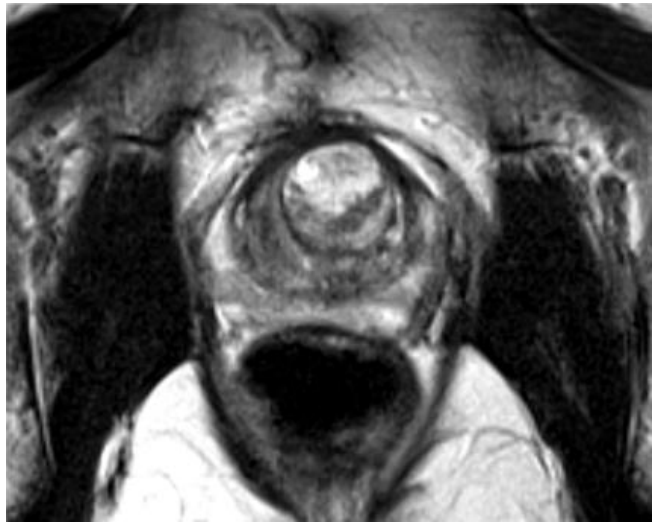
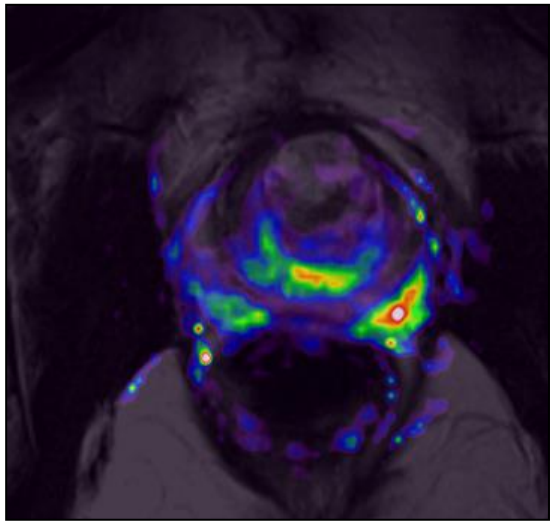
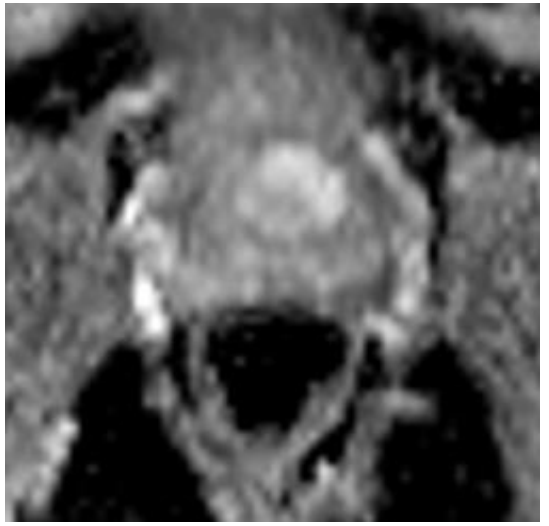
prostatic carcinoma

a role of radiologist in diagnosis and early detection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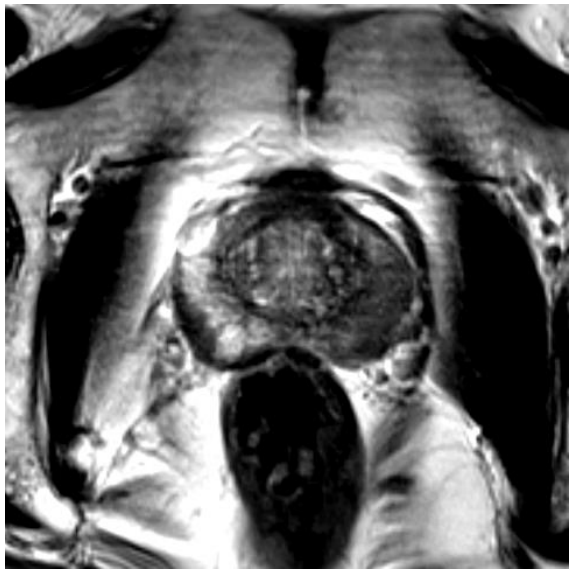
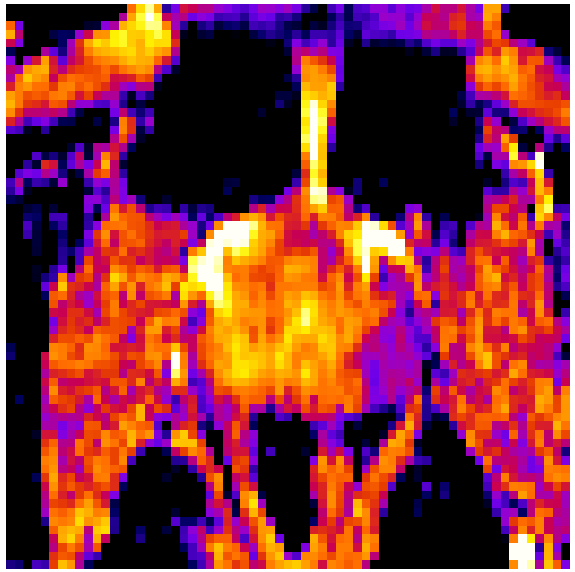
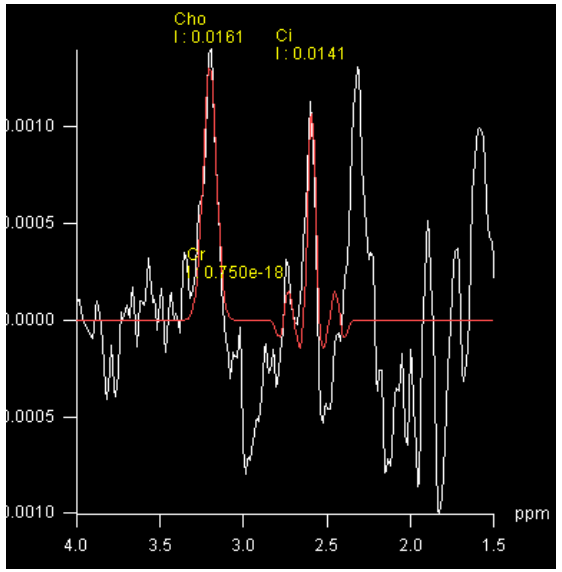
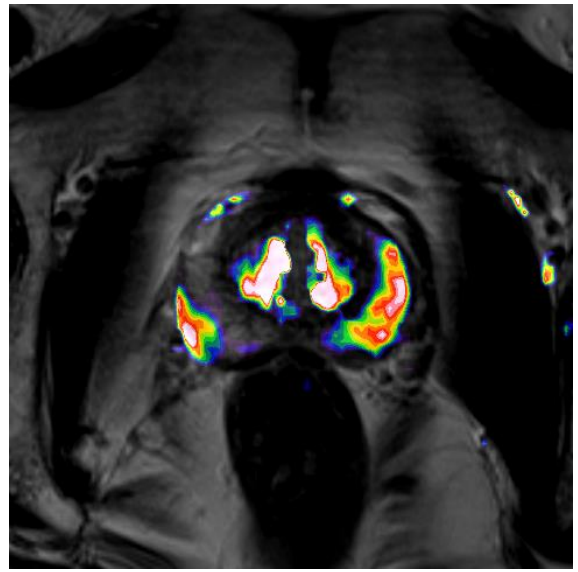
Why magnetic resonance imaging?

- **Acinary carcinoma of prostate**
  - ***2nd to 1st frequent malignant tumor in male population***
  - **Small CAP 1/3 males to 40y let, 2/3 in males over 70y (*)**
  - **detection: PSA, F/T ratio PSA, proPSA, TRUS guided or systemic biopsy**
- **High ratio of true negatives – 2/3 (**) and false negatives – 1/2 (**) findings in systematic biopsy**







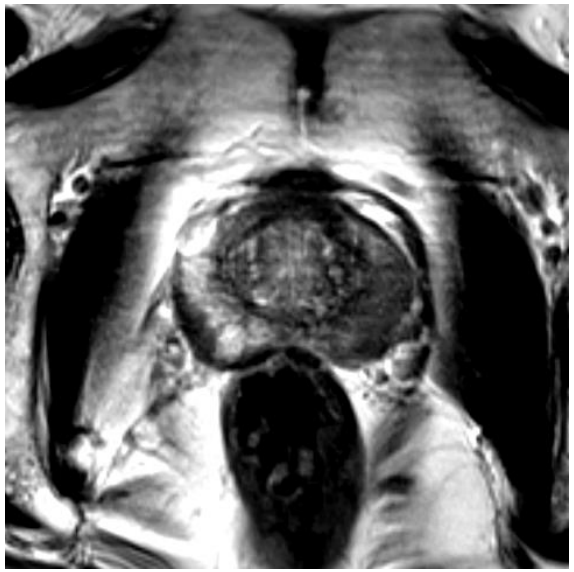


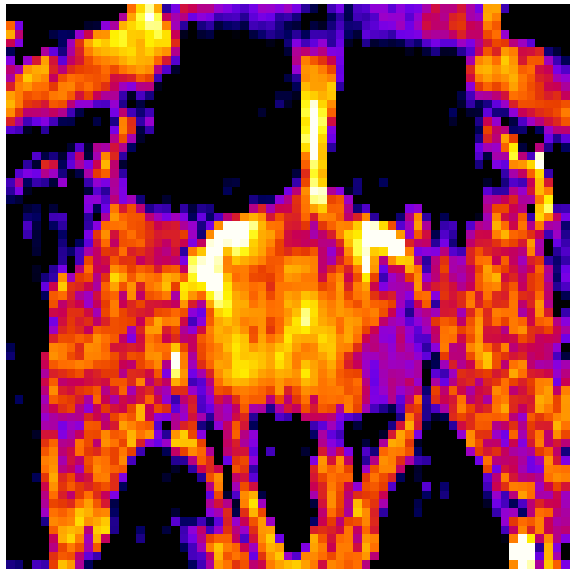
**Schillaci O , Calabria F, Tavolozza M et al.: Influence of PSA, PSA velocity and PSA doubling time on contrast enhanced ^{18}F-choline PET/CT detection rate in patients with rising PSA after radical prostatectomy. Eur J Nucl Med Mol Imaging 2012; 39:589-596*

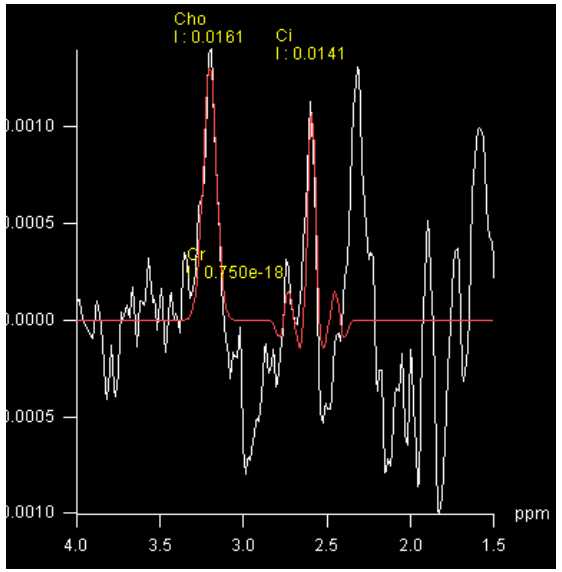
***Roehl KA, Antenor JA, Catalona WJ. Serial biopsy results in prostate cancer screening study. J Urol 2012: 167: 2435-2439*

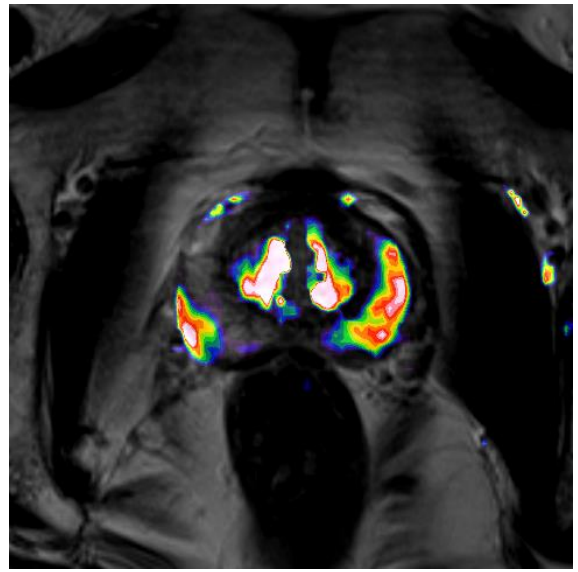
The characteristic of PCA in MRI

- Localization – peripheral or transitional zone
- Hypointense structure on T2 weighted images
- Cellularity properties – restriction of water molecules
- *Increased metabolites and specific molecules*
- Vascular mimicry developed by prostatic carcinoma tissue









Magnetic resonance imaging protocol

PI-RADS®

Prostate Imaging – Reporting and Data System

2019
Version 2.1

ACR American College of Radiology — Quality is Our Image

SUER

AdMeTech Foundation

1. **Magnetic Field Strength**

   The fundamental advantage of 3T compared with 1.5T lies in an increased signal-to-noise ratio (SNR), which theoretically increases linearly with the static magnetic field. This may be exploited to increase spatial resolution, temporal resolution, or both. Depending on the pulse sequence and specifics of implementation, power deposition, artifacts related to susceptibility, and signal heterogeneity could increase at 3T, and techniques that mitigate these concerns may result in some increase in imaging time and/or decrease in SNR. However, current state-of-the-art 3T MRI scanners can successfully address these issues, and most members of the PI-RADS Steering Committee agree that the advantages of 3T substantially outweigh these concerns.

3. **Computer-Aided Evaluation (CAE) Technology**

   Computer-aided evaluation (CAE) technology using specialized software or a dedicated workstation is not required for prostate mpMRI interpretation. However, CAE may improve workflow (display, analysis, interpretation, reporting, and communication), provide quantitative pharmacodynamic data, and enhance lesion detection and discrimination performance for some radiologists, especially those with less experience interpreting mpMRI exams. CAE can also facilitate integration of MRI data with some forms of MR targeted biopsy systems.

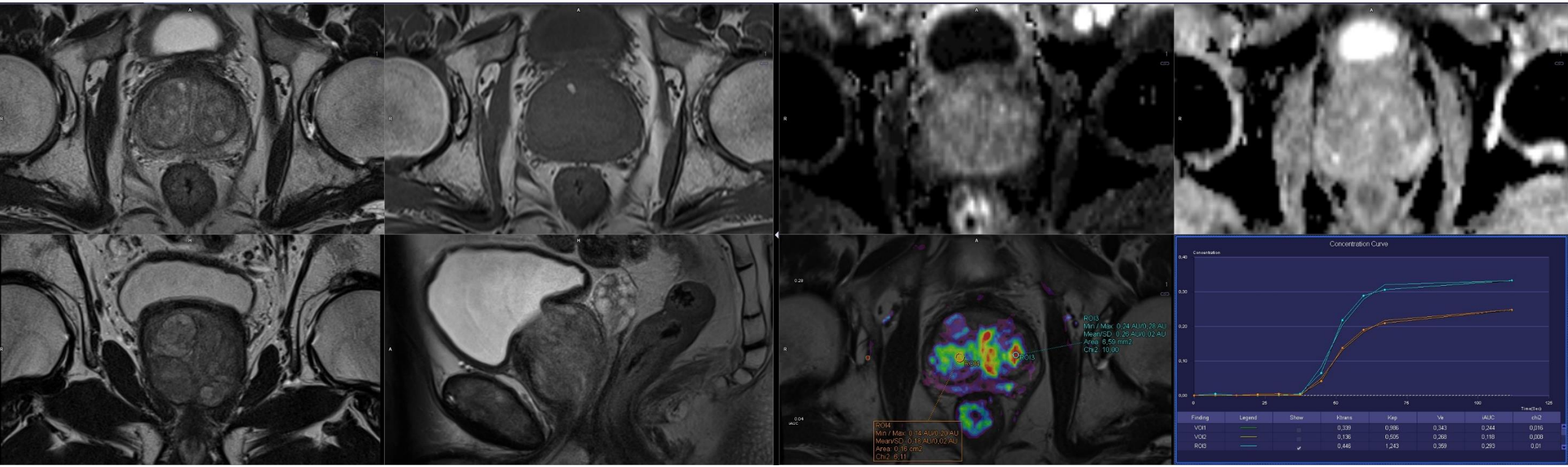
2. **Endorectal Coil (ERC)**

   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.

Magnetic resonance imaging protocol

- T2 weighted imaging – the best spatial resolution
- T1 weighted imaging – detection of methemoglobine
- Diffusion weighted imaging
- *Molecular imaging - MRS spectroscopy (CSI), PET – choline, PSMA-ligands, NaF*
- Dynamic contrast enhanced T1 wighted imaging with Gd-chelates

Turkbey B, Pinto PA, Mani H et al. Prostate cancer: value of multiparametric MR imaging at 3 T for detection – histopatologic correlation. Radiology 2010; 255:89 – 99



Biparametric protocol

Eur J Radiol. 2018 Apr;101:17-23. doi: 10.1016/j.ejrad.2018.01.028. Epub 2018 Feb 1.

Diagnostic accuracy of biparametric vs multiparametric MRI in clinically significant prostate cancer: Comparison between readers with different experience

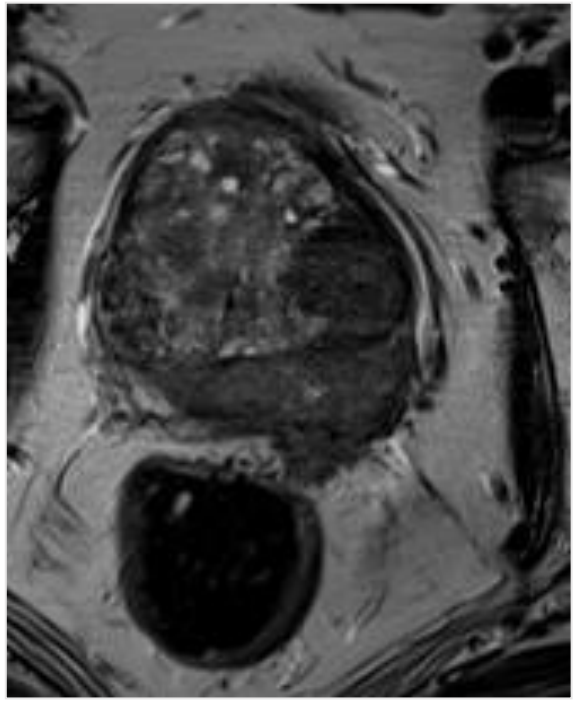
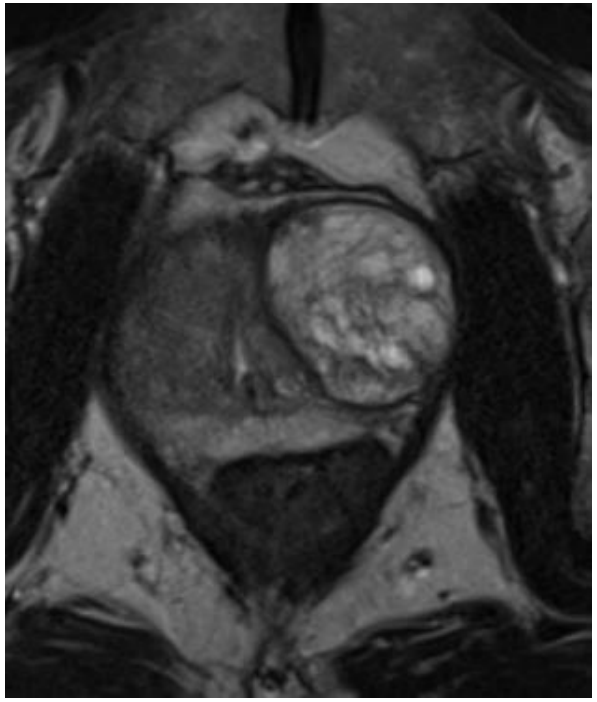
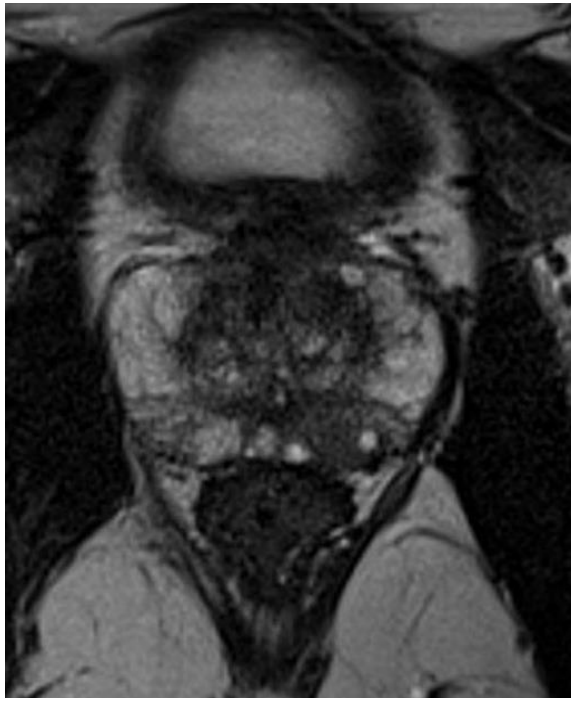
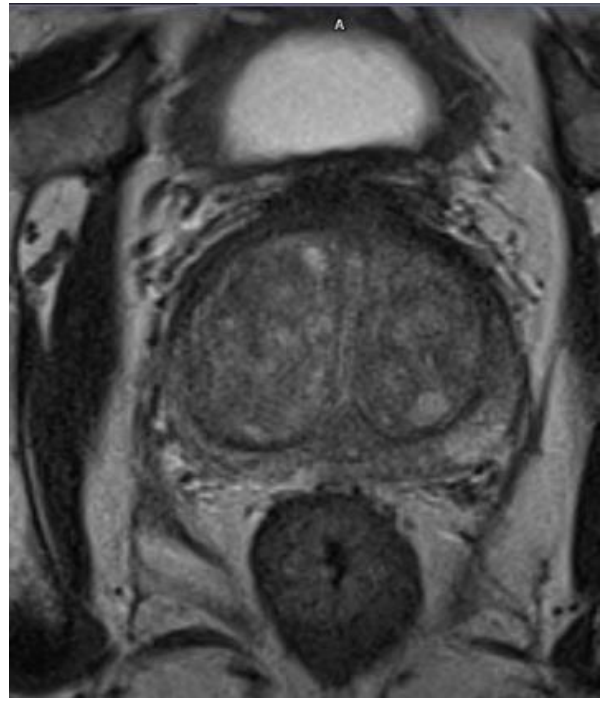
Eleonora Di Campli [1], Andrea Delli Pizzi [2], Barbara Seccia [1], Roberta Cianci [1], Martina d'Annibale [1], Antonella Colasante [3], Sebastiano Cinalli [4], Pietro Castellan [5], Riccardo Navarra [6], Romina Iantorno [4], Daniela Gabrielli [1], Angelica Buffone [1], Massimo Caulo [7], Raffaella Basilico [1]

Conclusion

The diagnostic accuracy of a bi-parametric MR imaging protocol consisting of T2-weighted imaging and DWI is comparable with that of a standard multi-parametric imaging protocol for the detection of clinically significant prostate cancer. The experience of the reader does not significantly modify the diagnostic performance of both MR protocols.

T2 weighted images

- Structure of gland
- Size and volume
- Sector localization
- Invasion
- Therapy planning

T2 weighted images

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	Normal appearing TZ (rare) or a round, completely encapsulated nodule. ("typical nodule")
2	A mostly encapsulated nodule OR a homogeneous circumscribed nodule without encapsulation. ("atypical nodule") OR a homogeneous mildly hypointense area between nodules
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

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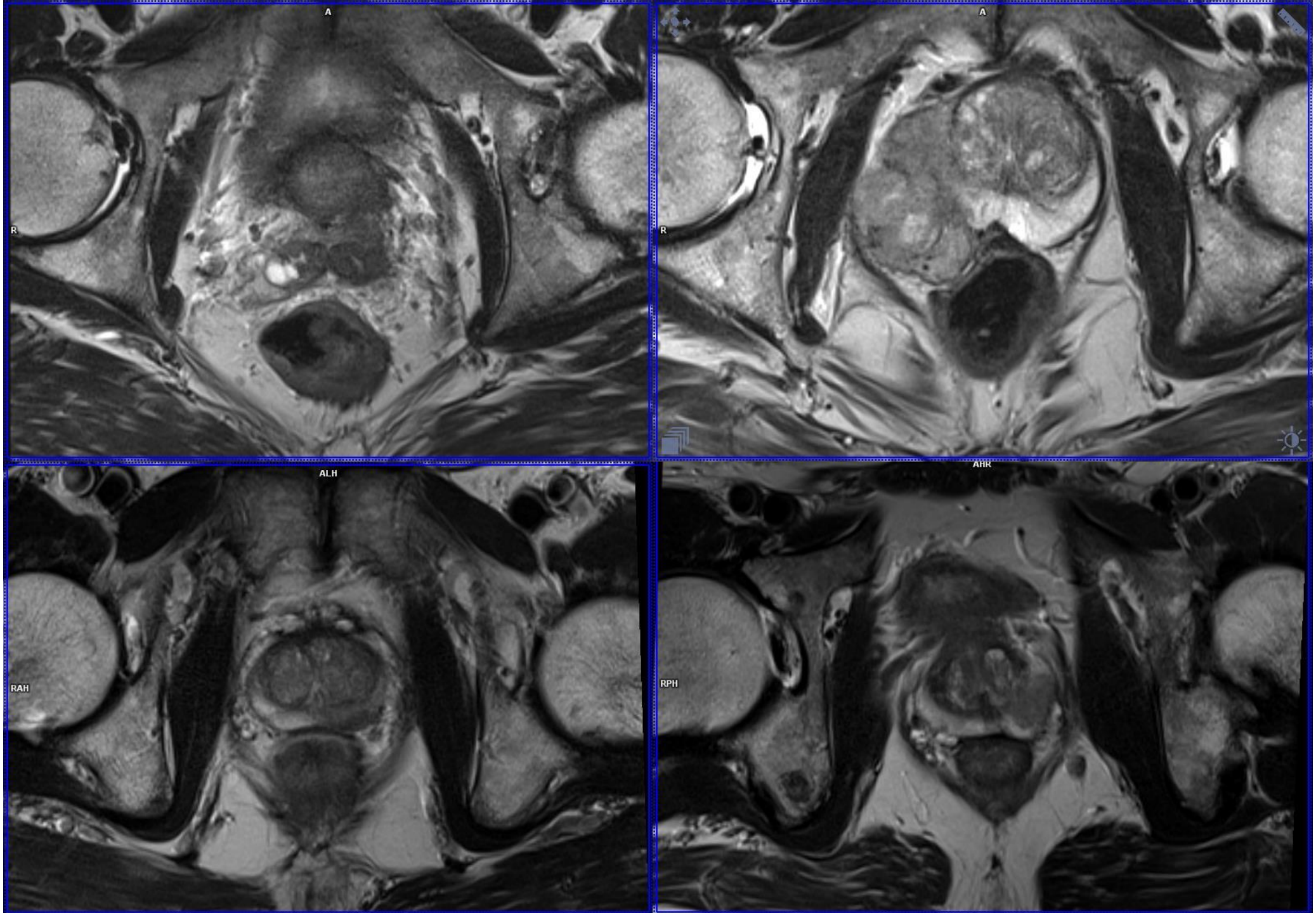
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R
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ALH
RAH
AHR
RPH

Diffusion weighted imaging

- Cellularisation – size of cells and volume of extracellular space
- Restriction of diffusion – water molecules mobility
- Susceptible effect of bleedings and calcifications
- Differential diagnosis of inflammations
- Apparent diffusion coefficient (ADC), high-b-value images




Diffusion weighted imaging

2. PI-RADS Assessment of DWI

Signal intensity in a lesion should be visually compared to the average signal of "normal" prostate tissue in the histologic zone in which it is located.

Score	Peripheral Zone (PZ) or Transition Zone (TZ)
1	No abnormality (i.e., normal) on ADC and high b-value DWI
2	Linear/wedge shaped hypointense on ADC and/or linear/wedge shaped hyperintense on high b-value DWI
3	Focal (discrete and different from the background) hypointense on ADC and/or focal hyperintense on high b-value DWI; may be markedly hypointense on ADC or markedly hyperintense on high b-value DWI, but not both.
4	Focal markedly hypontense on ADC and markedly hyperintense on high b-value DWI; <1.5cm in greatest dimension
5	Same as 4 but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

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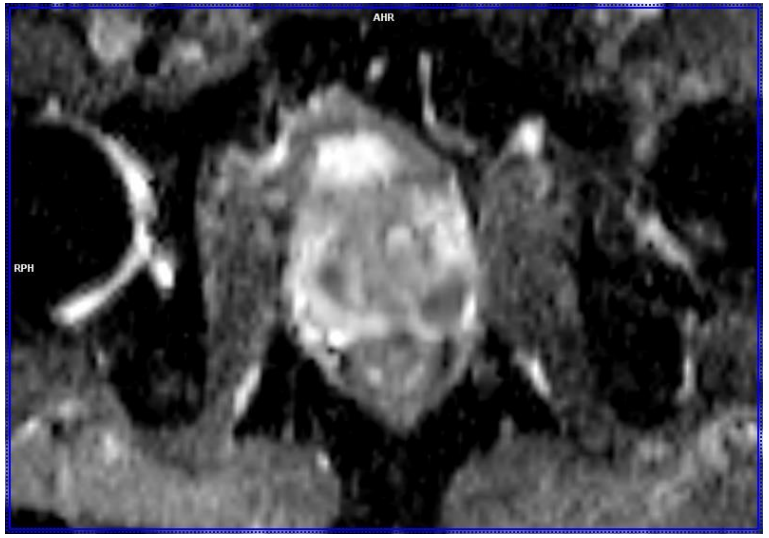
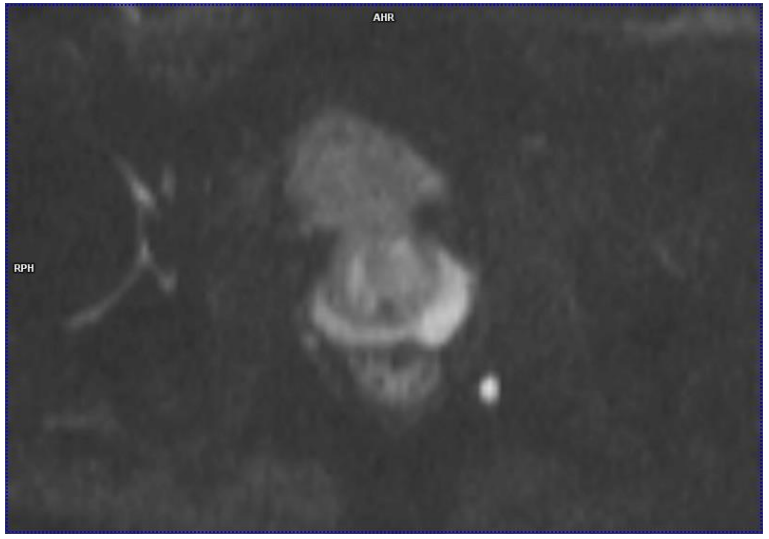
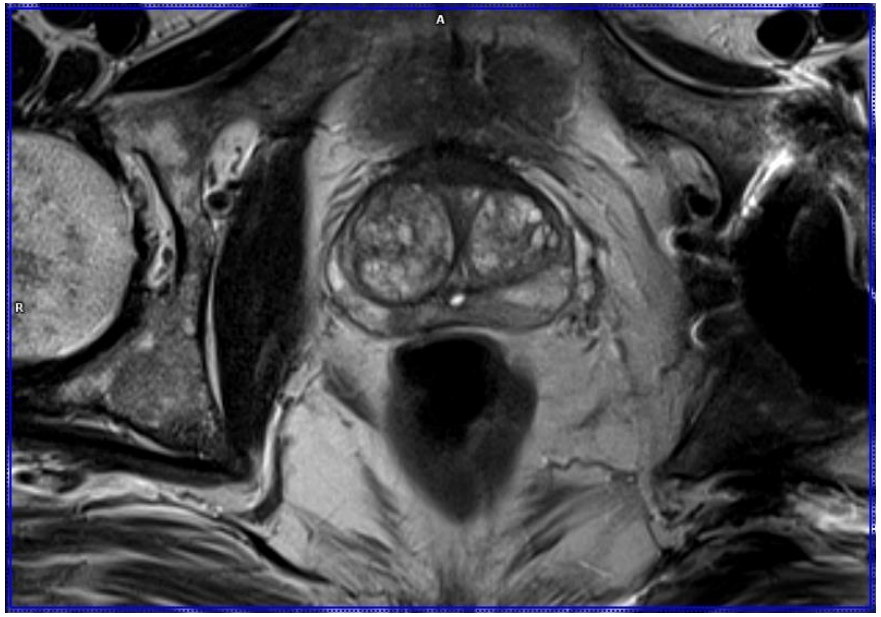
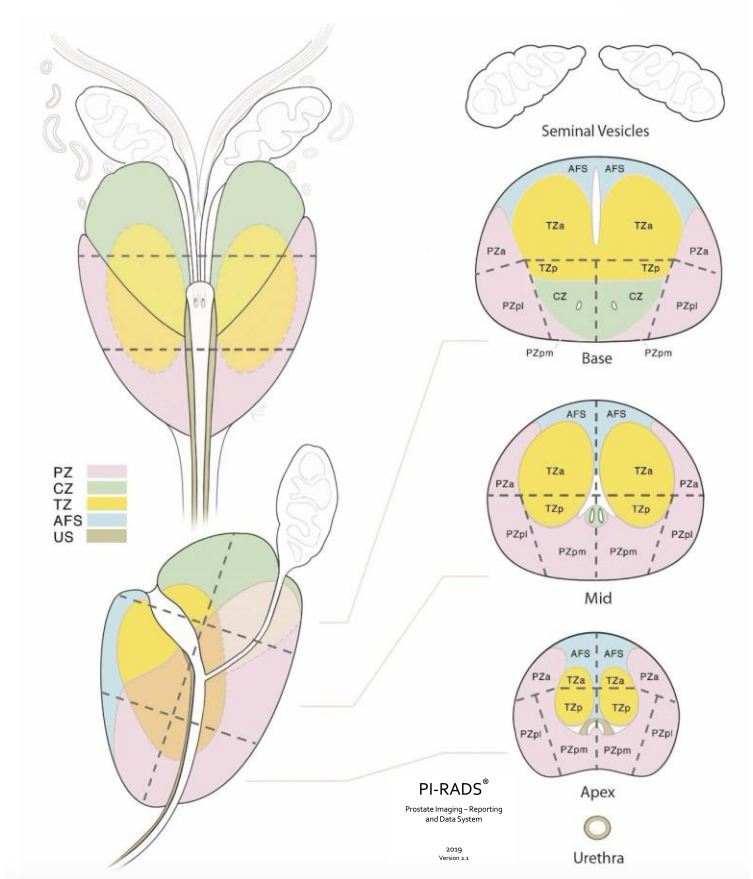


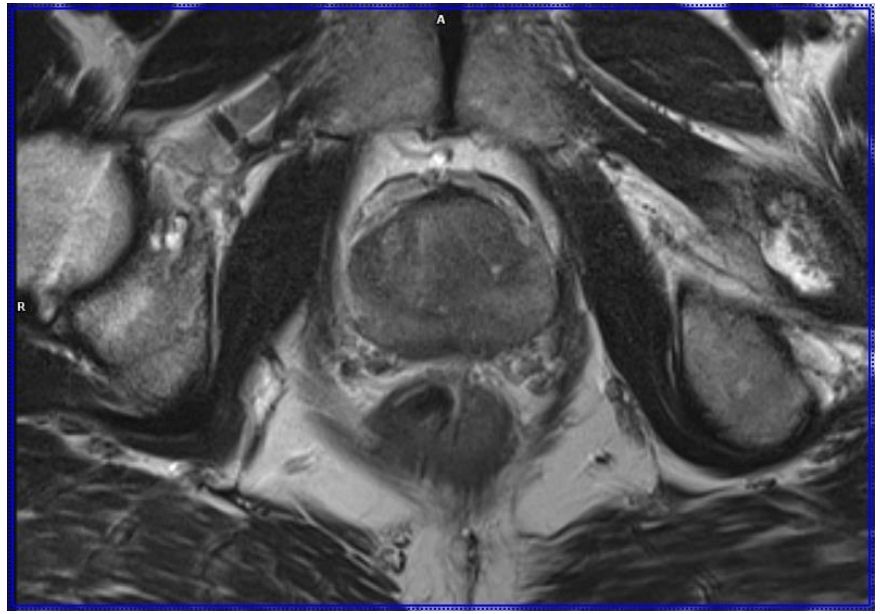


Reporting

PI-RADS^{R} v2.1 Assessment Categories
PI-RADS 1 – Very low (clinically significant cancer is highly unlikely to be present)
PI-RADS 2 – Low (clinically significant cancer is unlikely to be present)
PI-RADS 3 – Intermediate (the presence of clinically significant cancer is equivocal)
PI-RADS 4 – High (clinically significant cancer is likely to be present)
PI-RADS 5 – Very high (clinically significant cancer is highly likely to be present)







PIRADS v2.1 evaluation

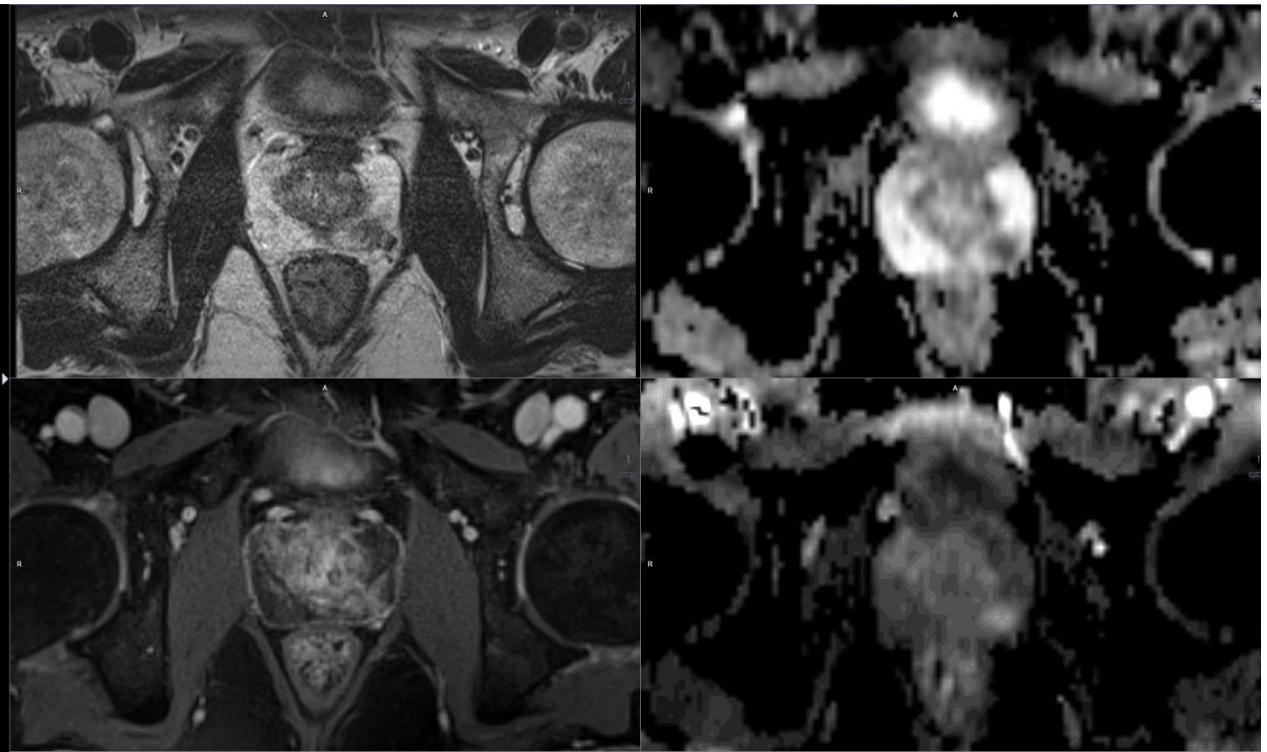
- T2
- DWI
- DCE
- score 1- 5

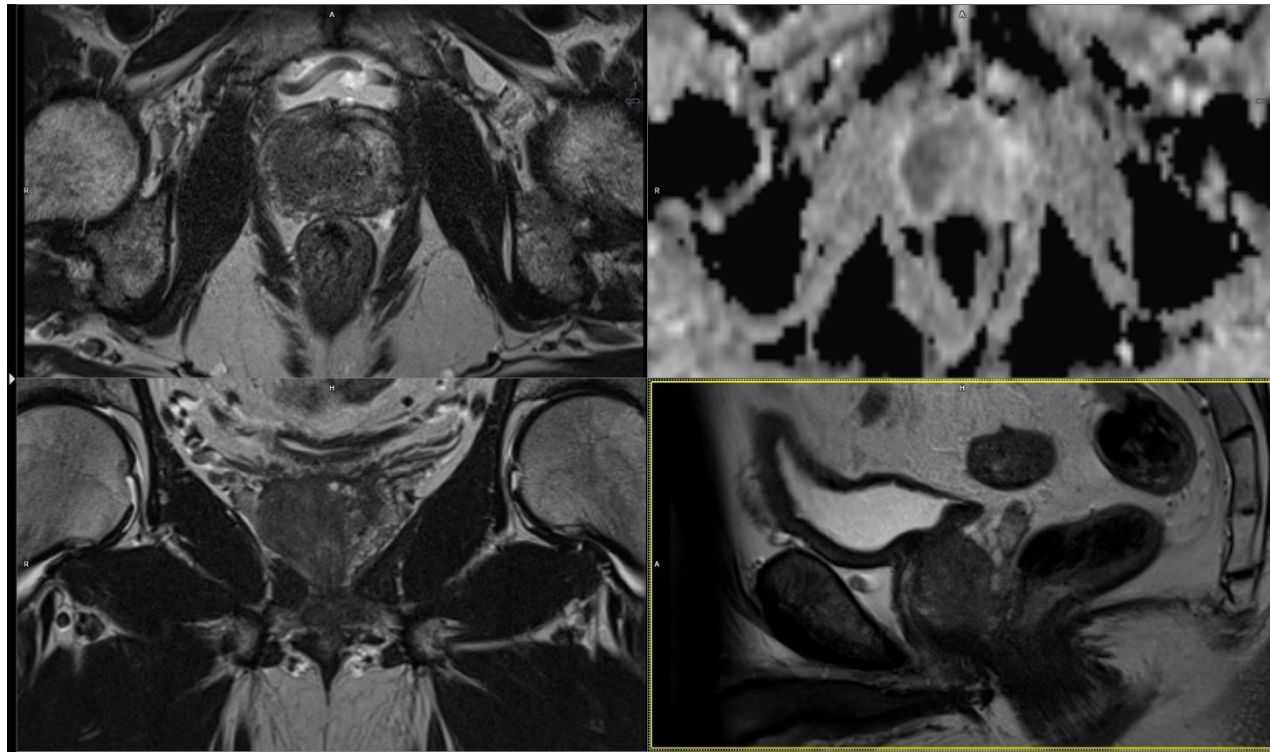
Peripheral zone

	DWI	T2	DCE	score
1		Any*	Any	1
2		Any	Any	2
3		Any	–	3
			+	4
4		Any	Any	4
5		Any	Any	5

	T2	DWI	DCE	score
1		Any*	Any	1
2		Any	Any	2
3		≤4	Any	3
		5	Any	4
4		Any	Any	4
5		Any	Any	5

Transitional zone





Effectivity of MRI

> Value Health. 2021 Dec;24(12):1763-1772. doi: 10.1016/j.jval.2021.06.001. Epub 2021 Aug 6.

Cost-Effectiveness of Magnetic Resonance Imaging in Prostate Cancer Screening: A Microsimulation Study

Shuang Hao [1], Andreas Karlsson [1], Emelie Heintz [2], K Miriam Elfström [3], Tobias Nordström [4], Mark Clements [5]

Affiliations + expand

PMID: 34838274 DOI: 10.1016/j.jval.2021.06.001

Abstract

Objective: This study aimed to assess the cost-effectiveness of magnetic resonance imaging (MRI) with combinations of targeted biopsy (TBx) and systematic biopsy (SBx) for early prostate cancer detection in Sweden.

Methods: A cost-utility analysis was conducted from a lifetime societal perspective using a microsimulation model. Five strategies included no screening and quadrennial screening for men aged 55 to 69 years using SBx alone, TBx on positive MRI (MRI + TBx), combined TBx/SBx on positive MRI (MRI + TBx/SBx), and SBx on negative MRI with TBx/SBx on positive MRI (MRI - SBx, MRI + TBx/SBx). Test characteristics were based on a recent Cochrane review. We predicted the number of biopsies, costs, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios.

Results: The screening strategies were classified in Sweden as high costs per QALY gained compared with no screening. Using MRI + TBx and MRI + TBx/SBx reduced the number of biopsy episodes across a lifetime by approximately 40% compared with SBx alone. Both strategies showed strong dominance over SBx alone and MRI - SBx, MRI + TBx. Compared with MRI + TBx, the MRI + TBx/SBx strategy had an incremental cost-effectiveness ratio of more than €200 000 per QALY gained, which was classified in Sweden as a very high cost. These predictions were robust in the probabilistic sensitivity analysis. Limitations included generalizability of the model assumptions and uncertainty regarding the health-state values and study heterogeneity from the Cochrane review.

Conclusions: MRI + TBx and MRI + TBx/SBx showed strong dominance over alternative screening strategies. MRI + TBx resulted in similar or marginally lower gains in QALYs and lower costs than MRI + TBx/SBx. MRI + TBx was considered the optimal choice among the screening strategies.

Keywords: Sweden; biopsy; cost-effectiveness; magnetic resonance imaging; microsimulation; prostate cancer; screening.

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Table 1. Input parameters used in the cost-effectiveness analysis.

Test characteristics—all countries			
No.	**Meta-analyses**	**Probability (*P*)**	**95% CI**
1	Probability of positive MRI results (GG = 0)	Pr (MRI + | GG = 0)	.452	(0.343, 0.565)
2	Probability of positive MRI results (GG = 1)	Pr (MRI + | GG = 1)	.715	(0.614, 0.798)
3	Probability of positive MRI results (GG ≥ 2)	Pr (MRI + | GG ≥ 2)	.931	(0.893, 0.956)
4	False-negative rate of SBx strategy (GG = 1)	Pr (SBx- | GG = 1)	.140	(0.111, 0.176)
5	False-negative rate of SBx strategy (GG ≥ 2)	Pr (SBx- | GG ≥ 2)	.103	(0.053, 0.191)
6	False-negative rate of TBx (GG = 1, MRI +)	Pr (TBx- | GG = 1, MRI +)	.247	(0.125, 0.432)
7	False-negative rate of TBx (GG ≥ 2, MRI +)	Pr (TBx- | GG ≥ 2, MRI +)	.066	(0.038, 0.111)

Unit costs per patient (€) and time of lost production—Sweden				
Module/procedure	**Unit costs/patient (€)**	**Remarks of unit costs**	**Lost production**	**Unit of lost production**
Diagnosis				
PSA test at primary care	35		2	Hour
SBx at outpatient care	888		2	Hour
MRI with TBx at outpatient care	1227		4	Hour
MRI with TBx/SBx at outpatient care	1376		4	Hour
Treatment				
Active surveillance at outpatient care: without MRI	496	*Annual cost*	8.66	Hour
Active surveillance at outpatient care: with MRI + TBx	608	*Annual cost*	9.32	Hour
Active surveillance at outpatient care: with MRI + TBx/SBx	657	*Annual cost*	9.32	Hour
Radical prostatectomy at inpatient care: robot-assistant	15 028		6	Week
Radiation therapy at outpatient care	14 930		8	Week
Metastatic: chemo + hormone therapy	6979	*Annual cost*	68*	Day
Metastatic: hormone therapy	6580	*Annual cost*	68*	Day
Post treatment follow-up				
Post treatment follow-up: first year	183		2	Hour
Post treatment follow-up: years after	55	*Annual cost*	2	Hour
Palliative therapy	15 755	*Annual cost*	68*	Day
Terminal illness	7878		6	Month

Effective MRI-guided flowchart?

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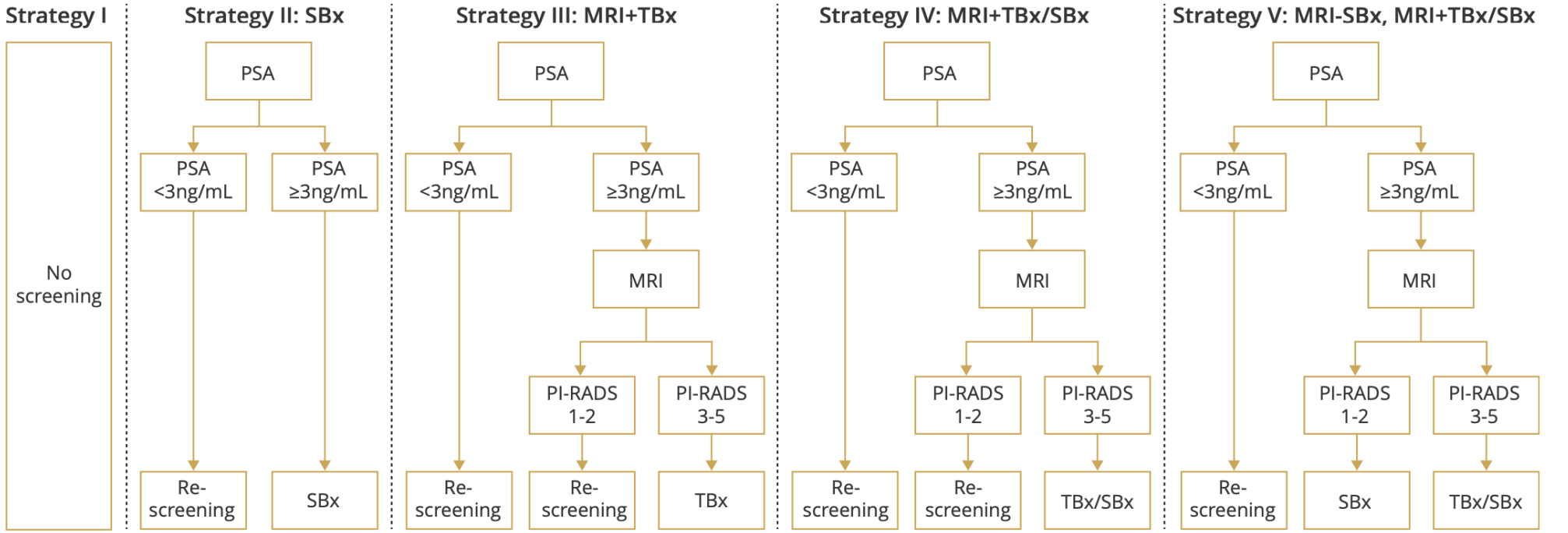
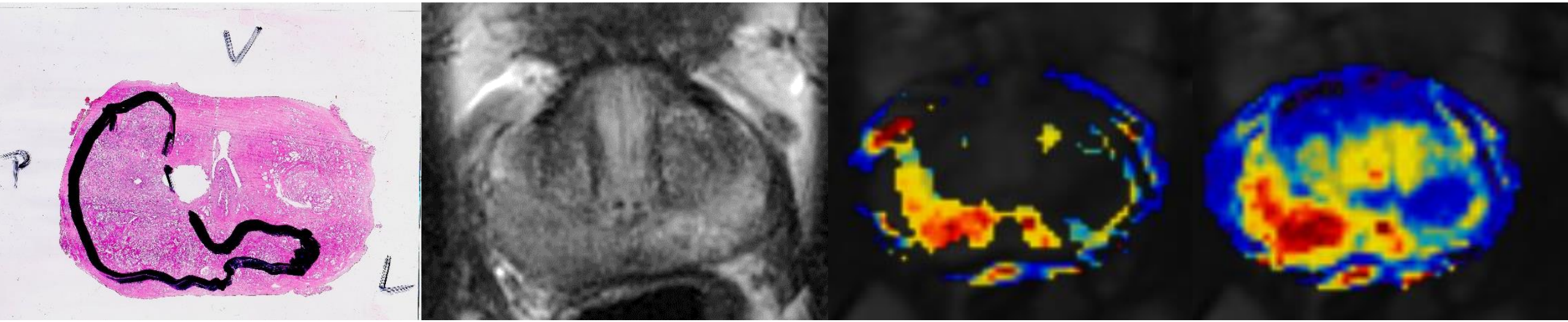
Figure 1. Illustration of the 5 strategies.



MRI indicates magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; SBx: systematic biopsy; Strategy I, no screening for prostate cancer; strategy II, quadrennial PSA screening using SBx alone; strategy III, quadrennial PSA screening using MRI, with TBx on positive MRI results; strategy IV, quadrennial PSA screening using MRI, with combined TBx/SBx on positive MRI results; strategy V, quadrennial PSA screening MRI, with SBx on negative MRI results and combined TBx/SBx on positive MRI results; TBx, targeted biopsy.

A role of DCE-MRI

- Neoangiogenesis – prostate carcinoma forming vascular mimicry
- Structural and functional changes of glandular tissue – different GS3 and GS5
- Adenomyomatous tissue is hyperperfused – typical finding in hyperplastic nodes
- Perfusion chages related redistribution of drugs (radiopharmaceuticals)



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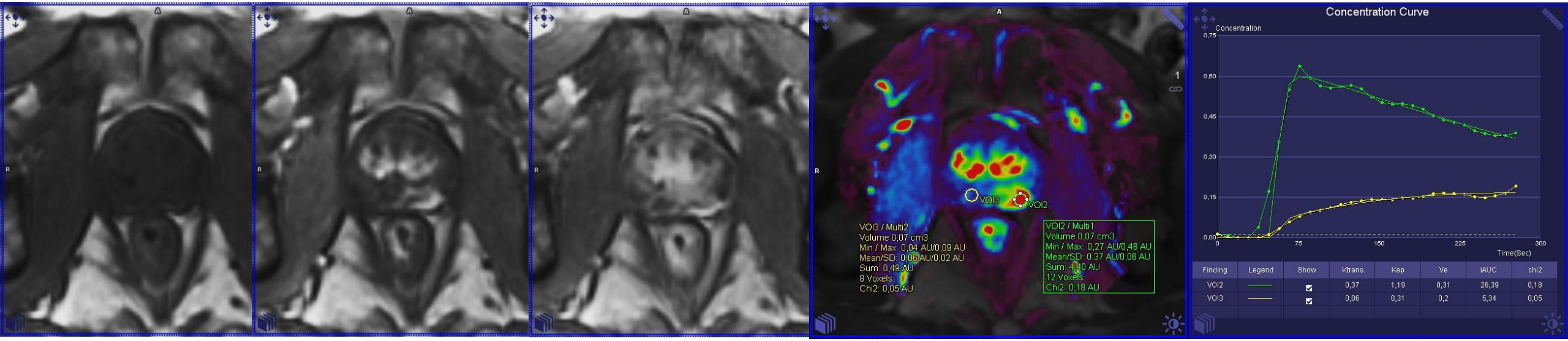
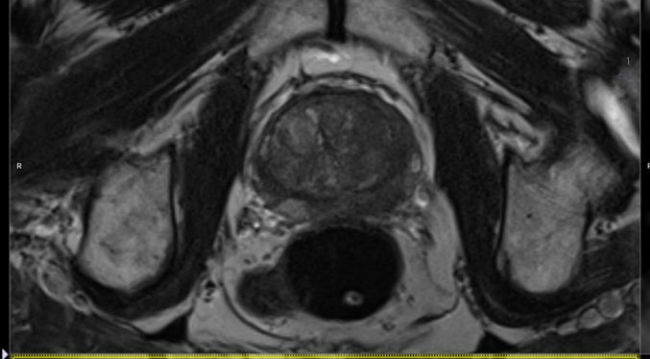
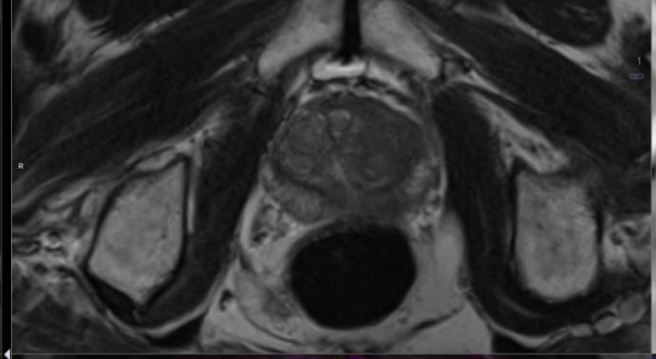
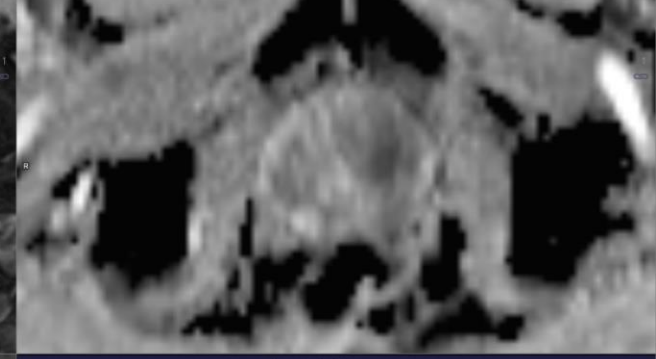
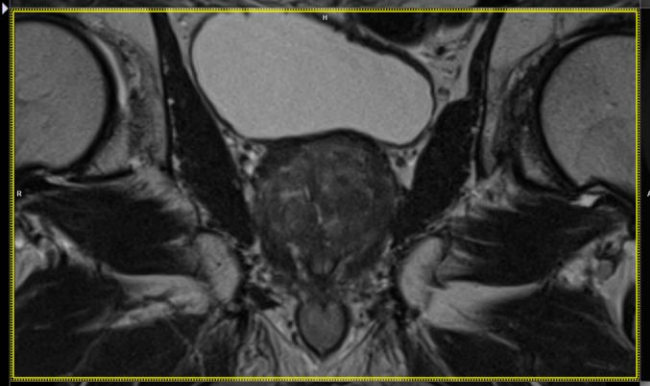
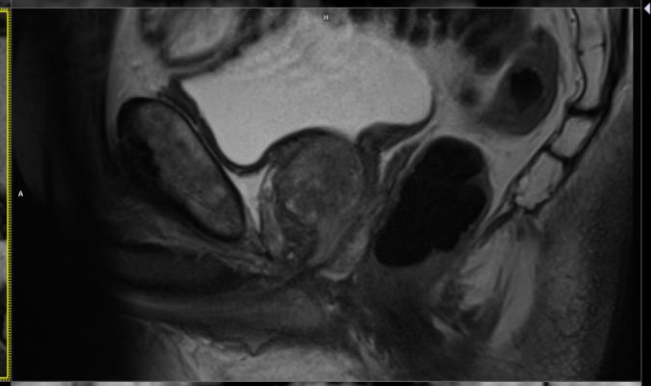
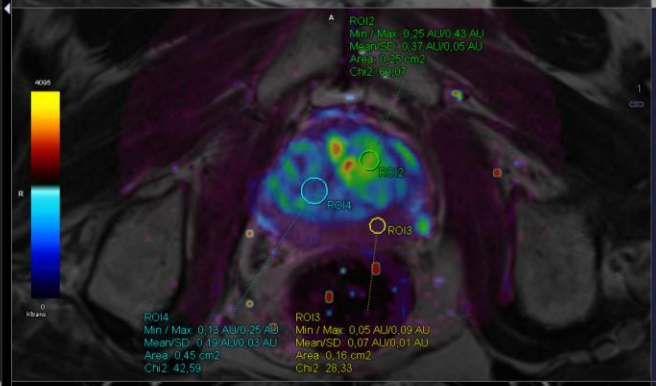
**Roehl KA, Antenor JA, Catalona WJ. Serial biopsy results in prostate cancer screening study. J Urol 2012: 167: 2435-2439

Dynamic contrast enhanced (DCE) MRI

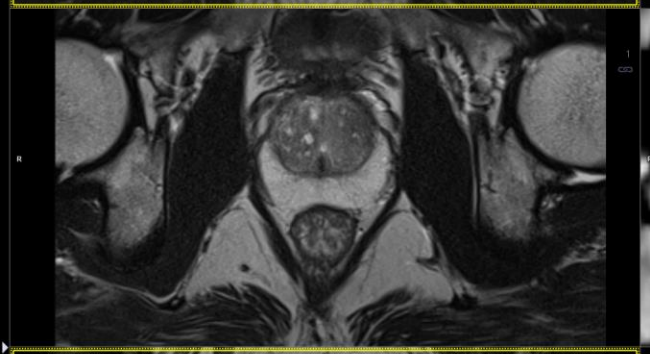
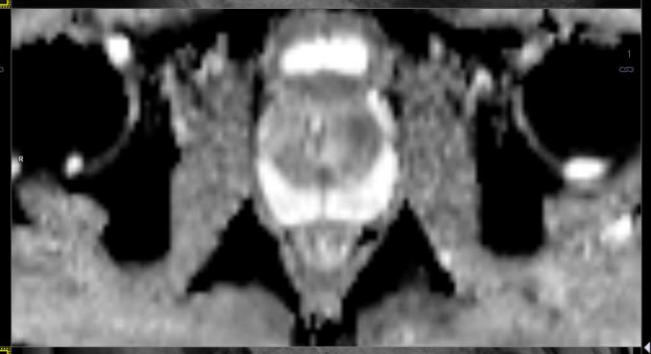
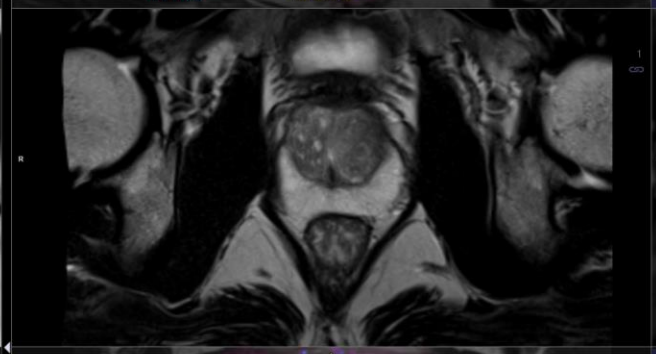
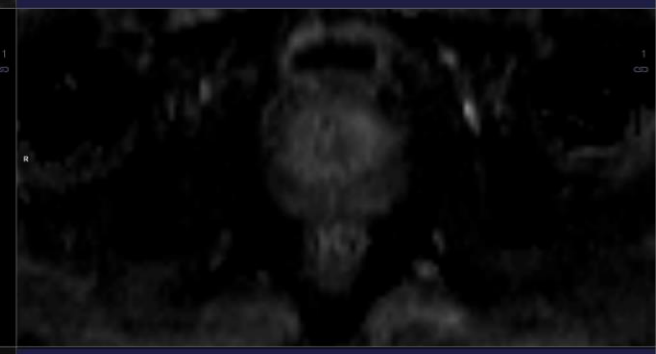
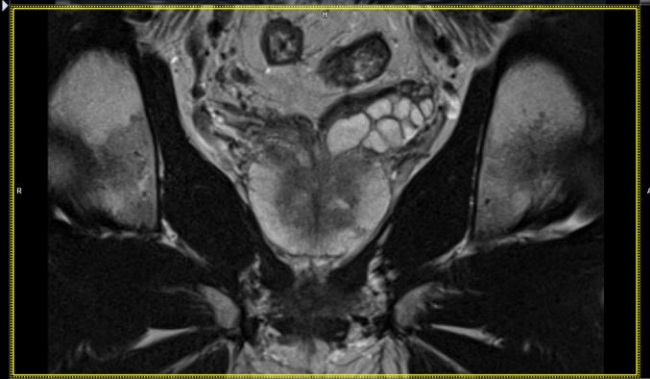
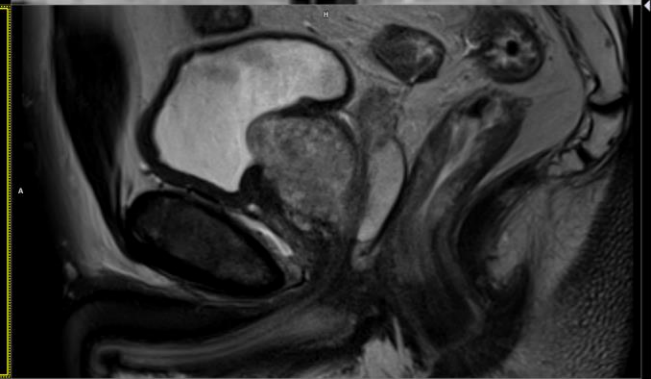
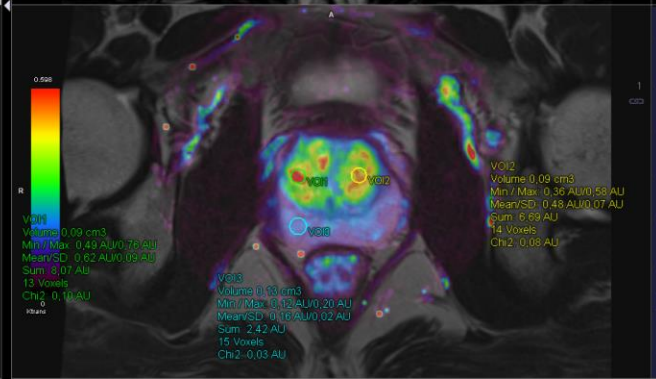
- Intravenous administration of gadolinium chelate
- Dynamic T1 weighted sequence of gradient echo
- Pharmacokinetic analysis
- Tofts‘ two-compartment model - K_{trans}, iAUC, V_e, K_e





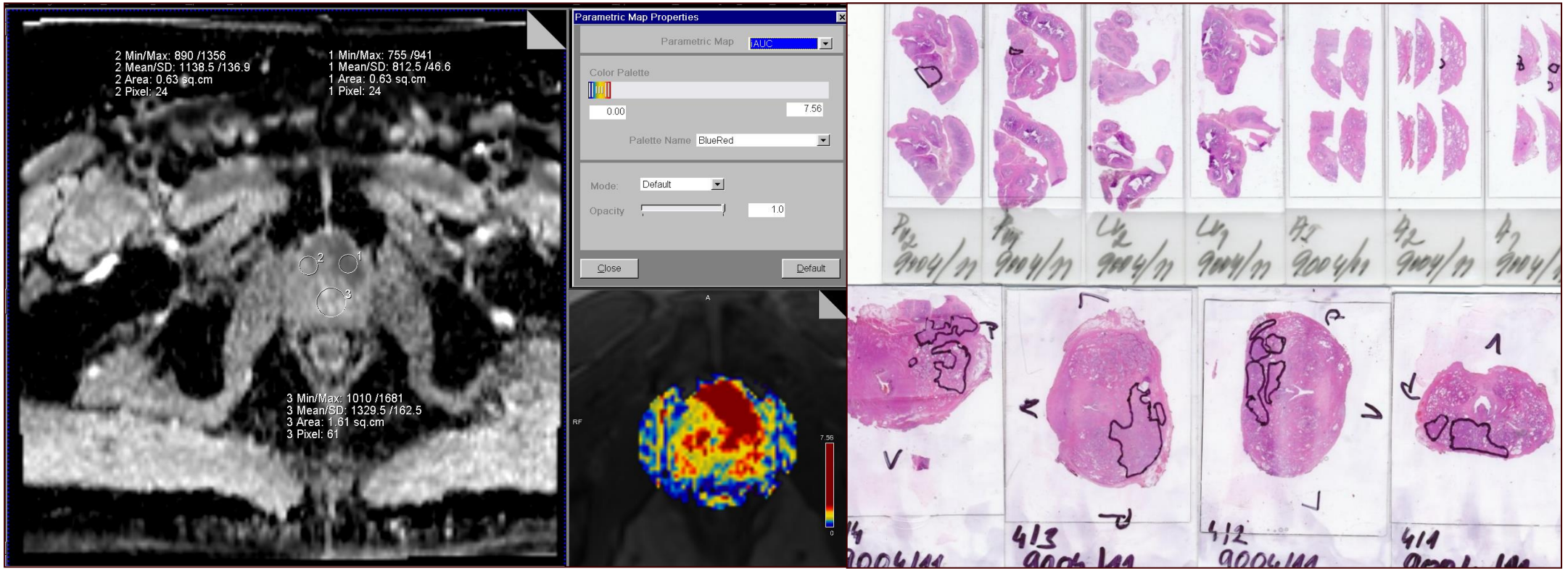
Finding	Legend	Show	Ktrans	Kep	Ve	iAUC	chi2
ROI2		✔	0,388	1,162	0,334	0,362	0,05
ROI3		✔	0,083	0,284	0,291	0,096	0,018
ROI4		✔	0,174	0,374	0,467	0,195	0,028

Finding	Legend	Show	Ktrans	Kep	Ve	iAUC	chi2
VOI1		✔	0,612	1,321	0,464	0,449	0,091
VOI2		✔	0,474	1,088	0,436	0,378	0,072
VOI3		✔	0,16	1,135	0,141	0,117	0,019

Effectivity of MRI-guided biopsy

- University Hospital Pilsen - 2012
- prospective study versus MRI-guided biopsy



Anticancer Res. 2013 Jun;33(6):2791-5.

A role of multifactorial evaluation of prostatic 3T MRI in patients with elevated prostatic-specific antigen levels: prospective comparison with ultrasound-guided transrectal biopsy.

Ferda J, Kastner J, Hora M, Hes O, Fínek J, Topolčan O, Kreuzberg B.

Author information

Abstract

AIM: To assess the role of multiparametric 3T magnetic resonance (3TMRI) of the prostate in detection of the prostatic carcinoma in a male population with elevated prostatic-specific antigen (PSA) and to compare the results with those of transrectal biopsies.

MATERIALS AND METHODS: A prospectively collected cohort of 191 men underwent 3T MRI before transrectal biopsy. The evaluation consisted of the assessment of T2-weighted images, diffusion-weighted images, MR spectroscopy and the pharmacokinetic evaluation of the data obtained during the dynamic post-contrast T1 imaging. The assessment included the calculation of the blood volume and transfer constant evaluations. The diagnosis of prostate carcinoma was based on a minimum of three positive signs obtained from MR studies--hypointensive T2 lesion, diffusion restriction, elevated choline/creatine peak in spectrum and malignant type of saturation by contrast agents. All biopsies were evaluated by a specialist in uropathology.

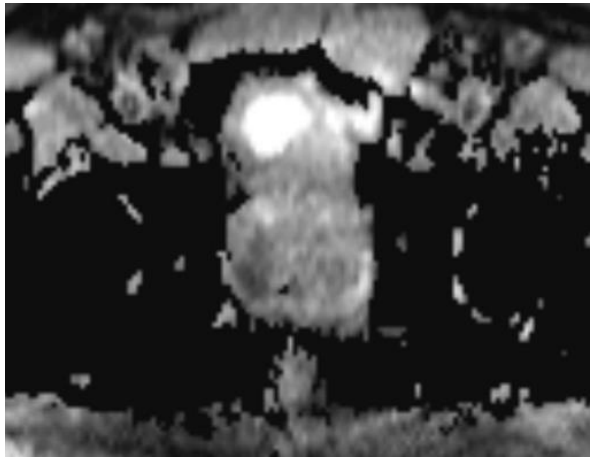
RESULTS: 164 patients underwent biopsy, in 27 the biopsy was omitted due to a lack or low probability of carcinoma: Overall, 84 carcinomas were found. Based on the comparison of biopsy results, 3T MRI reached a sensitivity of 97.6%, specificity of 85.0%, positive predictive value of 74.6% and negative predictive value of 96,3% respectively. There were only three false negative findings. In three patients with very suspicious MRI findings and PSA levels over 30 ng/ml, the biopsy did not confirm carcinoma, even though it was highly suspected.

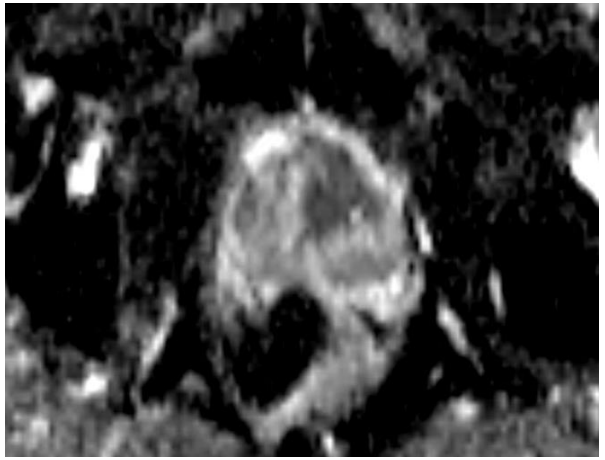
CONCLUSION: The implementation of 3T MRI in routine assessment of patients with elevated PSA should reduce the number of biopsies performed and improve the number of tumors detected due to better targeted biopsies.

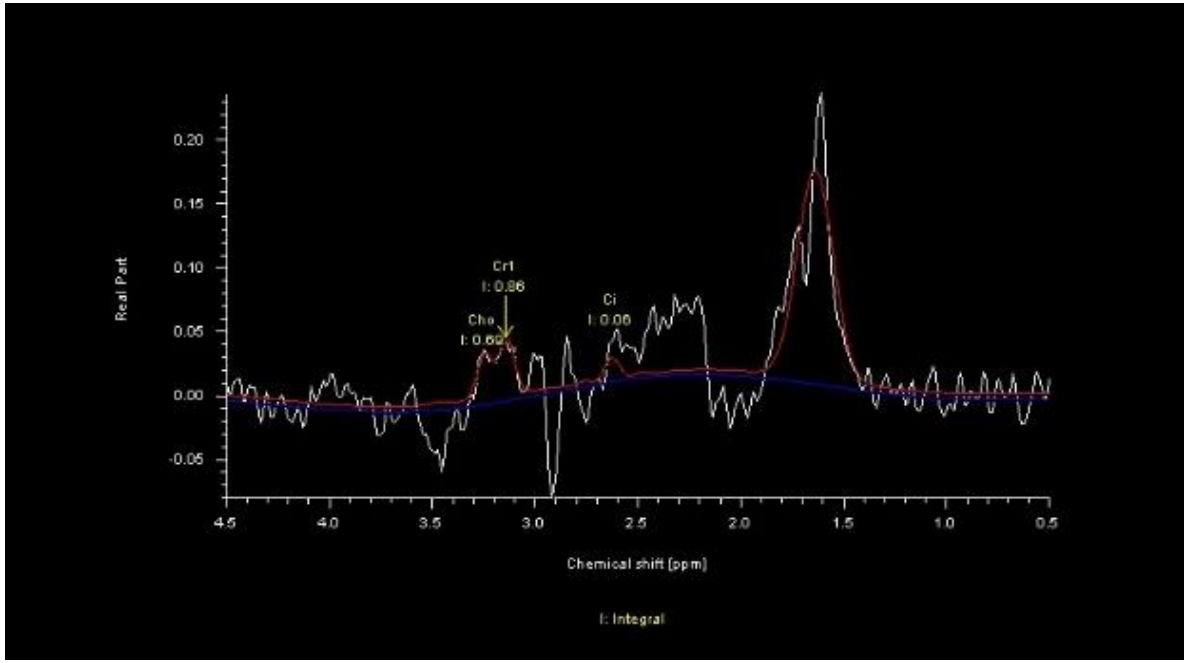
KEYWORDS: 3T magnetic resonance, PSA, prostatic carcinoma, transrectal biopsy

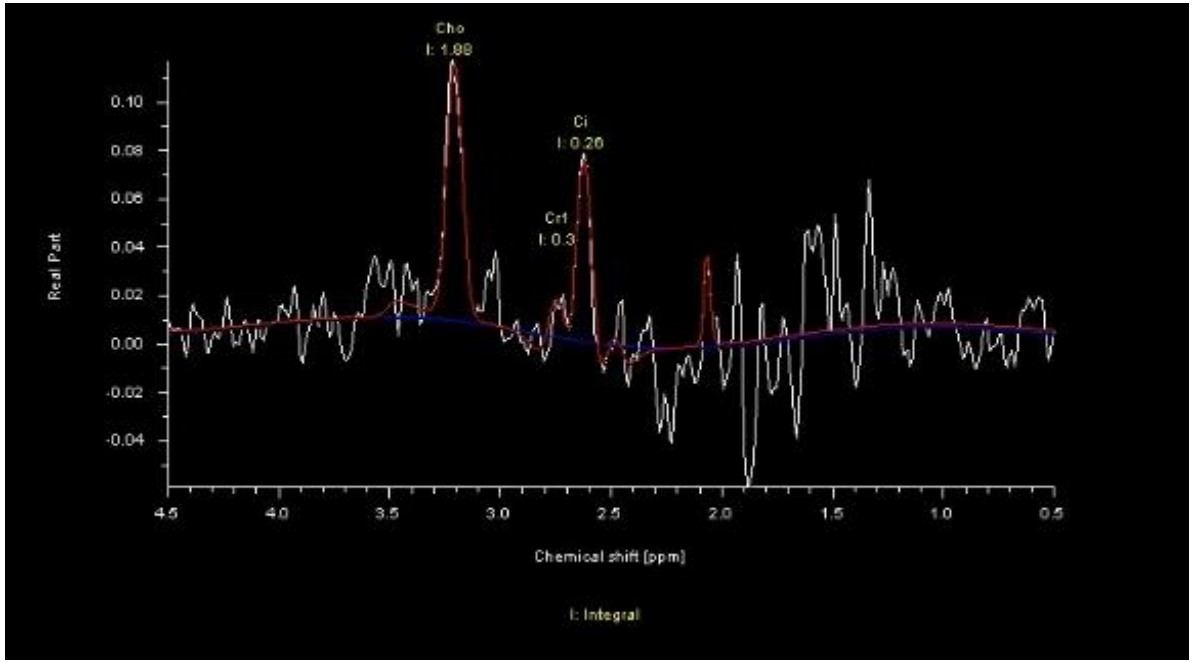
PMID: 23749943 [PubMed - indexed for MEDLINE]

A role of spectroscopy?









A role of ^{68}Ga-PSMA-11 PET

- **STAGING of risky PCA**
- **Glutamatecarboxypeptidase II (GCPII)**
  - *N-acetyl-L-aspartyl-L-glutamate-peptidase*
- **prostate-specific membrane antigen (PSMA)**
  - *750 aminoacids - membrane glycoprotein of II. class*
- **^{68}Ga-PSMA-11-PET**
  - *becoming current standard of the PCa staging*
  - **^{68}Ga-PSMA-11 related to PSMA expression**
  - **The relation of PSMA expression with GS**

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Assessment of Prostate Carcinoma Aggressiveness: Relation to ^{68}Ga-PSMA-11-PET/MRI and Gleason Score

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Abstract. *Aim: To test the correlation of ^{68}Ga-PSMA-11 uptake and the expression of PSMA (prostatic specific membrane antigen) with the Gleason score, apparent diffusion coefficient (ADC) and pharmacokinetic parameters obtained from dynamic contrast agent-enhanced MRI/PET. Patients and Methods: Forty newly diagnosed, therapy naïve patients with prostatic carcinoma (PC) (mean age of 56.7, range=34-79), who were referred for ^{68}Ga-PSMA-11-PET/MRI for primary staging and had undergone radical prostatectomy (RAPE) were included in this prospective study. Their blood samples were tested for serum levels of prostate-specific antigen (PSA) and proPSA. The patients' prostates were evaluated using whole-mount sections, which helped determine the extent and grade of the tumor; tests were performed to determine immunohistochemical PSMA expression. Results: A correlation between PSMA expression and the accumulation of ^{68}Ga-PSMA-11 was found using the Spearman correlation coefficient (p=0.0011). A stronger correlation was found between Gleason patterns 3 or 4 and PSMA expression (p=0.06). Furthermore, the correlation of Gleason score with the overall ^{68}Ga-PSMA-11 accumulation within the tumor or non-tumor tissue was found to be significant (p=0.0157). A significant relation was found only with the K_{ep} elimination rate constant, which was stronger in Gleason pattern 4 than in Gleason pattern 3. A weaker correlation was found between the accumulation of ^{68}Ga-PSMA-11 and K^{trans} in Gleason pattern 4: the most significant relation being between ADC_{min} and Gleason pattern 3 and 4 (p=0.0074). The total size of the tumor correlated with levels of proPSA (p<0.0001), and its extra prostatic extension correlated with levels of proPSA (p<0.0001). Conclusion: ^{68}Ga-PSMA-11 correlates well with the expression of PSMA. Gleason pattern 3 and 4 had a higher correlation with ^{68}Ga-PSMA-11 levels than did Gleason pattern 5. Either no correlation, or a weak correlation, was established with pharmacokinetics.*

In patients with newly detected prostate carcinoma (PC), the assessment of the exact tumor aggressiveness is most reliably determined by establishing the extent of the tumor along with its metastasis. This is the most reliable parameter for planning treatment.

The Gleason score is the gold standard measure of tumor aggressiveness in tissue samples collected in transrectal biopsies. Tumor behavior can furthermore be predicted based on the level of prostatic specific antigen (PSA) and, as of recent years, the level of the proPSA and its reflection in the prostate health index (PHI).

It is usually assumed that there is a pre-treatment risk of metastatic disease if the level of PSA is over 20 ng/ml and the Gleason score confirmed from the biopsy sample is 4+4 or higher. Over the past few years, the prostate specific membrane antigen (PSMA) ligand ^{68}Ga-PSMA-11 has become a promising PET radiopharmaceutical in

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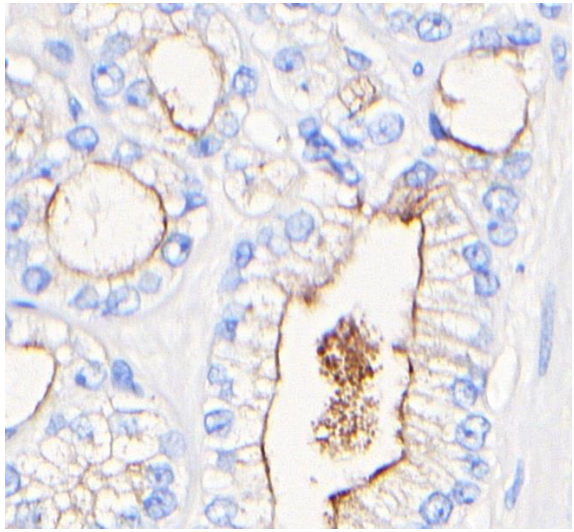
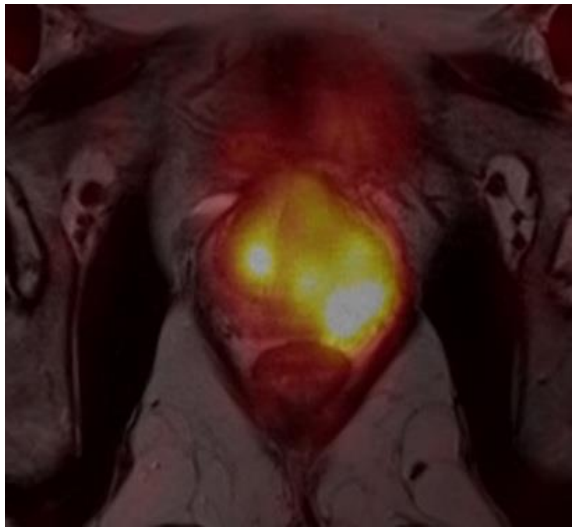
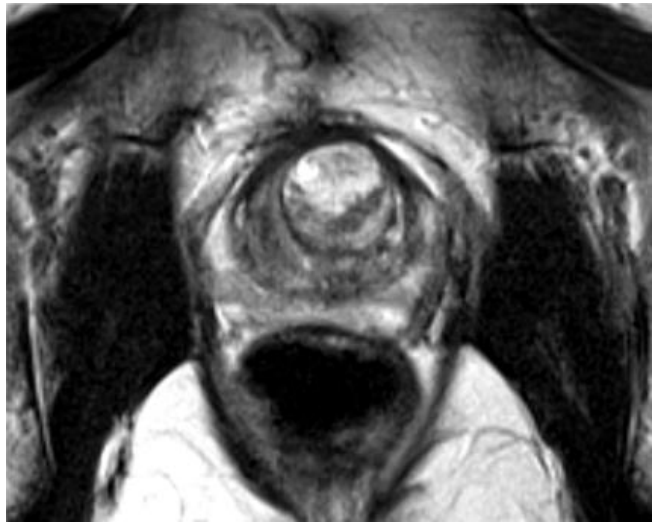
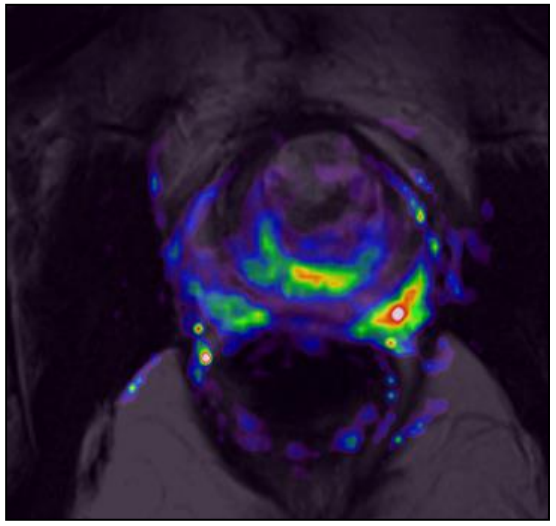
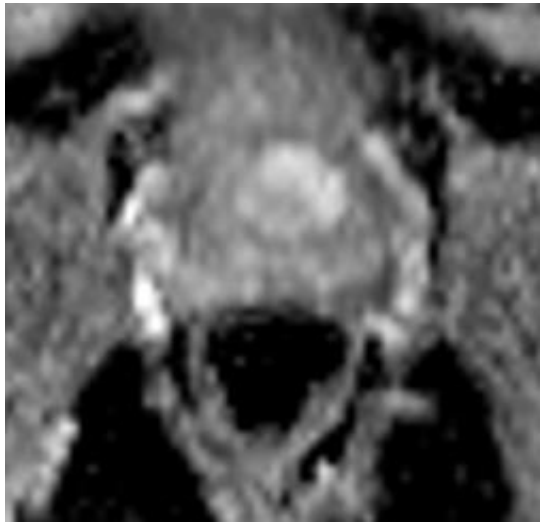
Key Words: Prostatic carcinoma, PET/MRI, ^{68}Ga-PSMA-11, tumor aggressiveness.





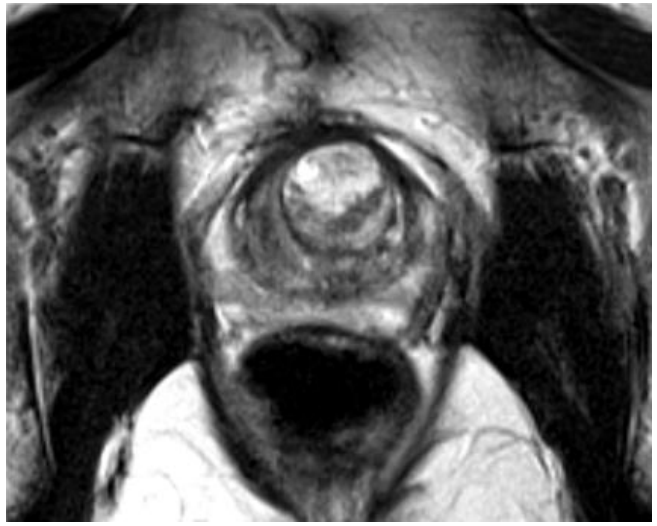
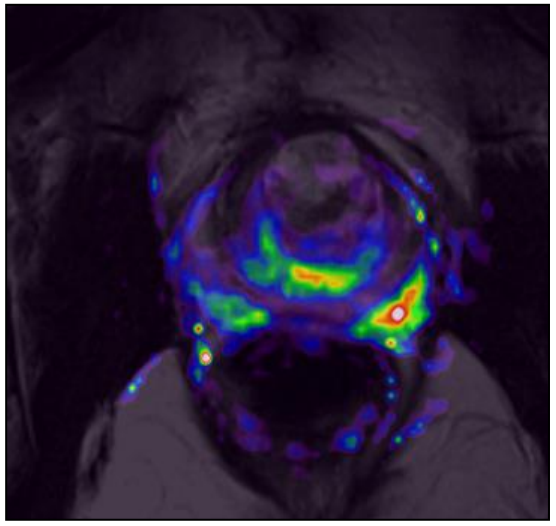
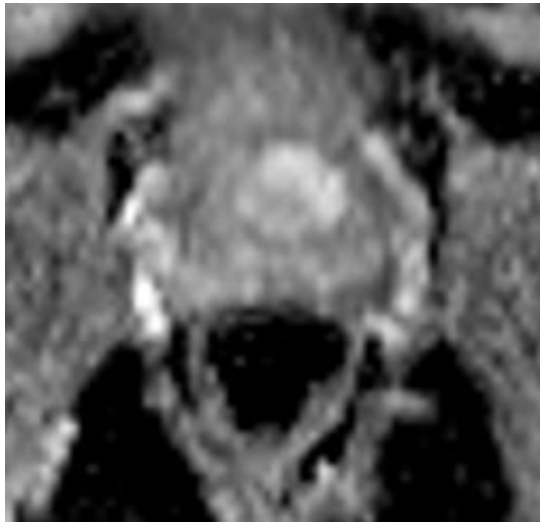
A role of radiologists?


- To evaluate prostatic lesions according PIRADS
- To guide the biopsy
- To detect the significant carcinoma
- To claim further strategy
- *To prepare the sufficient capability to maintain imaging demands*
- To evaluate effectivity and results of the imaging center

prostatic carcinoma

a role of radiologist in diagnosis and early detection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