

## Multi-Parametric Mri In Diagnosis Of Cancer Prostate In Patients With Elevated Prostatic Specific Antigen (Psa)

M.M.Refaat<sup>1</sup>, K.A.Elgamal<sup>2</sup>, H.M.Farouk<sup>1</sup>, A.E.M.Shalaan<sup>1</sup> and M.H.Shaker<sup>1</sup>

<sup>1</sup>Radiology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt

<sup>2</sup>Urology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt

E-Mail: Mariamafifi1188@gmail.com

### Abstract

Background and goal. Multiparametric resonance imaging (MRI) plays a vital role in the identification of prostate cancer. The aim of this study is to evaluate the function of MPMRI in 1,5-Tesla (1,5-T) prostatic carcinomas in high PSA patients. 50 patients were registered with PSA above 10 ng/ml for this prospective study authorised by this Ethics Board. Patients with a history of positive prostate biopsy and prostate cancer were excluded. All patients with 1,5-T MRI were targeted at transrectal ultrasound-led biopsies for confirming findings. The overall sensitivity, specificity, positive forecast value and negative predictive value with mp-MRI was 98.6%, 95%, 96% and 71%. Conclusion. Our results showed that the 1,5 T mp-MRI also serves as a triage method to avoid unnecessary invasive rectal biopsies which are very sensitive to prostate cancer.

**Keywords:** Prostate cancer, Multiparametric-MRI, Cancer imaging, •1.5-T MR

### 1. Introduction

Cancer Prostate is the most frequent disease among males 50 years of age and above and the third leading cause of cancer mortality among men [1].

The conventional diagnostic route in prostate cancer (PCa) is an increased prostate-specific antigen (PSA) and/or suspicious DRE, followed by a trans-rectal ultrasound-guided prostate (TRUS-GB) biopsy. TRUS is primarily used for anatomical guiding. Biopsies are usually collected from the peripheral zone where the majority of malignancies are present. Ultrasound can not detect high accuracy clinically significant (CSC) malignancy. [2].

Clinically relevant cancer prostate is often divided by three major forecast variables established by Stamey and Epstein (3&4) Gleason 7 or higher (3+4 = 7 or higher), Extra-prostatic tumours (T3a

disease or higher) and full-mount prostatectomy volume >0.5 cm<sup>3</sup>

During the initial biopsy procedure, more than 20% of prostate malignancies are overlooked or undersampled.

[5]. In addition, prostatitis or benign prostatic hyperplasia (BPH) can produce high levels of PSA.

Prostate multiparametric MRI is a potential new diagnostic technique for prostate cancer which may help decrease inconsequential prostate cancer. (6). It has become an increasingly essential tool for prostate cancer detection and characterisation.

MRI-directed biopsy includes targeted sampling of mpMRI suspected lesions. Many techniques for targeted prostate biopsy are being used: direct MRI-guided (in-bore) biopsy, cognitive fusion biopsy and MRI-TRUS fusion biopsy. [7]

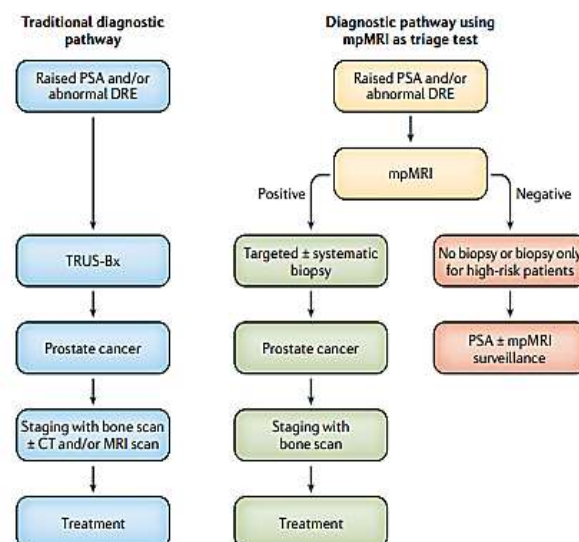


Fig. (1) Traditional and mpMRI-influenced prostate cancer diagnostic pathway (Stabile. A et al 2010 )

## 2. Aim of the Work

The aim of this study is to evaluate the role of the Multi-parametric MRI as a pre-biopsy non invasive imaging modality for detecting clinically significant cancer prostate in patients with elevated PSA.

## 3. Patients And Methods

### Patients selection

- A total of 50 patients ,with clinically elevated PSA>10ng/ml are going to be examined by mp-MR in a prospective single-center study at Banha university hospitals , radiology department . This prospective study was approved by the local ethics committee. Written informed consent was obtained from all the patients included in the study in order to use their laboratory, imaging and histopathologic data.
- **Patient preparation:** No specific patient preparation was requested other than the patients were inquired about the presence of ferromagnetic prosthesis or pacemakers, and these patients were excluded.
- **Patient position:** The patient laid down on the couch in the supine position with his arms beside his body with his foot first.

### Equipment:

- The study will be conducted on closed superconductive 1.5 Tesla MRI machine (Magnetom Avanto, Siemens Healthcare, Erlangen, Germany)
- The same mp-MRI protocol was used for all patients using phased array surface pelvic coil : axial T1WI , axial T2WI/ STIR , sagittal T2WI, coronal T2WI, axial DWI with ADC map, and for DCE-MRI a bolus injection of 0.1 mmol/kg body weight of gadolinium-based contrast agent followed by a saline flush of 20 ml was given.

Fast spin echo T2 weighted image: TR 4000/TE 110, Field of view 220(±20), Matrix size 224 x 320, Slice thickness 3 mm and no gap used

**Diffusion weighted images: (echo planer sequence):** TR 6000/TE 90, Matrix 128 x 128, field of view 220(±20), slice thickness 3mm without gap in between and 3 different b values were used (0,500,1000,1400 )

**ADC maps** were reconstructed on the workstation for qualitative and quantitative assessment of DWI images

### DCE images

- 2D FLASH , TR 4.5 , TE. 1.7 Field of view 220(±20), Matrix size 224 x 320, Slice thickness 2.5 mm and no gap used
- All cases will perform TRUS/biopsy to verify the diagnosis using GE Versana Essentials

### Inclusion criteria

- This study will include : Patients with elevated PSA>10ng/ml.

### Exclusion criteria:

- patients with a history of positive prostate biopsy, patients who were treated for prostate cancer. ,patients younger than 50 years old, Patients with renal impairment & Patients with bleeding tendency

### Examination

All patients will expose to 1) general examination.2)local examination: digital rectal examination ( DRE)

### Investigation

- Prostatic specific antigen (PSA).CBC,PC, PTT,INR, serum creatinine, blood urea, urine analysis &SGOT,SGPT

### MRI and TRUS biopsy Analysis

- The radiologist knew only the patient history of PSA & 1 Suspected lesions were reported in MRI and are classified in the PI-RADS V2 vocabulary; for all MR abnormalities, a five-point PIRADS score was given The 4 or 5 score was deemed positive for cancer, while the 3 or less score was regarded negative for cancer
- The standard systematic 12 core transrectal ultrasonography (TRUS)–guided biopsy covering the peripheral area from the prostate to the apex was done to all 50 patients. In patients with suspected MR lesions, additional, targeted cores were taken up. This was always determined on the basis of the highest level of suspicion, from each target lesion one to two biopsy core were obtained.
- If the lesion was undetectable on TRUS pictures and apparent on MR images, the target biopsy on the basis of nearby references like urethra or benign prostatic hyperplasia nodule was performed where it was suspected of occurring on MR images. Systemic core biopsies were done alone in patients with cancer-negative MRI results.
- As a clinically relevant system of PI-RADS was defined as a Gleason score of alternative 7, as well as/or volume of PI-RADS of Version 2 and/or Extraprostatic Extension.
- TREE: The findings of the systematic TRUS-led biopsy determined the standard of reference: a patient was regarded as a "true positive" when biopsy specimens had positive pathological outcomes and "true negative" if the outcome was negative. Then the radiological reports were matched to the histopathological data.

### Analysis of statistics

- The data obtained were processed and analysed using SPSS software version 21 (Spss Inc., Chicago, ILL Company) Number and percentages were categorical data, whereas quantitative data were represented as a mean ±standard deviation.
- The Chi square (X<sup>2</sup>) test, the exact Fisher tests, the student "t" tests and the pearson coefficient of correlation (r) have been used as meaning tests. The acceptable meaning level was set at 0.05 (P <0.05 was deemed significant).

**4. Result**

The current study included 50 male patients with PSA level above 10ng/ml and no prior prostatic biopsies performed .

The mean age of the examined patients was 66.9 years, ranging between 55 and 85 years. Patients less than 60 years old were about 36 % ,while those between 60-70 years represent about 32 % meanwhile about 32% were older than 70

The mean PSA value of the examined patient’s blood sample was 22.69ng/ml , ranging between 11 and 50 ng/ml. patient with PSA ranging from 10 to 20 ng/ml represent about 54.9% , patients with PSA above 20 ng/ml represent 43.1%

40 patients representing about 80.4% of the included sample have abnormal MRI findings based on the five points scoring system of PIRADS. As PIRADS 1 represents normal MP-MRI prostatic findings while PIRADS 2 and above denoting abnormal MP-MRI findings. Table (1)

The majority of the lesions were in the central gland representing about 76% , while about18% of the lesions were in the peripheral gland and about 6% were found implicating both central & peripheral zones .

The majority of the lesions were found at central gland(38 patients) which suspected on T2WI as a nodule, However on DWI, (50%) showed mild restricted diffusion corresponding measured high ADC value ranging from 1.132 to 1. 417 x 10<sup>-3</sup> mm<sup>2</sup>/s. The mean ADC value was 1.248( +14 x 10<sup>-3</sup> mm<sup>2</sup>/s.). in the dynamic study about 89% of the central lesions show normal or benign pattern of enhancement These imaging pattern can be sorted as PIRADS 2 according to PIRADS V2.1 ,2019 , After

TRUS guided biopsy it reveled to be adenomatous hyperplasia & prostatitis.Meanwhile there was 1 case presented with moderate restricted diffusion, mild hypointense on the ADC map,with crosseponding mild low in ADC value ( 0.9 x10<sup>-3</sup> mm/s<sup>2</sup> ) , These imaging pattern can be sorted as PIRADS 3 according to PIRADS V2.1 ,2019which was pathologically proven to be prostatitis.

Among the peripheral zone , 9 patients showed hypointense T2WI lesions On DWI, (about 22.2% of them) showed marked restricted diffusion with a corresponding low measured ADC ,The mean ADC value was 0.79 (± 0.14) x 10<sup>-3</sup> mm<sup>2</sup>/s).

while only 1 case show moderate DWI restriction, moderate low signal ADC map .These imaging pattern can be sorted as PIRADS 4 according to PIRADS V2.1 ,2019. Which was confirmed by TRUS biopsies to be adenocarcinoma while the 3rd case which is sorted as PIRADS 3 as it shows no positive contrast enhancement which was proven to be prostatitis by TRUS biopsy

Three patients had lesions involving both central and peripheral zones in the form of regional distribution. on DWI showed moderate to marked restricted diffusion , moderate to marked hypointense on the ADC map, the mean ADC value was 0.79 ( ± 0.14) x 10<sup>-3</sup> mm<sup>2</sup>/s) These imaging pattern can be sorted as PIRADS 4 according to PIRADS V2.1 ,2019.which was proved to be adenocarcinoma Table (2)

Overall Sensitivity (Se) was 95.6% , Specificity (Sp) 98.6%, Positive predictive value (PPV)97% and Negative predictive value (NPV)71% for PIRADS in prostate cancer detection Table (3).

**Table (1)** Distribution of patients according to the PIRADS scoring system.

PIRADS	No	%
1	10	19.6
2	33	64.7
3	2	4.9
4	5	10.8
<b>Total</b>	50	100

**Table (2)** Relation between radiological findings of the lesions on MP-MRI & pathological findings on biopsy.

	adenoma		prostatitis		Biopsy adenocarcinoma		prostatitis and fibrosis		Fisher exact test	P value	
	No	%	no	%	no	%	no	%			
PIRADS	1	3	13.6%	5	27.8%	0	0.0%	2	40.0%	52.7	.000*
	2	18	81.8%	12	66.7%	0	0.0%	3	60.0%		
	3	1	4.5%	1	5.6%	0	0.0%	0	0.0%		
	4	0	0.0%	0	0.0%	5	100.0%	0	0.0%		
Total	22	100.0%	18	100.0%	5	100.0%	5	100.0%			

**Table (3)** accuracy of MP-MRI in diagnosis of cancer prostate .

<b>sensitivity</b>	95.6%
<b>specificity</b>	% 98.6
<b>Predictive value positive</b>	98%
<b>Predictive value negative</b>	71%

## 5. Discussion

In our research, the greatest incidence of prostate cancer for men is over 60 years (about 64 percent) and the middle age is 66. This finding is compatible with the data [8] which have been published the incidence rate is over 60 percent for males over 65 years of age.

In our present study, PIRADS 3 & PIRADS 4 have been found to be prevalent for PSA patients < 20 ng/ml.

This finding is in accordance with [9] that PIRADS 1 and PIRADS 2 lesions were detected more often in PSA patients > 20 ng/ml. and predominate in PSA TEN 20 ng/ml, PIRADS 4 and PIRADS 5 lesions.

We carried out our experiment at 1.5 utilising pelvic surface coil of the phased array PiRADV2.1 demonstrates credible acceptable results for both 1.5 and 3T without using an ERC, despite the rise in SNR in the prostate at any magnetic field intensity in the endorectal coil (ERC). The use of this product may, however, increase examination costs and time, distort the gland and add artefacts. The committee thus suggested that supervising radiologists attempt to improve the imaging procedures such that the MRI scanner utilised can provide the highest and most consistent picture quality possible.

Our findings indicate that the majority of the lesions in the central gland exhibited positive characteristics that may be ascribed to the benign, central gland prostatic hyperplasia and also the relatively low incidence (about 30 percent) of central gland cancer of all prostate malignancies.

[10, 11] which states that the mean ADC value of the TZ indicators of benign lesions approx.  $1,212 \times 10^{-3}$ , higher than the tumour tissue of the same zone, and the mean ADC value of the tumour was significantly lower than that of non-tumor tissue of the PZ (0,842 versus  $1,138 \times 10^{-3}$ ) are almost identical in our findings with the mean value of  $1,248 \times 10^{-3}$  mm<sup>2</sup>/s for benign lesions of the CZ & the mean ADC value.

Overall sensitivity (Se) was 95.6%, 98.6%, positive predictive value (PPV) 97% and negative predictive value (NPV) 71%, for PIRADS, for prostate cancer diagnosis.

These findings have occurred w [12] who have carried out a meta-analysis of 14 trials, where pool sensitivity ranges from 0.82 (95 percent CI 0.72–0.89) to 0.82 (95 percent CI 0.67–0.92) & negative values in studies with proper usage of PI-RADS ranges from 0.58 to 0.95. They also noted that the diagnostic accuracy of PIRADS in PC detection

seems to be excellent but no recommendations about the optimum threshold can be given due to heterogeneity.

In [13] those who screened and examined more than 1500 cases the results were comparable to the prostatic naïve patients with high sensitivity (about 95 percent), but the findings showed greater specificity (about 98 percent) than that of [13] (only 37 percent), and can be attributed to PSA criteria for patients with <20 ng/ml with small numbers.

However, this is much lower than the research carried out in [14] the pre-PI-RADSV2 period, when 98% of NPV were found probable because of no additional investigation of possible variables linked to a false-negative MRI survey.

In the systematic review and meta-analysis, [15] the diagnostic advantages of MRI-TB vs. TRUS-GB in identification of PCa as a whole were identified.

MRI-TB and TRUS-GB did not vary substantially in the overall identification of prostate cancer (sensitivity 85 percent and 81 percent, respectively). The detection rate was greater than TRUS-GB (91 per cent vs. 76 per cent), while the detection rate for negligible prostate cancer was lower (sensitivity 44 percent vs. 83 percent).

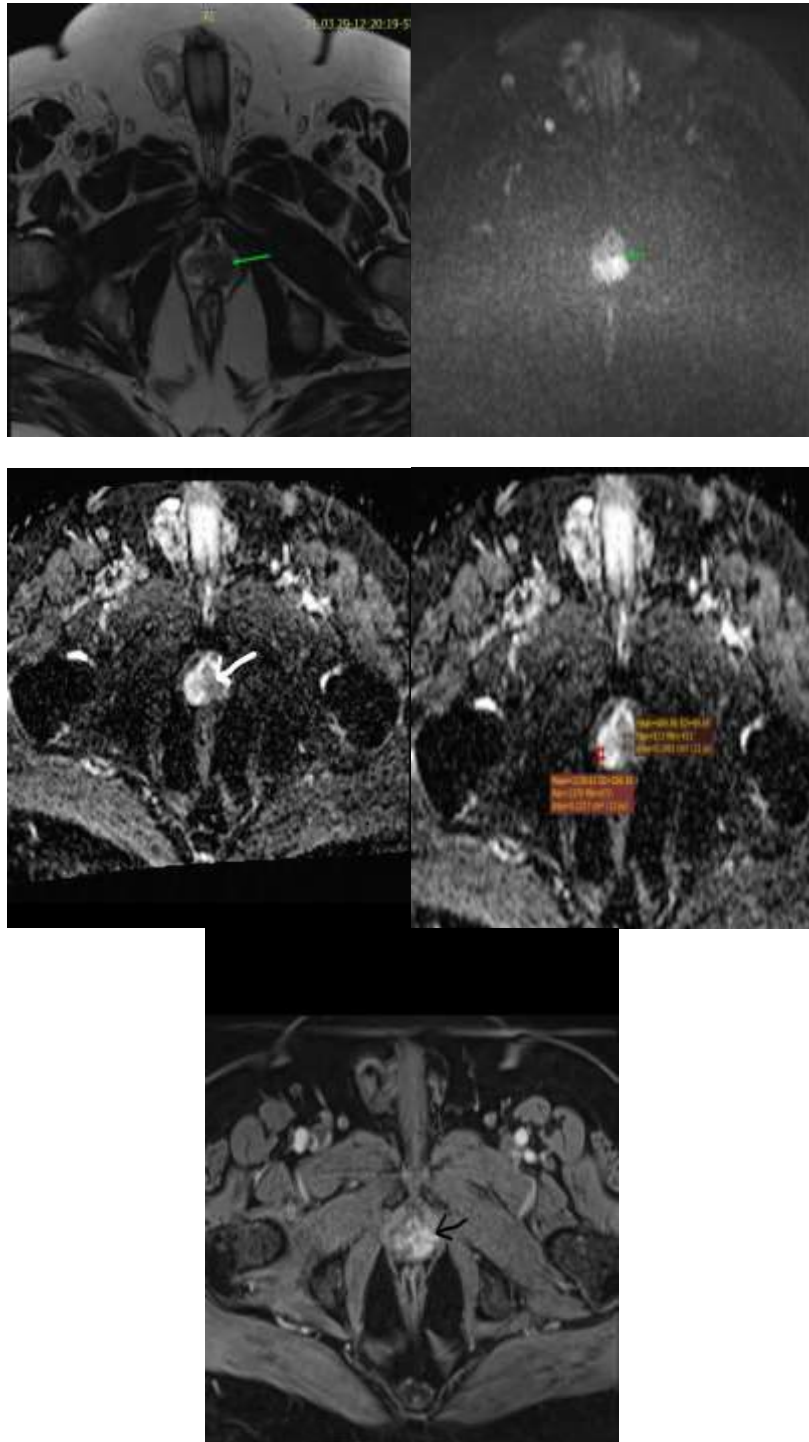
However, (16) the research showed that mpMRI diagnosis is accurate and made a significant step forward in introducing this radiological technique into the diagnostic pathways of men suspected of prostate cancer. In this research, mpMRI-targeted biopsy was more sensitive than TRUS-controlled biopsy (87% vs. 60%) and better NPV (72% vs. 65%) to identify prostate cancer with Gleason score + 4

It should be remembered that prostate mp MRI diagnosing capacity is inherently dependent on a number of factors including the technical acquisition of mpMRI images, radiologist image reporting expertise, the threshold used for mpMRI lesion definition and the definition of histologically relevant prostate cancer [17]

## 6. Conclusion

Our results show that 1,5 T mp-MRI is sensitive to clinically relevant identification of prostate cancer and that it has strong negative values to exclude serious illnesses. Our study therefore evaluates MPMRI for the detection of significant or small prostatic carcinoma as a diagnostic tool and a considerable triage system, as well as reduces the need for more invasive systemic biopsies, either by targeting susceptible lesions or by recommending to urologists that unnecessary biopsies be avoided.

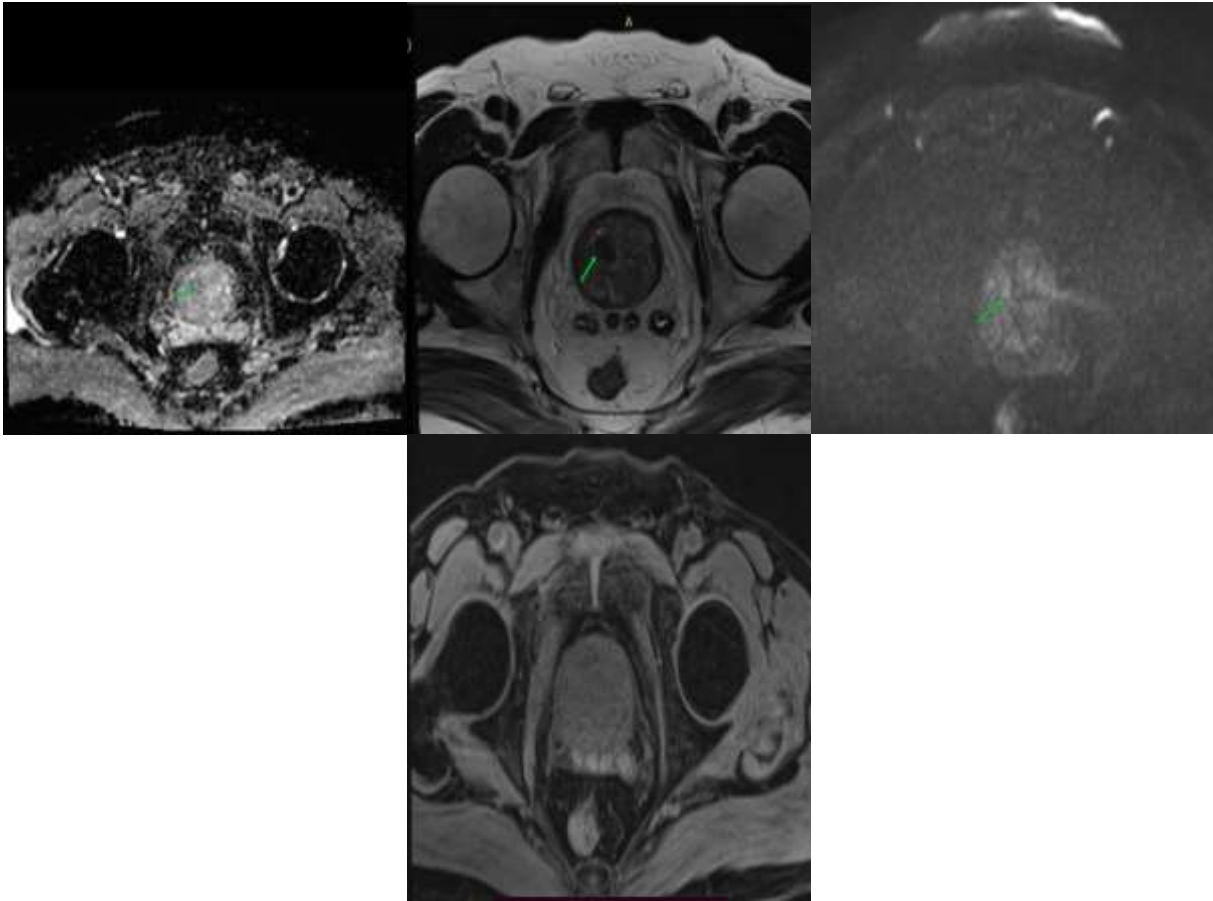
Cases



74 yrs male patient presented with gross hematuria. PSA was 55mng/ml. Axial T2WI (A) shows a hypointense lesion in the left PZ apical segment (on background of PZ hyperintensity with intact overlying hypointense capsule), which is seen restricted, hyperintense on the axial DWI (b-value 1400) (B), hypointense on the ADC map (C) and lowest mean ADC value was  $0.68 \times 10^{-3} \text{ mm}^2/\text{s}$  (ADC value on the right unaffected PZ was 1.1

$\text{mm}^2/\text{s}$ ). (D) . (E ) positive post IV contrast enhancement.

- T2W MRI PI-RADS=4, DWI PI-RADS=4, DCE-MRI PI-RADS=positive , PI-RADS Assessment Category=4
- TRUS guided targeted biopsy was performed and proved to be adenocarcinoma Gleason score 4+3. Imaging based staging: T2aN0 Mx.



70 years LUTS presented male patient. 14mg/ml PSA was. The oblique T2WI axial (a) reveals the "atypical" partly encapsulated nodule of T2WI. b) on the ADC map, the signal strength is modest below the backdrop c) moderate DWI limit (b-value 1400) over background in the axial DWI. d) disseminate homogeneous improvement of prostatic nodules PI-RADS=4, DWI PI-RADS=3, DCE-MRI PI-RADS=Negative, PI-RADS Evaluation Category=3 TRUS targeted biopsy was carried out and fibrosis linked with the diffuse adenomatous hyperplasia was found to be severe prostatitis.

#### References

- [1] J.Ferlay, H.R.Shin. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* .vol.127,pp.2893-2917,2010.
- [2] F.Uriburu-Pizarro, V.Kasivisvanathan. Pre-biopsy MRI as an adjunct for cancer detection in men with elevated PSA and no previous biopsy, *Transl Androl Urol*.vol.6(3),pp.387-394,2017.
- [3] J.W.Seo, S.J.Shin, Oh Y.Taik. PI-RADS Version 2: Detection of Clinically Significant Cancer in Patients With Biopsy Gleason Score 6 Prostate Cancer. *AJR Am J Roentgenol*.vol.209,pp.1-9,2017.
- [4] G.Ploussard, J.I.Epstein, R.Montironi. The contemporary concept of significant versus insignificant prostate cancer. *Eur Urol*.vol.60,pp.291-303,2011.
- [5] J.Fütterer, Jürgen. Multiparametric MRI in the Detection of Clinically Significant Prostate Cancer. *Korean J Radiol*.vol.18(4),pp.597-606,2017.
- [6] A.Stabile, F.Giganti. Multiparametric MRI for prostate cancer diagnosis: current status and future directions *Nature reviews*.vol.17,pp.155-190,2020.
- [7] M.Minhaj Siddiqui a, Soroush Rais-Bahrami. Magnetic Resonance Imaging/Ultrasound-Fusion Biopsy Significantly Upgrades Prostate Cancer Versus Systematic .vol.64,pp.713-719,2013.
- [8] Prashanth Rawla| Epidemiology of Prostate Cancer |*World J Oncol*.vol.10(2),pp.63-89,2019.
- [9] Cristian Popita, Anca Raluca Popita, Adela Sitar-Taut, Bogdan Petrut, Bogdan Fetica, Ioan Coman Tesla multiparametric-magnetic resonance imaging for the detection of clinically significant prostate cancer| *Clujul Medical*.vol.90,pp. 40-48,2017.
- [10] OTO.Aytekin, MD.Arda Kayhan, MD.Yulei Jiang, PhD.Maria Tretiakova, MD.Cheng Yang, PhD.Tatjana Antic, MD.Farid Dahi, MD.Arieh L.Shalhav, MD.Gregory Karczmar, PhD Walter, M. Stadler Prostate Cancer: Differentiation of Central Gland Cancer from

- Benign Prostatic Hyperplasia by Using Diffusion-weighted and Dynamic Contrast-enhanced MR Imaging| radiology.rsna.org n Radiology.vol. 257,pp.500-590, 2010.
- [11] Ragheb and Bassiouny Can mean ADC value and ADC ratio of benign prostate tissue to prostate cancer assist in the prediction of clinically significant prostate cancer within the PIRADSv2 scoring system .Egyptian Journal of Radiology and Nuclear Medicine.vol.51,pp.242 -347, 2020.
- [12] H.J. Esther Hamoen , Maarten de Rooij , J. Alfred Witjes , O.Jelle Barentsz , M.Maroeska Rovers |Use of the Prostate Imaging Reporting and Data System (PI-RADS) for Prostate Cancer Detection with Multiparametric Magnetic Resonance Imaging: A Diagnostic Meta-analysis.vol. 67,pp.1112–1121,2015.
- [13] G. Gaunay,Patel.V , P.Shah , D.Moreira , A.Simon, J. Hall , A.Manish Vira , M.Schwartz, Kreshover.J , E.R.Ben-Levi. Role of multi-parametric MRI of the prostate for screening and staging.vol.4,pp.68-74 ,2017.
- [14] JS.Wysock, N .Mendhiratta, F.Zattoni. Predictive value of negative 3T multiparametric magnetic resonance imaging of the prostate on 12- core biopsy results. BJU Int.vol.118,pp.515–520,2016.
- [15] G. Ivo Schoots , J.Monique Roobol , Daan Nieboer , H.Chris Bangma , W.Ewout Steyerberg , M.G. Myriam Hunink Magnetic Resonance Imaging–targeted Biopsy May Enhance the Diagnostic Accuracy of Significant Prostate Cancer Detection Compared to Standard Transrectal Ultrasound-guided Biopsy: A Systematic Review and Meta-analysis|| EURURO.vol.59,pp.530-566,2014.
- [16] U.Hashim Ahmed,Ahmed El-Shater Bosaily, C.Louise Brown,Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group|. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study|www.lacent.com.vol.25;389,pp.815-822,2017.
- [17] G. Gaziev, K.Wadhwa, T.Barrett. Defining the learning curve for multiparametric magnetic resonance imaging (MRI) of the prostate using MRI-transrectal ultrasonography (TRUS) fusion-guided transperineal prostate biopsies as a validation tool. BJU Int .vol.117,pp.80-6,2016.
- [18] A.Stabile, F. Giganti . Multiparametric MRI for prostate cancer diagnosis: current status and future directions Nature reviews .vol.17,pp.200-251,2020.