Original article

Efficacy of Pelvic Diffusion Weighted MRI Prior to Prostate Biopsy in Patients with elevated tPSA Level for Determination of Malignant Lesions

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Article Info

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Abstract:

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Aim: the aim of this research to examine the influence of TRUS-guided biopsy samples from specified lesions in diffusion-weighted MRI on the detection rate of prostate cancer (MRI). **Patients and Methods:** This study cross sectional analytical study with follow up the results of biopsy was conducted on 25 patients with elevated PSA from 2.5 to 20 ng/ml undergone diffusion weighted MRI before TRUS guided biopsy. Patients were referred to the diagnostic radiology department from the outpatient clinic of urology department at Beni-Suef University Hospital from September 2018 to December 2020.The study explained to all participants and written informed consent taken from them before starting the study and the approval of ethical

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committee of Beni-Suef was taken. **Results:** There were 72% of the studied patients had benign prostatic lesions and 28% had malignant lesions. There was a statistically significant higher level of PSA among patients with restricted MRI diffusion than who had normal MRI diffusion (P-value=0.030). The sensitivity of MRI diffusion in detection of malignant prostate masses was 71.4% its specificity was 94.4% %, the PPV was 83.3% and the NPV was 89.5%. **Conclusion:** In conclusion, transrectal ultrasonography (TRUS) guided biopsy samples from pre-determined lesions in diffusion-weighted MRI (MRI) resulted in an increase in the detection rate of prostate cancer while lowering the excessive biopsy rate.

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1. Introduction:

In the Nordic nations, prostate cancer (PCa) is the second greatest cause of cancer-related death and the most often diagnosed male malignancy. A man's lifetime chance of being diagnosed with PCa is around 17% (one in six), but just 3% (one in thirty) will die from it, indicating that the majority of men with PCa never acquire a clinically severe condition that would influence their morbidity or mortality [1].

Urologists discovered that people diagnosed with prostate cancer had a negative biopsy despite a normal PSA level and abnormal rectal examination, posing diagnostic problems [2].

Due to random sampling error (repeat biopsies using the same technique will detect tumor in around a quarter of cases) and the fact that up to a third of significant tumors are found in the anterior part of the gland, based on studies of radical prostatectomy specimens, transrectal biopsy may miss significant prostate cancers [3].

Different studies have shown that men with a negative biopsy but a consistently increased PSA level are more likely to develop malignancies. Research that used systematic trans perineal mapping biopsy

found malignancy in 57% of the cases, with most positive cores located anteriorly. When magnetic resonance imaging (MRI) data were utilized to target biopsy, 40% to 59% of males were found to have tumors [4].

In the detection and characterization of prostate cancer, multi-parametric magnetic resonance imaging (MP-MRI) has become an increasingly significant technique [5].

In patients with low-risk prostate cancer who have outstanding oncologic results, active monitoring has recently become a viable therapy option [6].

Diffusion-weighted MRI has been shown to be better than dynamic contrast-enhanced MRI in the diagnosis of prostate cancer in many trials [7].

According to some investigators, Gleason score based on prostatectomy sections associated better with targeted biopsy based on DWI results than Gleason score based on biopsy cores of systematic 10-core transrectal ultrasound-guided prostate biopsy [8].

DWI has previously been used to effectively identify and characterize cancers in the peripheral and transitional zones [9].

So,the aim of this research to examine the influence of TRUS-guided biopsy samples

from specified lesions in diffusion-weighted MRI on the detection rate of prostate cancer (MRI).

2. Patients and Methods:

Type of study:

This study is a cross sectional analytical studywith follow up the results of biopsy.

This study conducted on 25 patients with elevated PSA from 2.5 to 20 ng/ml undergone diffusion weighted MRI before TRUS guided biopsy.

Site of study:

25 patients referred to the diagnostic radiology department from the outpatient clinic of urology department at Beni-Suef University Hospital

Date and period of study:

This study done from September 2018 to December 2020.

Ethical consideration:

The study explained to all participants and written informed consent taken from them before starting the study and the approval of ethical committee of Beni-Suef was taken.

Inclusion criteria:

Patients having tPSA from 2.5 to 20 ng/ml & candidate for prostate tissue biopsy.

Exclusion criteria:

Patients having tPSA below 2.5 or above 20 ng/ml, patients with any prior biopsy,who already pathologically diagnosed as cancer prostate, anyone with contraindication for biopsy as bleeding tendency, rectal, perineal infection and who are with contraindication for MRI examination as cardiac pacemakers and cochlear implants were excluded from the study.

Procedure and technique:

All patients subjected to:

1. Full history taking as age, sex, symptoms, and any medical condition.
2. Clinical examination.
   - General examination:

• Many men have their first experience with prostate cancer screening at an annual physical screening.

• General signs of cancer as loss of weight, fatigue, pain, and cachexia

   - Urological examination:

• Pain in the bottom part of the pelvis

• Urinary incessantly

• Inability to urinate, such as a painful, scorching, or weak flow.

• Blood in the urine (Hematuria)

• Pain in ejaculation

   - Examination for any associated medical conditions.
3. Radiological investigations:
   - Patients underwent prostate MRI using SEIMENS Healthineers 1.5 Tesla with pelvic phased-array coil.

MRI sequences:

• T1 weighted images

• T2 weighted images

• Diffusion weighted images: Diffusion was performed using b-values of 800 and 1000

• ADC maps

4. Transrectal US guided biopsy (TRUS-GB)

Statistical analysis

SPSS v. 25 (Statistical Package for Social Science) for Windows was used to analyze the data. The mean and standard deviation were used to describe quantitative variables. Numbers (No.) and percentages were used to describe qualitative factors (percent). The Shapiro/ Kolmogorov tests of normalcy were used to examine the data for normality.

The independent t-test was used to analyze the comparison between the scale variables of the two groups. The best PSA cutoff threshold for predicting prostatic cancer was determined using a receiver operating characteristic curve. The significance of the findings was determined using the P-value, which was classified as non-significant when the P-value was more than 0.05 and significant when the P-value was less than or equal 0.05.

3. Results:

Table (1) showed that the study included 25 patients with mean age 64.5 ±6.5 years and ranged from 50 to 70 years

the mean PSA level of the studied patients was 10.1 ±4.3 ranged from 3.5 to 18 with median 9.5.

Table (1) Baseline characteristics of the studied patients:

Patients' characteristics (Mean±SD)	Number 25 (%)
Age	64.5 ±6.5
PSA	10.1 ±4.3

Table (2) Prostate Diffusion Weighted MRI of the studied patients:

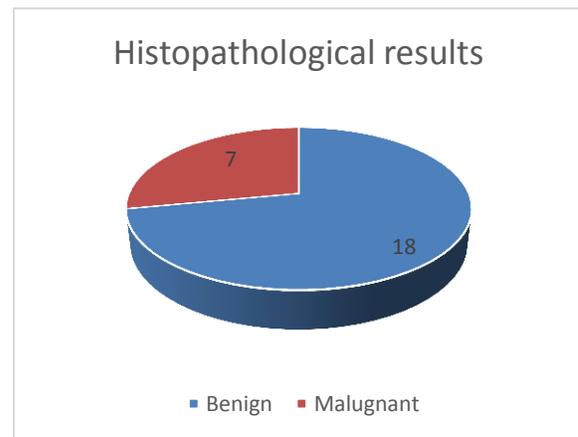| Lesion characteristics by Diffusion Weighted MRI	Number 25 (%)
Normal	19 (76.0)
Restricted	6 (24.0)
site of the restricted lesion detected by MRI diffusion according to zonal anatomy (no=6)	
- Transitional and peripheral	2 (33.3)
- Transitional	2 (33.3)
- Peripheral	2 (33.3)

Figure (1) Histopathological results of the studied biopsies

Figure (1) showed that there were 72% of the studied patients had benign prostatic lesions and 28% had malignant lesions.

Table (3) Comparison between patients with restricted and normal MRI diffusion regarding the PSA level of the studied patients:

Table (3) showed that there was a statistically significant higher level of PSA among patients with restricted MRI diffusion than who had normal MRI diffusion (P-value=0.030)

PSA	Restricted diffusion by MRI (n=6)	Normal diffusion by MRI (n=19)	P-value
Mean±SD	13.3±4	9.1±4	0.030*

Table (4) Sensitivity, specificity, positive predictive value, and negative predictive value of the MRI diffusion in detection of malignant prostate masses based on biopsy:

MRI Diffusion		Biopsy result		Total
		Negative malignancy	Positive Malignancy	
Negative restriction	Number	17	2	19
	% within MRI Diffusion	89.5%	10.5%	100.0%
	% within Biopsy result	94.4%	28.6%	76.0%
Positive restriction	Number	1	5	6
	% within MRI Diffusion	16.7%	83.3%	100.0%
	% within Biopsy result	5.6%	71.4%	24.0%
Total	Number	18	7	25
	% within MRI Diffusion	72.0%	28.0%	100.0%
	% within Biopsy result	100.0%	100.0%	100.0%

Table (4) showed that the sensitivity of MRI diffusion in detection of malignant prostate masses was 71.4% its specificity was 94.4% %, the PPV was 83.3% and the NPV was 89.5%.
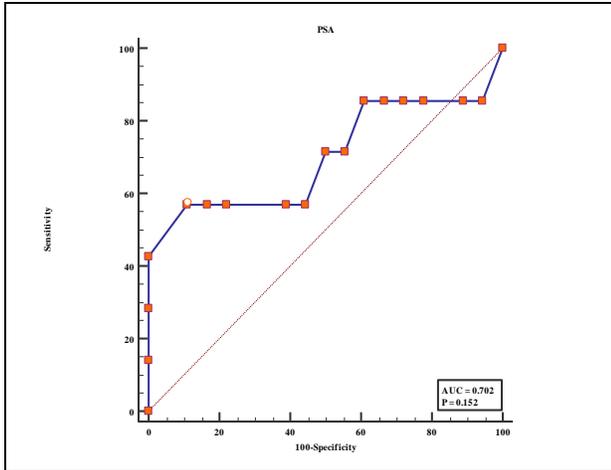
Figure (2) ROC curve for prediction of malignancy from PSA level

Table (5) Cut off point of PSA for prediction of prostatic malignancy:

Test Result Variable(s)	PSA
Area under the curve (95% CI)	0.702 (0.488 to 0.867)
Cut off	13
Sensitivity (95% CI)	57.14 (18.4 to 90. 1)
Specificity (95% CI)	88.89 (65.3 to 98.6)
PPV (95% CI)	66.7 (31.8 to 89.6)
NPV (95% CI)	84.2 (69.1 to 92.7)
+LR (95% CI)	5.14 (1.2 - 22.0)

Table (5) & figure (2) showed that the PSA is a good indicator for exclusion of malignancy as at a cut off of PSA 13 it can predict the malignancy with 57.14% sensitivity, 88.9% specificity, 66.7 Positive

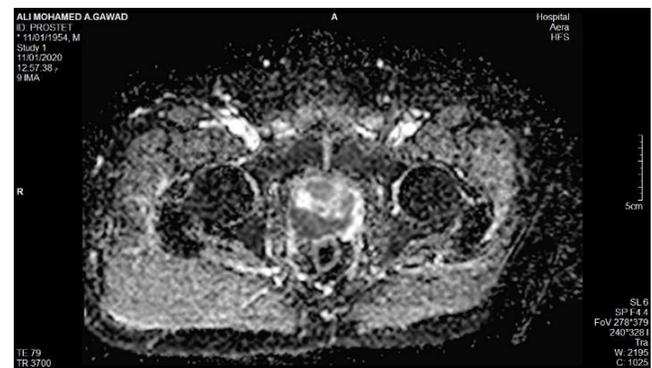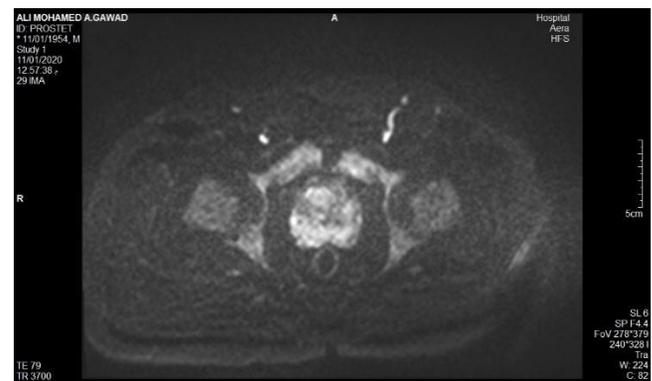predictive value and 84.2 negative predictive value.

Case presentation

Case 1

67-years-old male patient presented with hematuria

prostatic specific antigen: 12 ng/ml

MRI: showing restricted diffusion and low ADC in right and left mid gland

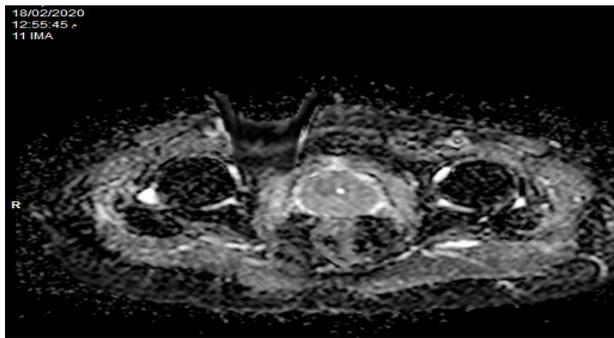TRUS guided by DWI: positive biopsy (Pca)

Case 2

71-years-old patient presented with weak and interrupted urine flow

 prostatic specific antigen: 10.5 ng/ml

MRI: showing restricted diffusion and low ADC in the right medial part of mid gland

TRUS guided by DWI: positive biopsy (Pca)
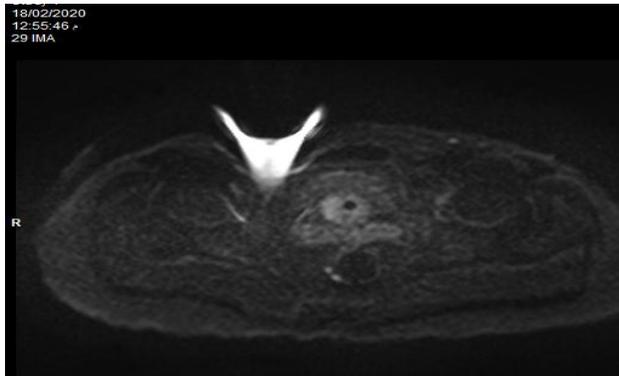
Case 3

68-years-old patient complaining of hematuria and frequency

 prostatic specific antigen 15 ng/ml

MRI: showing restricted diffusion and low ADC in the left lateral part of base of the gland

TRUS guided by DWI: positivebiopsy (Pca)
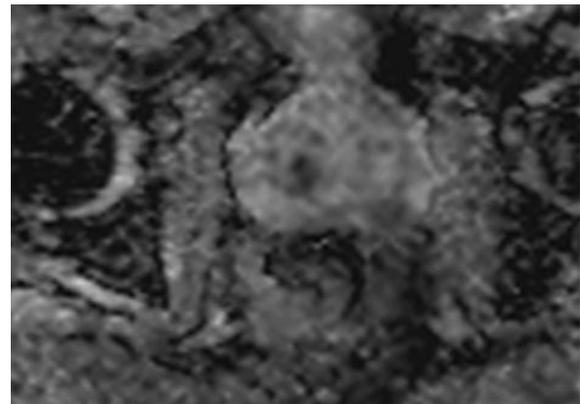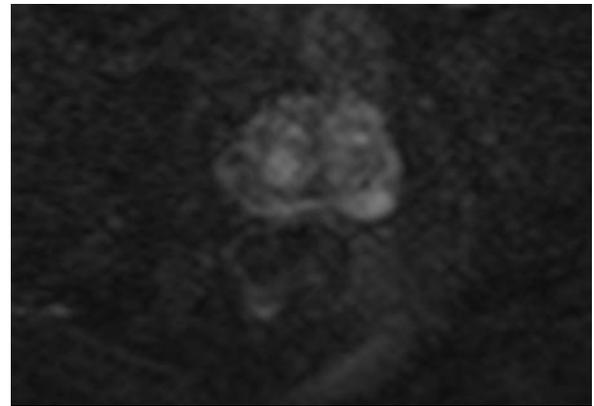
4. Discussion:

Prostate cancer is diagnosed and localized via a digital rectal examination (DRE) and serum prostate specific antigen (PSA) testing, followed by a transrectal ultrasonography (TRUS) guided biopsy, with a positive biopsy rate of 36.8%. [10]. Because standard sextant biopsy has a high probability of false negatives, we need more biopsy cores to boost prostate cancer diagnosis without increasing the number of needless biopsies [11].

Because roughly a quarter of tumors are found in the anterior region of the gland, and

between a quarter and a third of tumors are found in the front section of the gland, major prostate malignancies are missed [12].

The posterior region of the prostate is oversampled by transrectal biopsy, whereas the anterior, distal, apical, midline, and subcapsular prostates are under sampled. These locations may have clinically significant illness, which might change how patients are treated. The "prostatic evasive anterior tumor syndrome" (PEATS) is a kind of anterior tumor that is often overlooked with TRUS-guided biopsy [13].

Because of its lack of specificity in identifying clinically significant prostate cancer, PSA prostate cancer screening has several limitations in terms of diagnosis and treatment of clinically unimportant prostate cancer. This prompted the hunt for other screening methods aimed at reducing needless biopsies and overtreatment [14].

In order to reduce the high incidence of prostate cancer biopsy, we need to improve the accuracy of prostate cancer detection and localization. Because morphologic tests utilizing standard imaging methods have a limited specificity, they are not suggested as a first-line imaging tool for distinguishing between cancer and benign processes.

However, employing anatomical and functional MR methods such as diffusion weighted imaging (DWI), MR spectroscopy, and dynamic contrast enhancement investigations, the lesions are more visible, and the imaging assessment of localized prostate cancer is enhanced [15].

This measurement, T2WI, lies at the very heart of mp-MRI (Multiparametric MRI). Due to the excellent resolution and strong demarcation of the prostate capsule, T2WI may be used to assess prostate zonal anatomy and architecture, including identification of the peripheral zone, transition zone, prostatic urethra, prostatic capsule, and seminal vesicles, and to stage prostate cancer [16].

On T2WI, the vast quantity of water in the normal prostate gland shows as a high signal intensity, but prostate cancer appears as a low signal intensity. Because of this signal difference between normal and cancer tissue, diagnosing the gland-rich peripheral zone becomes simpler. However, since T2WI does not contain a lot of water, transitional zone cancer may be restricted [17].

The limits of T2WI for prostate cancer detection have been revealed in recent literature by Yoo and his colleagues in 2015 due to fluctuation in sensitivity and

specificity, i.e., 55 percent –88 percent for sensitivity and 67% –82% for specificity. Because of these limitations of T2WI, mp-MRI techniques such as DWI MRI and DCE MRI have been developed to increase the diagnostic accuracy of T2W MRI [17].

Prostate cancer diagnosis and characterisation is aided by the development and testing of MP-MRI, an anatomical and functional examination of the prostate [18].

PI-RADS 2.0, a standardized reporting system for prostate mp-MRI, was issued by the American College of Radiology as standards for the minimal needs for acquisition of an mp-MRI of the prostate [19].

Both 1.5T and 3T scanners are suitable for acquiring multiparametric MRI of the prostate; however, the 3T scanner is preferred because of its better signal/noise ratio, which allows images to be obtained in greater detail in T2 (3Dsequences, very high resolution and so on) and allows for images to be obtained more rapidly and in greater detail. Due to a high sensitivity to artefacts (gaseous, metallic, and aliasing), this inspection is often hampered. The presence of prostheses and implants (mostly) necessitates an increase in the number of exclusions from evaluation [20].

Although the use of an endorectal coil (ERC) is not necessary, the use of an ERC enhances the scan quality and increases the expense and pain of the process [21].

However, the cost and time required to conduct an MPMRI screening research raises questions about whether the healthcare system can afford it. This might lead to the development of new diagnostic tools that are similar to the mammography for breast cancer, if the research is simplified. As a result, researchers looked into the diagnostic value of a bi-parametric MRI that only uses T2W, DWI sequences and requires half the in-bore magnet time of our institution's complete MPMRI while also removing the need for a contrast-enhanced study, which saves money and time by eliminating the need for an intravenous access catheter replacement for MR contrast agent administration [22].

The combination of BMRI with PSA screening should help reduce the number of biopsies that produce benign results or clinically inconsequential illness, therefore directing resources toward men with more aggressive disease [23].

DWI has previously been used effectively to identify and characterize cancers in the peripheral and transitional regions of the

brain [24]. The high cellularity and abundance of intra and intercellular membranes in prostate cancer tissue results in diffusion limitation, making DWI a useful tool for detecting the disease. Furthermore, the use of DWI to measure tumor aggressiveness is garnering a lot of interest, despite the difficulty of accurately predicting Gleason scores [25].

In our study we selected group of patients with elevated PSA (2.5-20 ng/ml) based on previous papers and because of PSA less than 2.5 is commonly with benign lesions and performing DWI before transrectal biopsy and we found results; sensitivity was 71.4%, specificity was 94.4% %, the positive predictive value was 83.3% and the negative predictive value was 89.5%.

A similar study done by **Yagciand his colleagues in 2011** that mentioned that DWI may be utilized as a screening and guiding technique before a biopsy in patients with suspected prostate cancer. They discovered this (sensitivity 81%, specificity 92%, positive predictive value 78 %, negative predictive value 93%) [26].

Another study performed MRI diffusion to detect suspicious lesions before transrectal biopsy with almost similar results (Sensitivity 75.8%, Specificity 94.2%,

Positive predictive value 79.8% Negative predictive value 92.7%) [27].

So, our results are almost similar regarding specificity and to a lesser extent specificity with slightly higher positive predictive value and lower negative predictive value. Even better sensitivity and specificity were attained when B-MRI was used in conjunction with PSA levels and PSAD, according to research done by **Rais-Bahramiand his colleagues in 2015.** Prostate cancer diagnosis may benefit from the use of a restricted non-contrast MRI, as shown by these findings. High specificity (90%) was achieved by combining B-MRI with PSA levels (63%). In contrast, the combination of B-MRI and PSAD resulted in a high specificity (86%) but a modest sensitivity (74%). PSAD with B-MRI had an NPV of 70%, while PSA with B-MRI had an NPV of 82% [23].

Another study done by **Haider and his colleagues in 2007** found that T2 + DWI imaging had greater sensitivity and specificity than T2 imaging alone, both of which were over 80%. T2 + DWI imaging have a much greater negative predictive value than T2 imaging alone. Both T2 and T2+DWI have limited sensitivities for the

identification of cancer in the transition zone [28].

However, in our study 33.3 % of the studied patient with diffusion restriction were found in the transitional zone and 33.3 % were found in both transitional and peripheral zone

Despite the fact that DWI may boost the sensitivity of prostate cancer diagnosis, it is nevertheless restricted in its ability to see cancer tissue in the transitional zone since BPH-related nodules also show reduced diffusion. Additionally, tumour necrosis may show up as a high signal intensity on an ADC map, i.e., enhanced water diffusion. DWI has a number of potential downsides, including a poor signal-to-noise ratio, artefacts, and a limited spatial resolution [30].

DWI enhances diagnostic accuracy to T2 imaging, although the method by which it does so is unknown, according to **Haider et al., 2007** study. Cancer, inflammation, fibrosis, and bleeding are all possible causes of T2 signal reduction in the peripheral zone [28].

DWI and T2WI combined have showed substantial diversity in sensitivity (65–84 percent) and specificity (77–87 %) according

to another research by **Yoo et al. in 2015** [17].

ADC is a better indicator of cancer than bleeding, inflammation, or fibrosis, hence it is used in this study. Prostate cancer may have a lower ADC value because of the numerous closely packed glandular components seen in tumors that replace the fluid-containing peripheral zone ducts in the prostate. This might lead to a decrease in the ADC value in a certain area. For cancer diagnosis, researchers have shown that using the ADC map in conjunction with T2WI results in a significant increase in the detection rate [29].

5. Conclusion:

In conclusion, transrectal ultrasonography (TRUS) guided biopsy samples from pre-determined lesions in diffusion-weighted MRI (MRI) resulted in an increase in the detection rate of prostate cancer while lowering the excessive biopsy rate.

Recommendations:

According to the findings of this research, diffusion-weighted imaging should be employed in conjunction with conventional MRI sequences in the analysis of prostatic lesions, rather than as a stand-alone imaging study. Prostate tissue features may be studied

using DWI in conjunction with T2WI, which is based on T2WI.

We further recommend that diffusion image be analyzed in combination with traditional sequences to avoid any possible mistakes or limits of the technology.

Also, we urge that future research be done out on the many uses of diffusion weighted method in the prostate, such as the evaluation of treatment response and the recurrence of the tumor, as well.

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