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Research Article

The Value of Diffusion Weighted MRI in the Detection and Localization of Prostate Cancer among a Sample of Iraqi Patients

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Abstract

Background: Prostatic adenocarcinoma is the most widely recognized malignancy in men and the second cause of cancer-related mortality encountered in male patients after lung cancer.
Aim of the study: To assess the diagnostic value of diffusion-weighted imaging (DWI) and its quantitative measurement, apparent diffusion coefficient (ADC), in the identification and localization of prostatic cancer compared with T2 weighted image sequence (T2WI).
Type of the study: a prospective analytic study
Subjects and methods: forty-one male patients with suspected prostatic cancer were examined by pelvic MRI at the MRI department of the Oncology Teaching Hospital/Medical City in Baghdad from September 2017 to September 2018. Thin sections axial T2 and DWI sequences were performed for each patient. Two patients were excluded from the study due to poor image quality (motion artifact). Regions with a hypointense signal on T2WI and/or restricted lesion in DWI were determined. The ADC values were measured and the results were registered and sent for biopsy correlation. The sensitivity, specificity, accuracy, and other parameters were calculated for T2WI and DWI.
Results: The sensitivity and specificity of T2WI in the detection of prostate cancer were about 76.6% and 77% respectively. These improved to 96% and 88.8% by performing the DWI and measuring the ADC value. The mean ADC value was greatly lower in prostatic cancer (about 650x 10-6 mm2 /s) than in normal prostate parenchyma (about 1250 x10-6 mm2 /s) with a significant difference between them (p-value about 0.04)
Conclusion: In practice, using diffusion-weighted MRI sequence and its ADC quantitative measurement greatly increases tumor detection in patients suspected to have prostatic cancer and should be routinely used when doing pelvic MRI for patients with high clinical suspicion.

Introduction

Prostatic adenocarcinoma is the most widely recognized malignancy in men and the second cause of cancer-related mortality encountered in male patients after lung cancer [1, 2].
Precise identification and localization of the prostatic malignancy are of great importance for best management especially after the emergence of targeted therapies such as brachytherapy, cryosurgery, and intensity adjusted radiotherapy [3].
This allows maximum therapy to be directed to the focus of the lesion with limited destructive effects to the adjacent structures such as the neurovascular bundles, the urinary bladder, and the rectum [3].
Digital rectal examination (DRE), serum prostate-specific antigen (PSA), and transrectal ultrasound (TRUS)-guided prostate biopsy are the mainstay of the diagnostic process used for the detection of prostatic malignancy [4].
The use of PSA in the screening of prostate malignancy has shown no significant effect on the reduction of mortality. Furthermore, the detection of clinically significant prostate cancer using transrectal ultrasound (TRUS) is not easy [5, 6].

The exact depiction and localization of the lesion within the prostate gland would greatly reduce the unnecessary biopsies [7].
Only some information about the localization of prostate malignant lesions was obtained by T1WI and T2WI which were considered the cornerstone and the routine sequences in prostate MRI examination. They are used mainly for providing anatomical and morphological information. The T2WI clearly demonstrates the zonal anatomy of the prostate [8]. Normally the peripheral zone is hyperintense while the central and transitional zones are hypointense on T2WI.

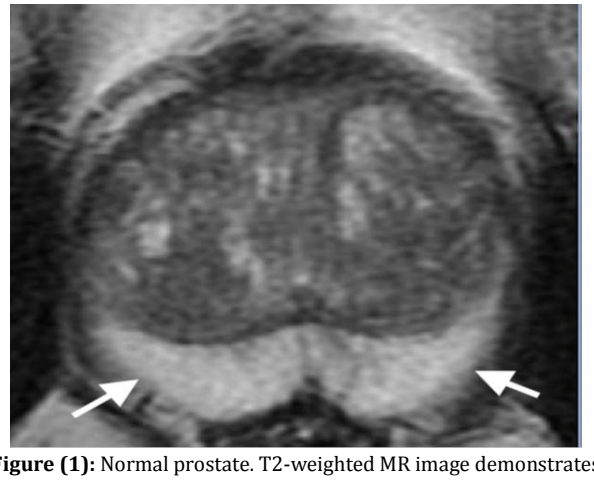


Figure (1): Normal prostate. T2-weighted MR image demonstrates normal prostate parenchyma with hyperintense peripheral zone (white arrow) and low signal central zone (black arrow) [9].

At present multiparametric MRI, approaches are added and involve one or more functional MRI sequences, which include diffusion-weighted (DW), dynamic contrast-enhanced (DCE), and/or MR-spectroscopy (MRS) techniques [10].
Diffusion-weighted sequence (DW) depends on the diffusion of water molecules in various biological tissues and can be achieved at different b values where the restriction increases as the b value increases [11].
The apparent diffusion coefficient (ADC) value is a quantitative parameter of DW MRI reflecting the magnitude of diffusion of water molecules in extracellular and extravascular spaces and capillary perfusion [12].
In general, malignant lesions tend to be hypercellular compared with normal tissue with a resultant decrease in ADC value [13,14]. Many previous studies have reported that the benign and malignant lesions of the prostate can be differentiated by measuring the ADC value [15,16,17].
Aim of the study: To evaluate the diagnostic value of DWI and its quantitative measurement (ADC) in the identification and localization of prostatic cancer compared to the T2WI sequence.

Subjects and Methods

A prospective analytic study was performed in the MRI department of the Oncology Teaching Hospital - the medical city in Baghdad from September 2017 to September 2018. Forty-one male patients with suspected prostatic cancer (either by positive digital rectal examination (DRE) or elevated levels of PSA) were referred to the MRI department from the urosurgery outpatient clinic. A pelvic MRI was done for each patient. Two patients were excluded; due to poor image quality (motion artifact) and the pelvic MRI of 39 patients was analyzed. Their ages were ranging from 49 years to 80 years old with a mean of 64 years old. A biopsy was done for 32 patients based on MRI findings or clinical suspicion or both.

MRI protocol
All the patients were examined using an MR Scanner of 1.5 Tesla (Siemens) with the pelvic phased-array coil. The patients were examined in the supine position. The prostate gland was localized in the center of the MRI field. The MRI protocol includes axial T1WI, axial and sagittal T2WI, and axial diffusion-weighted sequence (DWI). The axial T2WI and DWI were used in the analysis of the imaging findings. The parameters for T2WI were as follows: TR/TE: 7500/108 slices thickness: 3 mm, the field of view: 20 cm, number of excitations is 100, matrix: 320 x80 phase-encoding direction, right to left.
The parameters for DWI were: b values: 100, 400, and 1000 s/mm2, TR/TE: 4800/68.0, the field of view: 38 cm, bandwidth: 250 kHz, slice thickness: 3mm, the matrix of 192x80, number of excitations: 10.

Image interpretation
For all patients, T2WI alone was reviewed first. The images were studied on a workstation by two expert radiologists. The size of the prostate gland was measured. The prostatic zonal anatomy was demonstrated on T2WI, the peripheral zone is of high signal, the central zone and transitional zones (both are of low signal intensities). The peripheral zone was further divided into right and left halves. On T2WI, any apparent hypointense area in the peripheral zone was considered suspicious. These were correlated with its appearance on DWI and its ADC value. These areas were further studied and analyzed according to their site, size, and distance of contact with the prostatic capsule. The integrity of the low signal prostatic capsule was also recorded for any interruption as well as any extracapsular extension (manifested as capsular bulge or retraction) or involvement of the neurovascular bundle (which is located at 5 and 7 o'clock of the prostate gland). DWI was done using three different b values (100, 400, and 1000 mm/s), this allows for quantitative measurement of the ADC.
The ADC values were measured by placing the region of interest (ROI) circles in the center of the hypointense suspicious area. Then the ADC values were measured in the adjacent normal prostate tissue. The readings were registered for each patient.
Other associated findings such as pelvic LNs enlargement, adjacent organ invasion, and any abnormal bone marrow signal intensity within the pelvic MRI examination field were also evaluated and recorded.
Finally, the results obtained from T2 & DWI were compared together and correlated with biopsy results in indicated cases.

Statistical analysis
The collected data were tabulated and analyzed using computer software Statistical Package for Social Science (SPSS version 22) and Microsoft Excel 2010; the data documented regarding percentage, sensitivity, specificity, accuracy, Chi-squared test; P value of less than 0.05 was considered significant.
Ethical approval was obtained from the University of Baghdad.

Results

Forty-one male patients suspicious of prostatic cancer (either elevated PSA level or abnormal DRE) were examined by pelvic MRI. Two patients were excluded; due to poor image quality (motion artifact) and the pelvic MRI of 39 patients was analyzed. Their ages were ranging from 49 years to 80 years and the mean age was about 64. Twenty-four patients (61.5%) had abnormal signal intensity lesions detected on T2WI, DWI, and its quantitative measurement (ADC) images. Twenty-three cases (58.9%) of them subsequently proved to be prostatic cancer histopathologically but one patient (2.56%) proved to be benign histopathologically.
Six patients (15.3 %) had abnormal signal intensity lesions on DWI and ADC images with no definitive abnormality on T2WI and the histopathological results were prostatic adenocarcinoma.
The pelvic MRI of one patient (2.56%) showed an abnormal hypointense area on T2WI but it was not restricted on DWI; the biopsy result was of benign finding due to the previous prostatitis.
A note was made on 1 patient (2.56%) who had no definitive lesion neither on T2WI nor on DWI, however, a biopsy was done for him because there was high clinical suspicion (highly elevated PSA level) and the result was prostatic cancer.
Seven patients, of the total, had mildly elevated PSA levels (less than 12 ng/ml), their pelvic MRI showing an enlarged prostate gland with a heterogeneous appearance on T2WI but no definitive lesion was found neither on T2WI nor on DWI. These imaging findings were consistent

with benign prostatic hyperplasia (BPH) and biopsy was not performed for those patients.

The above-mentioned findings are summarized in table 1.

The mean ADC value was greatly lower in prostatic cancer than in the normal prostate parenchyma (mean ADC value for prostatic cancer was 650 x 10-6 mm2 /s) and for normal prostate, gland parenchyma was (1250 x10-6 mm2 /s) with a significant difference between them (p-value about 0.04) (less than 0.05).

For the malignant lesions, the minimum ADC value was 500 x 10-6 mm2/s, while the maximum ADC value was 920 x 10-6 mm2/s and the mean ADC value was 690 x 10-6 mm2/s.

Similarly, the minimum ADC value for normal prostate parenchyma was 1050 x 10-6 mm2/s and the maximum ADC value was 1700 x 10-6 mm2/s; the mean ADC value was 1250 x 10-6mm2/s.

The sensitivity, specificity, accuracy, negative predictive values (NPV), and positive predictive values (PPV) of T2WI and DWI were illustrated in table 2.

In this study, we found that among the patients with proved prostatic cancer (30 patients), 11 patients had a prostatic-confined lesion (36.6%), 19 patients had extracapsular extension (63.3 %) (Of those 19 patients, 13 had seminal vesicle involvement). Pelvic LNs involvement was reported in 8 patients (27.5%). Bony metastasis within visualized pelvic MRI fields was reported in 7 patients (23.3 %).

Table (1) Preoperative Clinical Characteristics associated with Accidental Gallbladder Perforation.

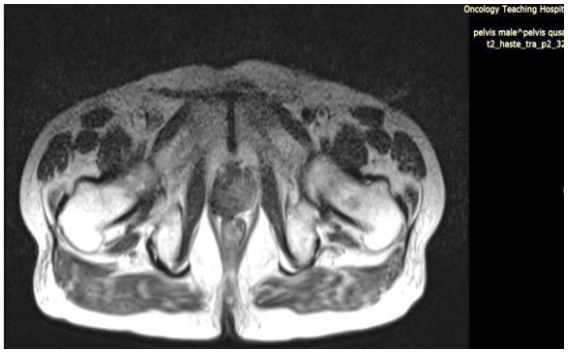
	Cases had undergone biopsy (32 cases)								**Patients with low clinical suspicion & no biopsy done**	
	Both T2WI &DWI*		DWI only*		T2 only*		Neither*		(no abnormal signal detected on T2 &DWI)	
	NO	%	No.	%	No	%	No	%	No.	%
	24	61.5%	6	15.3%	1	2.5	1	2.5	7	17.9
Final diagnosis	Prostate cancer in 23 Benign in 0ne		Prostatic ca in 6		Benign		Prostatic cancer		BPH	

*Both T2WI&DWI: lesions were detected on both these sequences.
*DWI only: lesions were detected only on DWI and not depicted on T2WI.
*T2WI only: lesions only detected on T2WI and not appeared on DWI.
*Neither: lesions not detected neither on T2WI nor DWI.

Table (2) The sensitivity, specifity, accuracy, PPV and NPV for T2WI and DWI with its ADC value are summarized.

Diagnostic performance parameters	**T2WI**	**DWI and ADC**
Sensitivity	76.6 %	96.6%
Specifity	77%	88.8%
Accuracy	76.9%	94.8%
PPV*	92%	96.6%
NPV*	50%	88.8%

*PPV applied for positive predictive value
*NPV applied for negative predictive value



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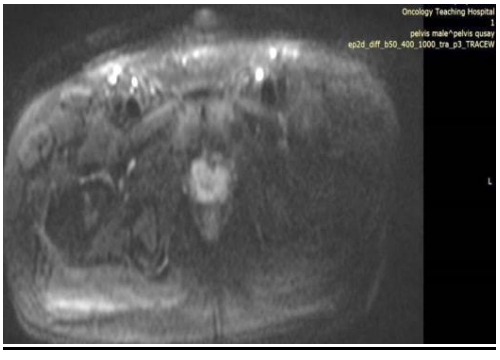

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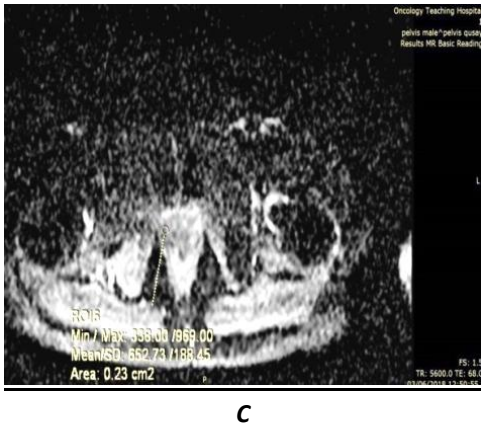
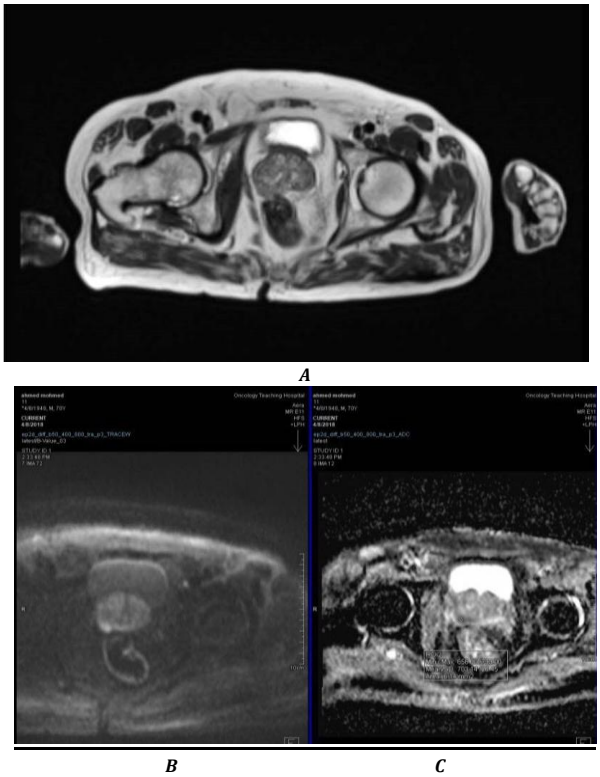


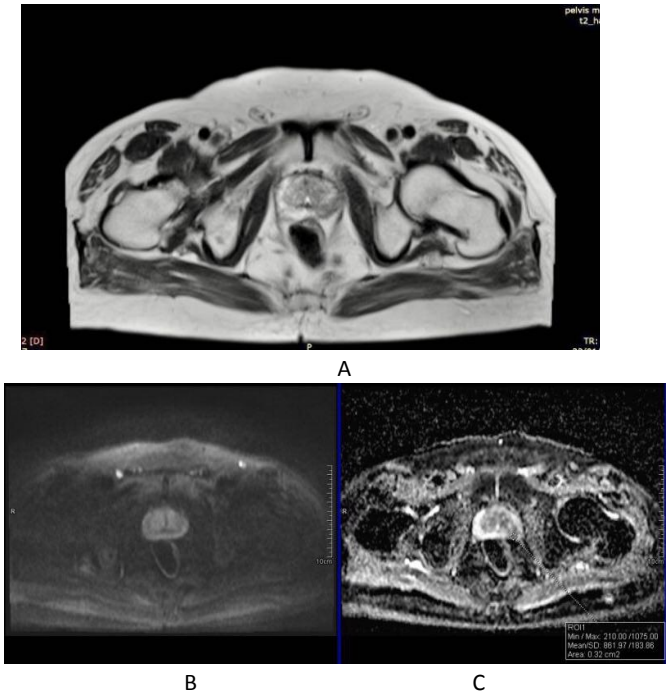
C

Figure (2): 73 years old male axial T2WI showing ill-defined hypointense lesion involving the right peripheral zone and part of central zone, crossing the midline and in contact with prostatic capsule for more than 12mm causing capsular bulge (A). On DWI (B), there is area of restricted diffusion appearing high signal intensity on DWI and low signal intensity on ADC image(C) with ADC value of about 670 x10-6 mm2 /s compared with 1560 x10-6 mm2 /s for normal adjacent area. Prostate cancer was the biopsy result.



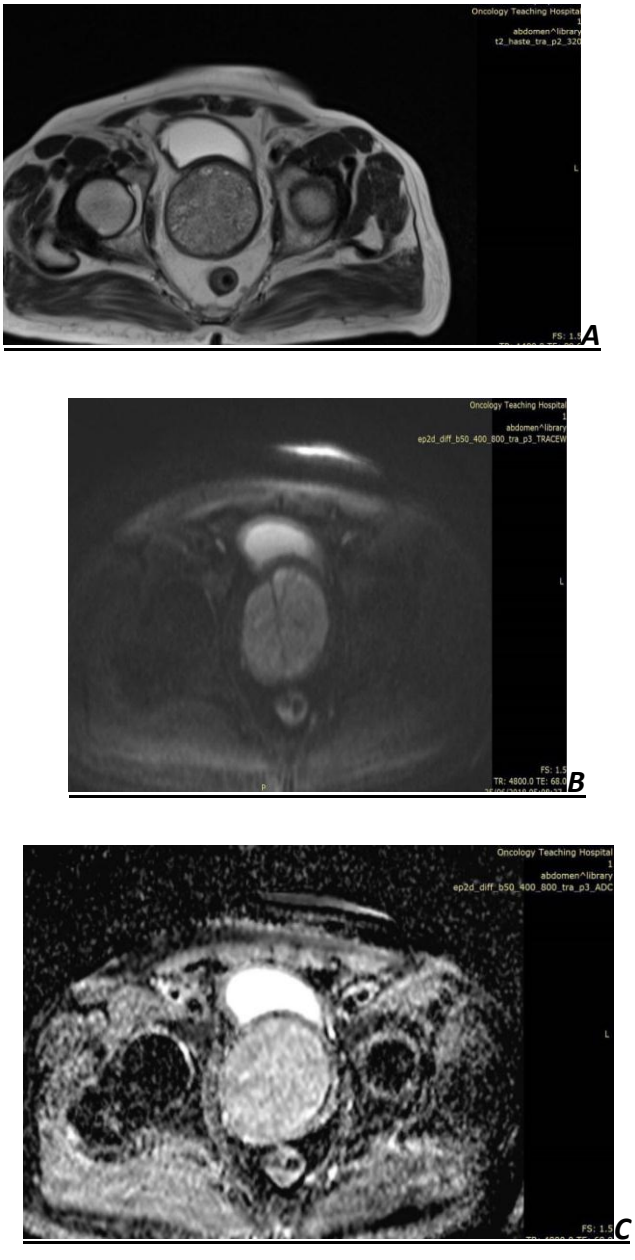
A B C

Figure (3): 65 years old male with elevated PSA level. Pelvic MRI was done and there is abnormal hypointense lesion in the right peripheral zone in contact with prostatic capsule causing capsular bulge (red arrow) (A).The same lesion appeared hyperintense on DWI (blue arrow) (B) and hypointense on ADC image (C) (restricted diffusion) with ADC value 7 30x10-6mm2/s as compared with 1150x10-6 mm2/s for normal adjacent prostate parenchyma. The histopathological result was prostate cancer.



A B C

Figure (4) :70 years old male presented with elevated PSA level, pelvic MRI showing ill-defined hypointense lesion in the left peripheral zone, the low signal intensity prostatic capsule appears intact and continuous, (A). DWI and ADC image showing corresponding restricted area with ADC value about 860 x10-6 mm2/s. Prostate cancer was the histopathological results.



A B C

Figure (*5*): 69 years old male presented with mildly elevated PSA level (about 7 ng/ml).Pelvic MRI T2WI (A) revealed enlarged prostate gland (markedly enlarged transitional zone with intact hypointense prostatic capsule, heterogeneous prostate gland signal intensity but no definitive focal lesion.(B&C)No abnormal restricted lesion on DWI and ADC image with average ADC value about 1300 x10-6 mm2/s in different areas of the prostate …Picture was consistent with BPH.

Discussion

Although prostate cancer diagnosis has been mainly dependent on biopsy guided by TRUS, it was reported that TRUS guided biopsy had 40% false-negative rates [18, 19].

DW-MRI is a developing imaging sequence that can reveal changes in signal intensity due to the restriction of movement of water molecules in biological tissues. The histopathological study of prostate cancer shows hypercellularity and alteration in the glandular structure of prostate parenchyma [15, 16, 20].

the literature revealed that significant differences in the ADC values between prostate cancer and benign prostatic lesions are present.

In prostate cancer, the ADC value was found to be lower than normal prostatic parenchyma [16, 21]. This was in agreement with the results of

this study which showed significant differences in ADC values between suspicious regions and normal prostatic gland tissue at a b value of 1000 s/mm2.

In this study, the sensitivity of T2WI in the detection of abnormality in the prostate gland peripheral zone was 76.6% and the specificity was 77%. By performing the DWI and measuring the ADC value at (b=1000); the sensitivity in the detection rate increases to 96.6 % and the specificity increases to 88.8%. So DWI had obviously raised the sensitivity and specificity (but to a lesser extent) of prostate cancer detection than T2 WI alone. These results were comparable to the study of Yağcı A.B et al, in which, the sensitivity of T2WI alone was 71% and the specificity was about 77% while those for DWI were 84% and 82%, respectively (22).In the study of Haider et al., the sensitivity also increased from (44-65%) with T2WI to 74-86% by using DWI, while the specificity was about (86-95%) with T2WI and (77-89%) with DWI [23].

In the current study, the accuracy of T2WI was 76.9% and even higher accuracy was reported by using DWI (about 94.8%). This was comparable to Yagci et al. who found that the accuracy of T2WI was 76% and for DWI was 83% [22].

Both T2WI and DWI had nearly similar positive predictive values; 92% for T2WI and 96%for DWI. This was higher than the results obtained by Yağcı. et al. who found that the positive predictive values were 53% and 63% for T2WI and DWI respectively in their study[22].

In the current study, the negative predictive value was markedly increased from 50% with T2WI to 88.8% with DWI.

The ADC value was found to be markedly lower in malignant lesions as compared with normal prostate gland parenchyma. This was in accordance with many previous studies as Issa et. al., Sato et al., and Tanimoto et. al. studies [15,16,17]. The mean ADC value in malignant prostate lesions in this study was about (680 x 10-6 mm2/s) and for normal parenchyma was about (1300x10-6mm/s) with a significant difference between them. This was comparable to Yağcı et al study [22].

We found that the diagnostic performance of DWI in the depiction of prostatic cancer was higher than T2WI alone. The lesions appear as poorly defined hypointense areas on T2WI. However; this hypointensity within a normal hyperintense peripheral zone may be caused by other benign lesions as non-specific prostatitis, hemorrhage, post-biopsy changes, post-radiation fibrosis, and changes of benign prostatic hyperplasia [7]. While by using DWI there will be a decrement in ADC value mostly related to increased cellularity in the tumoral lesion with tightly packed tissue architecture and decreased extracellular fluid in comparison with the normal parenchyma of the prostatic gland [24,25]; hence yielding more accurate results.

A second cause for the improved role of DWI could be the measurement of ADC, which removes the influence of T2 signal differences and, by this means fixed numerical value is obtained. While T2 imaging is non-quantitative depending on visual assessment of the morphologic alterations and the signal changes of the abnormal hypointense regions, making it a subjective assessment [23].

The fact that the size of the suspicious prostatic lesion will greatly affect its depiction by MRI [23] may explain that one case in this study, which was not clearly depicted by MRI (Neither on T2WI nor DWI) mostly due to its small size, has subsequently been diagnosed as malignant lesion depending on biopsy which was done based on high clinical suspicion.

Conclusion

In practice, using diffusion-weighted MRI sequence and its ADC quantitative measurement greatly increases tumor detection in patients suspected to have prostatic cancer and therefore should be routinely used when doing pelvic MRI for a patient with high clinical suspicion.

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Conflicting Interest

No conflict of interest.

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