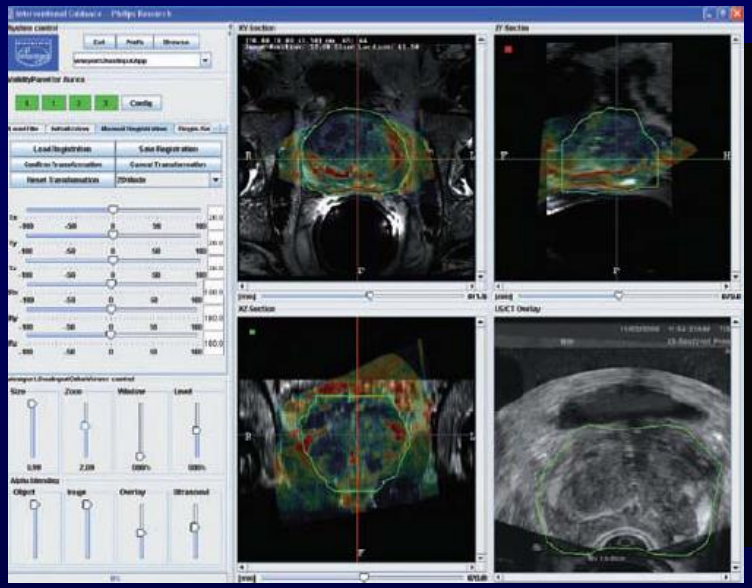


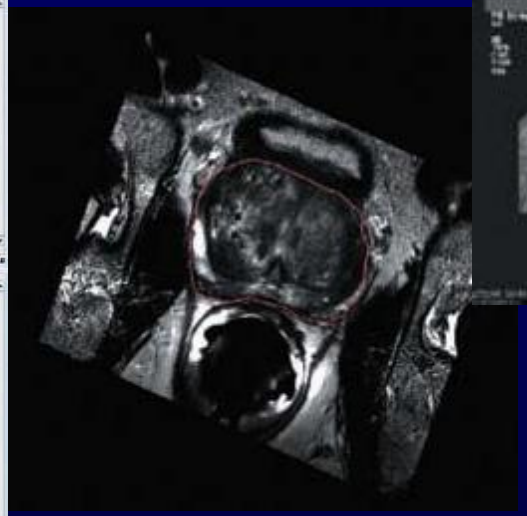


Weinreb C et al
Eur Urol 2016

COME RENDERE PIU' ACCURATE LE BIOPSIE?

- *SOFTWARE DI FUSIONE DELLE IMMAGINI*





Xu S, Comput Aided Surg. 2008

Singh A, BJU 2008

COME RENDERE PIU' ACCURATE LE BIOPSIE?

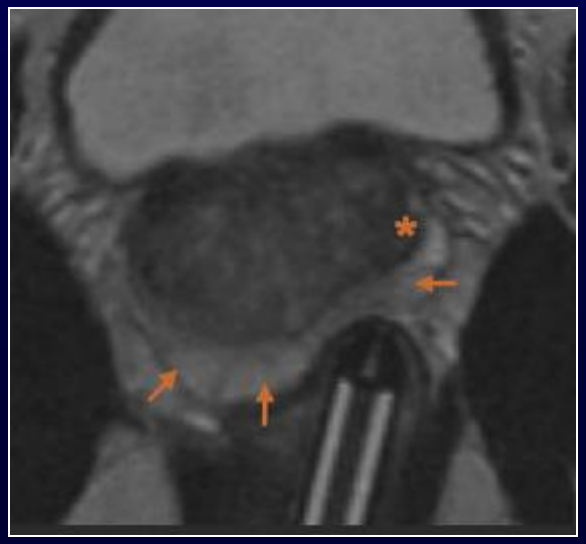
- *ESECUZIONE DI PRELIEVI BIOPTICI DIRETTAMENTE SOTTO GUIDA RM*

MRI-Guided Biopsy of the Prostate Increases Diagnostic Performance in Men with Elevated or Increasing PSA Levels after Previous Negative TRUS Biopsies

Aristotelis G. Anastasiadis[a,,1], Matthias P. Lichy[b,1], Udo Nagele[a], Markus A. Kuczyk[a], Axel S. Merseburger[a], Joerg Hennenlotter[a], Stefan Corvin[a], Karl-Dietrich Sievert[a], Claus D. Claussen[b], Arnulf Stenzl[a], Heinz-Peter Schlemmer[b]*

EUROPEAN UROLOGY

2006



Podman, European Urology 2008

ACCURATEZZA DELLA mpRM NELLA DIAGNOSI DI NEOPLASIA PROSTATICA

Metanalisi PI-RADS 1: sensibilità 78% e specificità 79%

Hamoen EHJ, Eur Urol 2015

PI-RADS 2: sensibilità e specificità> 80%

Nei pazienti ***senza precedenti biopsie*** la mpRM pre-biopsia incrementa di poco la diagnosi di neoplasie clinicamente significative (+10%) e riduce di molto la diagnosi di neoplasie clinicamente non significative (-49%)

NEOPLASIE NON SIGNIFICATIVE:
≤3-5 mm e GS≤3+4

Schoots IG; Eur Urol 2015

QUANDO ESEGUIRE LA RM PRE-BIOPSIA?

Dopo biopsie negative ma con persistenza di PSA elevato

80% dei tumori prostatici già diagnosticati con biopsie random

RM: scarsa disponibilità di apparecchiature e costi elevati

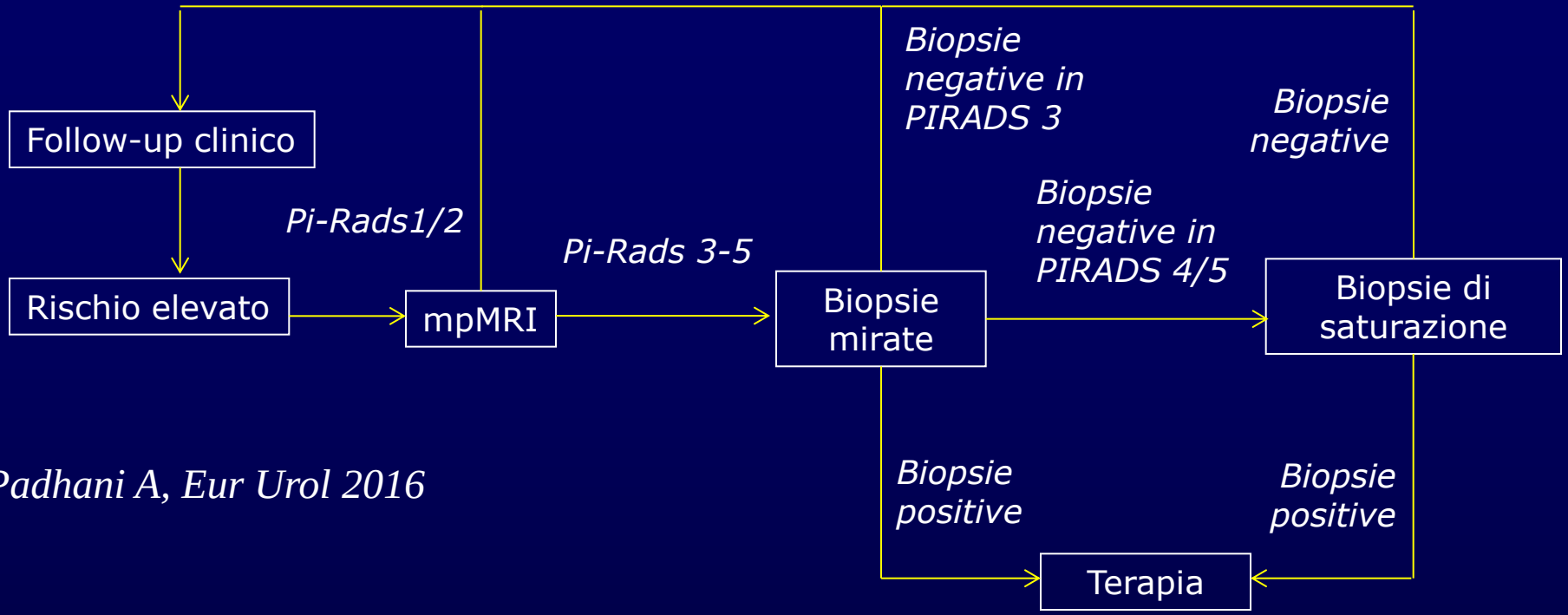
In pazienti «naive»

Prelievi mirati: meno complicanze

Minore diagnosi di tumori clinicamente non significativi

Necessità di ampi studi costo-beneficio

PROPOSTA DI ITER DIAGNOSTICO



Padhani A, Eur Urol 2016

VANTAGGI:
Meno biopsie
Biopsie mirate
Meno diagnosi di neoplasie non significative
Migliore stratificazioni di classi di rischio

TAKE HOME POINTS

- Fondamentale «***ottimizzare***» le immagini
- ***Sequenze funzionali*** indispensabili nella identificazione di neoplasia prostatica (RM multiparametrica!)
- Uniformità di refertazione secondo i criteri ***Pi-Rads2***
- Studi su ampia casistica su ***quando eseguire la RM*** (dopo biopsie preliminari o in pazienti «naive»?)
- Biopsie ***mirate*** ***«realmente»*** con tecnica fusion (o direttamente sotto guida RM)