MULTI-PARAMETRIC MRI IN DIAGNOSIS OF CANCER PROSTATE IN PATIENTS WITH ELEVATED PROSTATIC SPECIFIC ANTIGEN (PSA)

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Abstract

Background and aim.

Multiparametric-magnetic resonance imaging (mp-MRI) plays an important role in diagnosis in prostate cancer The aim of this study is to evaluate the role of MPMRI for detection of prostatic carcinoma in patients with elevated PSA at 1.5-Tesla (1.5-T)

Methods. In this ethical board approved prospective study, 50 patients with elevated PSA above 10ng/ml were included. Patients with a history of positive prostate biopsy and patients treated for prostate cancer were excluded. All patients were examined at 1.5-T MRI, with targeted transrectal ultrasonography–guided biopsy for confirmation

Results. The overall sensitivity, specificity, positive predictive value and negative predictive value for mp-MRI were 98.6%, 95 %, 96% and 71%, respectively.

Conclusion. Our results showed that 1.5 T mp-MRI has a high sensitivity& also specificity for detection of prostatic carcinoma also act as a triage system to avoid the unnecessary invasive trasrectal biopsies

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

INTRODUCTION

Cancer prostate is the most common cancer among men aged 50 years and older and the third leading cause of cancer-related death in men (**1).**

The classical pathway for the diagnosis of prostate cancer (PCa) is an elevated prostate-specific antigen (PSA) and/or a suspicious digital rectal examination (DRE) followed by a trans-rectal ultrasound guided biopsy (TRUS-GB) of the prostate. TRUS is performed mainly for anatomic guidance .Biopsies are taken mainly from the peripheral zone, which have the majority of cancers ,Ultrasound does not identify clinically significant cancer (CSC) with high accuracy. **(2).**

Clinically significant cancer prostate is frequently categorized according to three main prognostic factors as defined by Stamey and Epstein (**3& 4)** Gleason score 7 or greater (3+4=7 or higher), Extraprostatic tumor extension (T3a disease or greater) & Tumor volume on whole-mount prostatectomy >0.5 cm3

Over 20% of the prostate cancers are missed or undersampled during the first biopsy session.**(5).** Moreover, prostatitis or benign prostatic hyperplasia (BPH) also cause elevated PSA levels.

Multiparametric MRI (mpMRI) of the prostate is a novel promising tool for diagnosis of prostate cancer that might help to reduce over diagnosis of insignificant prostate cancer. (**6).** It has become an increasingly important tool in the diagnosis and characterization of prostate cancer .

MRI-guided biopsy involves selective sampling of lesions identified as suspicious on mpMRI. There are several methods currently in use for targeted prostate biopsy: direct MRI-guided (in-bore) biopsy, cognitive fusion biopsy and MRI–TRUS fusion biopsy.(**7)**

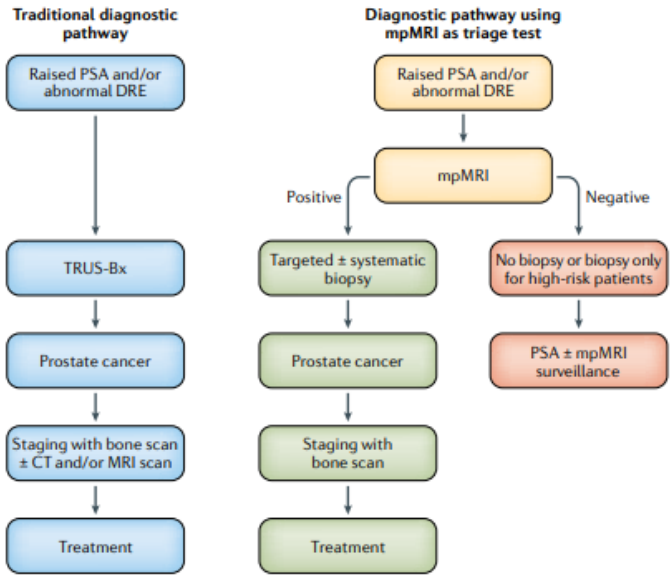


Fig1: Traditional and mpMRI-influenced prostate cancer diagnostic pathway **(Stabile. A et al 2010)**

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.

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 superconductive1.5 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: (echoplaner 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 PSA history
- Suspected lesions were noticed in MRI reports and were categorized according to the PI-RADS V2 lexicon ; a five points PIRADS score was assigned for all MR abnormalities. a score of 4 or 5 was considered cancer positive, whereas a score of 3 or less was considered cancer negative

- All 50 patients underwent a standard systematic 12 core transrectal ultrasonography (TRUS)–guided biopsy covering the peripheral zone from the prostate base to the apex bilaterally., additional targeted cores were picked up in patients with MR suspected lesions.. which was always defined on the basis of the highest suspicion level, One or two biopsy cores were obtained from each target lesion.
- When a lesion was invisible on TRUS images but visible on MR images, the target biopsy was conducted where it was suspected on the MR images on the basis of adjacent references, such as urethra, or benign prostatic hyperplasia nodule. In cases with cancer-negative MRI findings, systemic core biopsies alone were performed.
- The clinically significant cancer was defined, according to PI-RADS version 2 system, as Gleason score ≥7, and/or volume ≥0.5 cc, and/or extraprostatic extension.
- The standard of reference was settled by the results of systematic TRUS-guided biopsy: a patient was considered "true positive" if biopsy specimens showed pathologically positive results and "true negative" if biopsy result was negative. The radiological reports were then compared with the histopathologic data.

Statistical analysis

The collected data were tabulated and analyzed using SPSS version 21 soft ware (Spss Inc, Chicago, ILL Company) . Categorical data were presented as number and percentages while quantitative data were expressed as mean ±standard deviation.

Chi square (X^2) test, Fisher's exact test, student “t” tests, and pearson’s correlation coefficient (r) were used as tests of significance.. The accepted level of significance in this work was stated at 0.05 (P <0.05 was considered significant),.

RESULTS

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 ٦٠years 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)**

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
	Total	50	100

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 -3 mm^2/s. The mean ADC value was 1.248(-+14 x 10 -3 mm^2/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 x10-3 mm/s2) , 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 -3 mm^2/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 -3 mm²/s) These imaging pattern can be sorted as PIRADS 4 according to PIRADS V2.1 ,2019.which was proved to be adenocarcinoma (**Table 2)**

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

		Biopsy								Fisher exact test	F v
		adenoma		prostatitis		adenocarcinoma		prostatitis and fibrosis			
		No	%	no	%	no	%	no	%	52.7	.
ADS	1	3	13.6%	5	27.8%	0	0.0%	2	40.0%		
	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%		
		22	100.0%	18	100.0%	5	100.0%	5	100.0%		

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)**

sensitivity	95.6%
specificity	% 98.6

Predictive value positive	98%
Predictive value negative	71%

DISCUSSION :

In our study The highest incidence of prostate cancer was for males is seen above 60 years (about 64%) with mean age of presentation at 66 years . This result is consistent with data reported by **(Rawla.P , 2019) (8)**that stated The incidence rate is nearly 60% in men over the age of 65 years .

It was noticed in our current work that PIRADS 3& PIRADS 4 were predominant in patients with PSA level > 20 ng/ ml ,.This observation is coincide with **(Popita. C et al 2017)(9)** which stated that PIRADS 1 and PIRADS 2 lesions were found more frequently in patients with PSA value < 20ng/ml . and the group with PSA≥20 ng/ml, PIRADS 4 and PIRADS 5 lesions were predominant.

we performed our work at 1.5 using phased array surface pelvic coil **According to the PIRADV2.1** credible satisfactory results have been obtained at both 1.5T and 3T without the use of an ERC, in spite that endorectal coil (ERC) shows increase

SNR in the prostate at any magnetic field strength.. However, its use may increase the cost and time of the examination, deform the gland, and introduce artifacts. so the committee recommended that supervising radiologists try to optimize imaging protocols in order to obtain the best and most consistent image quality possible with the MRI scanner used.

Our results showed that the majority of the lesions that arising within the central gland showed benign features which is could be attributed to that benign prostatic hyperplasia arising from the central gland and also the relatively low incidence of central gland cancers (approximately 30%) of all prostate cancers according **to Aytekin Oto, et al .2010 .(10)**

Rhageb S. et al 2020(11) which stated that mean ADC value denoting benign lesions within the TZ about 1.212x10-3 which is higher than the tumoral tissue within the same zone & also the mean ADC value were significantly lower in tumor than non-tumor tissue in in the PZ (0.842 versus 1.138x10-3), our results were nearly the same as the value of 1.248x 10 -3 mm^2/s for benign lesions within CZ & The mean ADC value was 0.79 (± 0.14) x 10 -3 mm^2/s)for suspicious lesion within the PZ .

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

These results are come up w **Hamoen.Eet al 2015 (12)**who conducted a meta -analysis over about 14 studies stated that pooled sensitivity of 0.82 (95% CI 0.72–0.89) and specificity of 0.82 (95% CI 0.67–0.92)& negative predictive values ranging from 0.58 to 0.95 in studies with correct use of PI-RADS They also stated that PIRADS appears to have good diagnostic accuracy in PC detection, but no recommendation regarding the best threshold can be provided because of heterogeneity.

In Gaunay .G et al 2017(13) who performed a screening and staging over 1500 cases the results were comparable regarding the prostatic Naïve patients with high sensitivity nearly as our study (about 95 %), however , our results showed higher specificity (about 98%) than the **Gaunay .G et al 2017(**only 37%), may attributable to patients selection criteria with PSA >20 ng/ml with small patients numbers as well as out targeted biopsies upon the suspicious lesions not the standred saturation biopsies

However it is significally lower than the study by **Wysock and colleagues 2016** (**14)**was conducted in the pre-PI-RADSv2

era who stated NPV of 98% likely due to no further analysis of potential factors associated with a false-negative MRI study

In systematic review and meta-analysis, **Schoots et al.2014(15)** looked for evidence regarding the diagnostic benefits of MRI-TB versus TRUS-GB in detection of overall PCa .MRI-TB and TRUS-GB did not significantly differ in overall prostate cancer detection (sensitivity 85% and 81%, respectively). MRI-TB had a higher rate of detection of significant prostate cancer compared to TRUS-GB (sensitivity 91% vs. 76%) and a lower rate of detection of insignificant prostate cancer (sensitivity 44% vs. 83%).

However, **the PROMIS 2017(16)** study provided evidence for diagnostic accuracy of an mpMRI and took a major step towards the introduction of this radiological test in the diagnostic pathway of men in whom prostate cancer is suspected. In this study, mpMRI-targeted biopsy had greater sensitivity than TRUS-guided biopsy (87% versus 60%) and a higher NPV (72% versus 65%) for detecting Gleason score prostate cancer ≥3 + 4

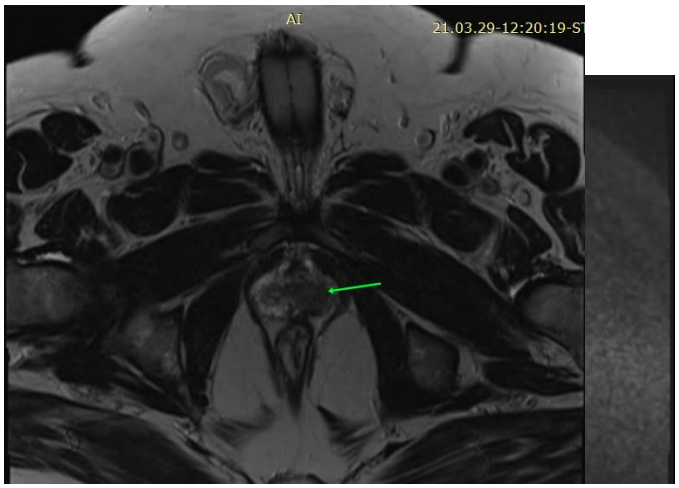
it should keep in mind that the diagnostic capability of prostate mpMRI is inherently dependent on a number of factors including the technical acquisition of the mpMRI images, the expertise of the radiologist reporting the images, the threshold

used to define a lesion on mpMRI, and the definition of histologically significant prostate cancer **as Gaziev Get al 2016 stated (17)**

CONCLUSION

Our results show that 1.5 T mp-MRI has a high sensitivity for the detection of clinically significant prostate cancer and high negative predictive value in order to rule out significant disease So Our study to evaluate ,support the role of the MPMRI as a diagnostic tool & a considerable triage system to detect the possible significant or insignificant prostatic carcinoma & also minimize the need for the more invasive systematic biopsies by targeting the suspicious lesions or recommending the referral urologist to avoid the unnecessary biopsies.

cases



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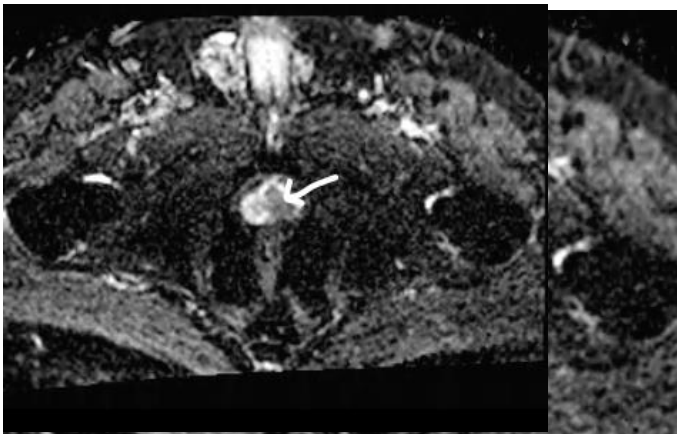

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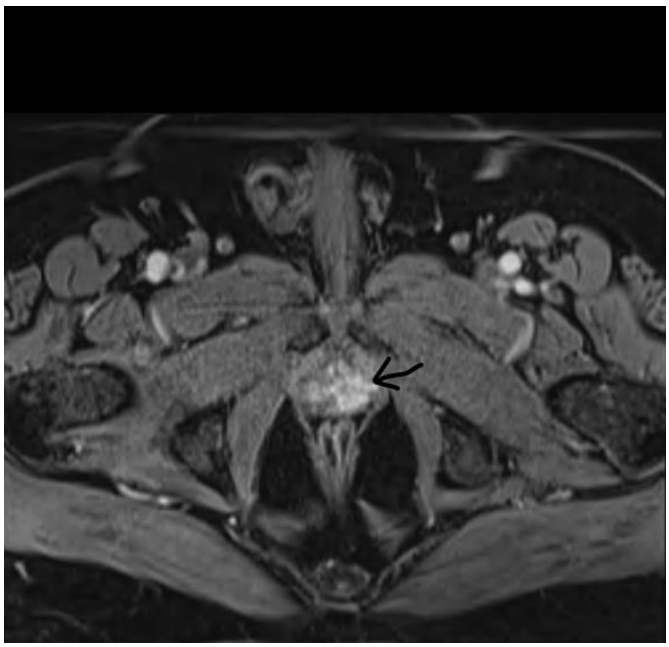
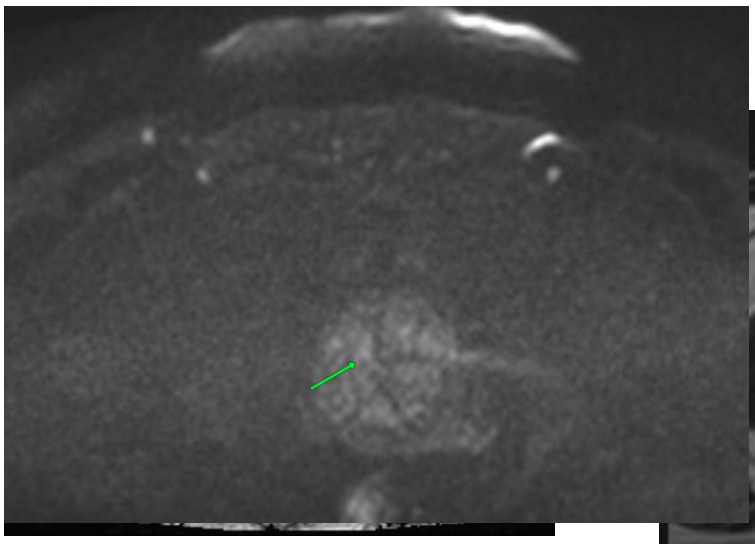


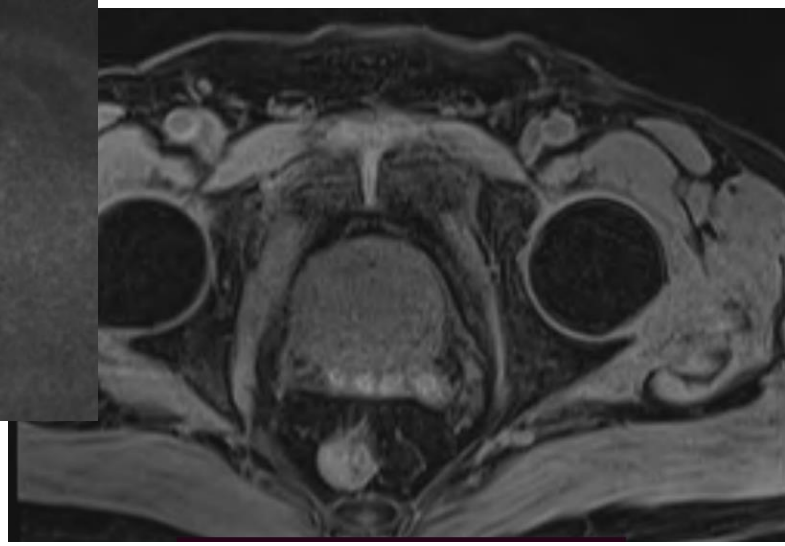
e

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 x 10-

3 mm²/s (ADC value on the right unaffected PZ was 1.1 mm²/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.





d)

a b c

70 yrs male patient presented with LUTS. PSAwas 14mng/ml. oblique axial T2WI (a) shows partially encapsulated “atypical” nodule in T2WI . b)on ADC map shows moderate low signal

intensity below the background c) mild DWI restriction in the axial DWI (b-value 1400)above the background .d)diffuse homogenous enhancement of the prostatic nodules

T2W MRI PI-RADS=4, DWI PI-RADS=3, DCE-MRI PI-RADS=negative, PI-RADS Assessment Category=3

- TRUS guided targeted biopsy was performed and proved sever prostatitis with fibrosis associated with diffuse adenomatous hyperplasia

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