Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2022.118671.2463 Volume 30, Issue 1.2, February 2024, Supplement Issue
Manuscript ID ZUMJ-2201-2463 (R1)
DOI 10.21608/ZUMJ.2022.118671.2463

ORIGINAL ARTICLE

Applicability of Abbreviated Biparametric MRI for Detection of Suspected Prostate Cancer: Comparative Study to Standard Multiparametric MRI Using PI-RADS V2.1

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Submit Date 2022-01-27
Revise Date 2022-03-10
Accept Date 2022-04-02

ABSTRACT

Background: The abbreviated biparametric MRI (bpMRI) uses T2 and diffusion-weighted images without dynamic contrast-enhancement (DCE-MRI) to avoid the adverse effects, reduce testing time and cost, compared to multiparametric MRI (mpMRI). Its capability to detect prostate cancer with the Prostate Imaging and Reporting Data System version 2.1 needs more comprehensive studies.
We aim To assess the reliability and diagnostic performance of the abbreviated bpMRI in the detection of prostate cancer using 3.0 tesla machine, compared to standard mpMRI using PI-RADS v2.1
Methods: Using 3.0T MRI machine, 180 biopsy-naïve patients suspected of prostatic cancer underwent an abbreviated bpMRI, then, the standard mpMRI was completed by DCE-MRI. Four experienced uroradiologists independently assessed each suspected PC lesion and the diagnostic performances of the two approaches were analyzed. Finally, transrectal US- guided targeted 12-core biopsies were performed for histopathology.
Results: In this patient-based analysis, the mpMRI showed higher detection rates than the bpMRI approach, when considering category-three lesions as benign, with sensitivity, specificity, accuracy, positive and negative predictive values of 88.57%, 96%, 91.7%, 96.8%, 85.7% for the mpMRI protocol vs. 57.14%, 92%, 71.7%, 90.9%, 60.5% for the bpMRI protocol, respectively ($P<0.001$). ROC curve analysis exhibited a greater AUC for the full over the abbreviated protocol (0.937 vs. 0.883). However, this was not evident when considering the same category as malignant.
Conclusions: When considering PI-RADS category three lesions as malignant, biparametric MRI could be considered as effective as multiparametric MRI. However, when considering category three lesions as benign, multiparametric MRI had a higher detection rate.
Keywords: Biparametric; Magnetic resonance imaging; Multi-parametric; Prostate cancer; Prostate Imaging Reporting and Data System version 2.1

INTRODUCTION

Prostate cancer (PC) is regarded as one of the most prevalent malignancies as well as a leading cause of cancer-related mortalities amongst men worldwide. As a result, the need for diagnostic modalities that could detect the disease in an early stage has progressively increased **[1].**

Currently, the standard pathway for diagnosing PC includes measurement of the prostate-specific antigen (PSA) levels in addition to a digital rectal examination. Based on such a workup, a decision would be made on whether to subsequently perform a transrectal ultrasound-guided systematic (TRUS) biopsy [2]. However, the current body of evidence has demonstrated a vast range of drawbacks to such a diagnostic pathway, including over diagnosis, treatment complications, and even a higher mortality rate **[3,4].**

For now, multi-parametric magnetic resonance imaging (mpMRI) is extensively used as a further step to detect cases unidentified by the conventional systematic TRUS biopsy **[5–8]**. mpMRI can be described as an approach that utilizes a minimum of three techniques, including high-resolution T2-weighted imaging (T2WI) for morphological evaluation, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced imaging (DCE-MRI) **[9].**

Occasionally, a fourth element is used to add to the procedure's specificity as regards PC lesion distinguishment. Such a technique operates through the employment of magnetic resonance spectroscopy (MRS) in visualizing choline levels and ratios **[10,11].** The American College of Radiology had released the Prostate Imaging and Reporting Data System (PI-RADS) as version 1 in 2012, version 2 (v2) in 2015, and version 2.1 (v2.1) in 2019. PI-RADS™ v2.1 has five categories according to the mpMRI findings probability of lesion in the prostate gland to be malignant or nonmalignant. These Categories are:

PIRADS 1: Very low risk for malignancy
PIRADS 2: Low risk for malignancy
PIRADS 3 : Intermediate risk (equivocal)
PIRADS 4 : High risk for malignancy
PIRADS 5 : Very high risk for malignancy **[12]**.

The mpMRI, involves both anatomical and functional assessment methods, the acquisition and interpretation of such imaging protocols is usually an overly lengthy process. Moreover, the high cost for each given test would negatively influence the procedure's availability **[13]**. This has raised up the need for an edited protocol that both reduces cost and time consumption and significantly increases the availability of the test. Accordingly, many studies have reported the usefulness of the abbreviated biparametric MRI (bpMRI) in detecting clinically significant PC **[13–16**].

In this imaging technique, the same components of mpMRI are used, except for DCE-MRI. This assumes that the DCE-MRI component of mpMRI has a limited contribution to the diagnostic performance of mpMRI. In addition, the use of gadolinium contrast materials has recent safety concerns (e.g., nephrogenic systemic fibrosis, etc.) **[17,18]**. Frequent studies have reported bpMRI to be superior or as accurate as mpMRI **[12,13,19–21]**. On the other hand, several trials had concluded that DCE-MRI significantly contributes to the sensitivity of mpMRI and that such a component can be regarded as a crucial part of the procedure [22,23].

The current study compares the two techniques, bpMRI and mpMRI, in terms of diagnostic accuracy and performance, through analysis of PC detection rates in men with high PSA levels.

METHODS

This retrospective study was approved by the local institutional ethics committee and review board. The informed written consents were waived. The work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion and exclusion criteria

Between August 2019 and April 2021, we included male patients suspected of prostatic cancer with abnormal PSA levels and has only one suspicious lesion. Cases excluded from our study if they had undergone previous prostate mpMR imaging, patients with multiple lesions, had a previous prostate biopsy, or had received radiotherapy for a PC condition. In addition, images obtained in bad quality (e.g., due to motion artifacts or server issues) were not considered for review. Moreover, incomplete mpMRI examinations (e.g., lacking the DCE-MRI component) were ruled out **Fig.1**. As a result, 180 patients were identified for inclusion in our study with the mean age being 65±8 years (range= 48 to 82 years).

MRI Acquisition

All MRI studies were performed on 3.0-T MRI systems (Ingenia, Philips Medical Systems) with a multichannel phased-array external surface coil. All patients received intramuscular Butylscopolamine (i.e., Buscopan) or Glucagon as an anti-peristaltic agent. A full prostate mpMRI protocol was implemented for all patients, including T2WI, DWI, and DCE-MRI.

The MRI protocol obtained for all patients included:
- (1) T2-weighted images (FOV: 200 mm, TR: 5000 msec, TE: 110 msec, slice thickness: 3 mm, no interslice gap, and matrix: 288 × 192), were acquired in axial, sagittal, and coronal planes according to the recommendations of the PI-RADS version 2.1 **[2]** Diffusion-weighted images (DWI) (FOV: 350 mm, TR: 7255 msec, TE: 85 msec, slice thickness: 3 mm, no interslice gap, and matrix: 128 × 96), using low (0 s/mm2), intermediate (800 s/mm2), and high (1400 s/mm2) b values and ADC maps were obtained at b0 and b1400 s/mm2 gradients. **[3]** Dynamic contrast enhancement (DCE) images (FOV: 200 mm, TR: 19 msec, TE: 1.93 msec, slice thickness: 4 mm, no interslice gap temporal resolution ≤ 15 s and matrix: 320 × 192), were obtained after IV injection of

contrast media (Magnifest) at a dose of 0.1 mmol/kg (maximum dose 15 mmol) at a rate of 3 mL/s.

Image Interpretation

The obtained mpMRI datasets were evaluated by four trained Uroradiologists with seven to twelve years of experience in prostate MR imaging, reading, and interpretation, through an Extended Brilliance Workstation (Philips Medical System). Blinded to any specific findings of subsequent images obtained during the biopsy, any histopathological, clinical, or laboratory information while assigning each lesion a PI-RADS v2.1 category, according to the published recommendations and guidelines. In a two-step classification process, only T2W and DW images, through ADC maps, were first interpreted and assigned a category according to the recommendations of PI-RADS v2.1, in a bpMRI manner (i.e., without DCE-MRI). Then, DCE-MR images were considered for the full mpMRI protocol, which was reclassified into a PI-RADS v2.1 category. Eventually, the diagnostic performances of the two techniques were analyzed and compared.

Confirmation of the MR Results

For this study, trans rectal US-guided targeted 12 core biopsies and the histopathological features of the specimens retrieved during the process were the reference standard used to determine the diagnostic accuracy of the two techniques.

TRUS-Guided Targeted Biopsy

All TRUS procedures were performed using an (EPIQ 7, Philips Healthcare, Best, Netherlands) system, a high-frequency Trans rectal transducer (5-9 MHz), and an 18G biopsy needle. Both axial and coronal planes were used for scanning the entire volume of the prostate, to target lesions detected by MRI. Additional cores were taken on a case-by-case rationale. Antibiotics (i.e., quinolones) were the standard regimen used for countering any infections. Samples obtained were then retrieved and sent for pathological evaluation.

Histopathological Evaluation

Histopathological validation of the retrieved specimens was carried out by a certified Uropathologist who reported and assessed the lesions in concordance with the European Association of Urology guidelines **[24]**. A final diagnosis was established as regards the presence of PC lesions in the biopsied specimens. Furthermore, a Gleason score (GS) and classification were assigned to each lesion, according to the 2005 recommendations of the International Society of Urological Pathology (ISUP) **[25]**.

STATISTICAL ANALYSIS

All analyses were performed using Statistical Package of Social Science (SPSS) version 22 (SPSS Inc., Chicago, Illinois, USA). Continuous data were presented as mean ± SD or median and range as appropriate. We presented the qualitative data in frequencies and percentages. Chi-squared test ($\chi 2$) was used to assess the association between two or more qualitative variables. For comparing quantitative variables between two groups, the Student t-test and Mann-Whitney U test were used as appropriate. The receiver operator characteristics (ROC) analysis was performed to assess the validity of the bi-parametric and multi-parametric PI-RADs scoring system regarding the nature of the lesion by histopathology, with respective maximum accuracy points for both sensitivity and specificity. Also, the positive predictive value (PPV) and negative predictive value (NPV) were calculated. The significant difference was considered when the p-value was less than 0.05.

RESULTS

Patients

180 patients were included in this study, the mean age was higher in patients suffering from malignant lesions than those with benign tumors (67.8 ± 7.5 vs. 60.2 ± 6.9 years). According to histopathology, of the 180 considered lesions, 105 (58.30%) were malignant, and 75 (41.70%) were non-malignant.

All 105 malignancies were adenocarcinomas, with the vast majority (54.8%) of the lesions scoring 4+4 on the Gleason scale used. On the other hand, 66 of the non-malignant lesions were cases of Benign Prostatic Hyperplasia, while the remaining 9 were due to prostatitis. Cancerous lesions were more located in the peripheral zone (PZ); 93 out of 105 (88.57%), while benign lesions were found more in the transitional zone (TZ); 66 out of 75 (88%). No lesions were reported in the central zone (CZ). The most reported clinical symptoms amongst the studied sample were hematuria (33%) and urine retention (27%). The average PSA level was 35 ± 33.9 ng/dl (range, 4.8 to 100 ng/dl). The mean PSA level was significantly higher among patients with malignant lesions ($p<0.0001$). (**Table 1)**.

Analysis of the Diagnostic Accuracies of bpMRI and mpMRI

In terms of detection rates, the PI-RADS v2.1 scores for the bpMRI-produced images were highly indicative of malignancy (score, 4-5) in 66 of the 180 inspected lesions, 60 of which were found to be truly malignant (True Positive, TP) through histopathology. Meanwhile, 96 mpMRI-scanned

lesions had a PI-RADS v2.1 score of 4 to 5, with 93 of these (TP) proven to be malignant by histopathological assessment. As for the negative observations, 63 lesions were not suggestive of malignancy on both bpMRI and mpMRI protocols, of which 54 and 57 lesions, respectively, were consistent with the diagnosis of a benign tumor (True Negative, TN). Score-three (i.e., intermediate) lesions were 51 according to bpMRI scanning, of which 36 were histopathologically determined as malignant, while 15 were found benign. In the case of mpMRI, intermediate lesions were lower than bpMRI (21 observations), the final diagnosis in 15 of which was benign. Accordingly, when considering category-three lesions as benign, the diagnostic sensitivity, specificity, accuracy, PPV and NPV were higher in mpMRI than bpMRI (88.57%, 96%, 91.7%, 96.8%, and 85.7%) vs. (57.14%, 92%, 71.7%, 90.9%, and 60.5%). Meanwhile, when regarding category-three lesions as malignant, the diagnostic sensitivity, specificity, accuracy, PPV and NPV were comparable among the two protocols (94.3%, 76%, 86.6%, 84.6% and 90.5% for mpMRI versus 91.4%, 72%, 83.3%, 82.1% and 85.7% for bpMRI). An image example of findings from the abbreviated biparametric and complete multiparametric approaches is provided in **Figure 2** and **Figure 3**. ROC-curve analysis showed a greater AUC in mpMRI (0.937) than bpMRI (0.883). Illustrations of the diagnostic sensitivities and specificities of the two techniques are shown in **Figure 4**. A summary of the diagnostic performances of the two approaches is listed in **Table 2** and **Table 3**.

ADC and DCE-MRI

Using the standard monoexponential regression model, the Apparent Diffusion Coefficient (ADC) maps were calculated, by employing different b-values for both malignant and benign lesions, (mean ± SD = 0.63 + 0.14 x 10-3 and 1.31 + 0.24 x 10-3 s/mm2, respectively), with the diffusion gradients applied on three orthogonal directions for each value, and an overall b-value range from 0.4 x 10-3 to 1.7 x 10-3, as well as a mean ± (SD) of 0.91 x 10-3 ± 0.39 x 10-3s/mm2. ADC results showed a significant predictive value in the discrimination between benign and malignant observations (P<0.001). Secondary use of DCE-MRI followed the PI-RADS 3 scoring of 36 lesions, according to the DWI technique, of these observations, 30 showed positive contrast enhancement and were subsequently assigned a PI-RADS 4 score, while the remaining 6 lesions halted at PI-RADS 3 score due to negative enhancement. According to the DCE-MRI sequence, 93 (51.7%) of the lesions were defined as positive observations, while 87 (48.3%) were regarded as negative.

Table 1: shows the demographic features and clinicopathological data of the study's population

		All patients (n= 180)	*Benign lesions (n= 75)*	*Malignant lesions (n= 105)*	*P value*
Age (years)	***Mean± SD***	***65.0 ± 8.0***	***60.2 ± 6.9***	***67.8 ± 7.5***	***0.0011***
Age groups, n (%)	***40-50***	***12 (7%)***	***12 (16%)***	***0 (0%)***	***0.0082***
	51-60	***45 (25%)***	***24 (32%)***	***21 (20%)***	
	61-70	***69 (38%)***	***33 (44%)***	***36 (34%)***	
	71-80	***48 (27%)***	***6 (8%)***	***42 (40%)***	
	≥81	***6 (3%)***	***0 (0%)***	***6 (6%)***	
Presenting symptoms, n (%)	***Dysuria***	***27 (15%)***			
	Hematuria	***60 (33%)***			
	Urine retention	***48 (27%)***			
	Burning micturition	***15 (8%)***			
	Weak stream of urine	***9 (5%)***			
	Urinary frequency	***21 (12%)***			
Tumor Gleason score at TRUS biopsy, n (%)	***3+3***			***6 (5.7%)***	
	3+4			***21 (20%)***	
	4+3			***27 (25.7%)***	
	4+4			***48 (54.8%)***	
	4+5			***3 (2.8%)***	
PSA level (ng/dl)	***Mean± SD***	***35 ± 33.9***	***13.7 ± 11.7***	***50.3 ± 36.3***	***<0.0001***

Table 2: shows the validity of the bi-parametric and multi-parametric PI-RADs scoring system regarding the nature of the lesion by histopathology when the score-three lesions were regarded as malignant

	Bi-parametric PI-RADs scoring system				multi-parametric PI-RADs scoring system			
	Benign (n=75)	Malignant (n=105)	N	p-value	Benign (n=75)	Malignant (n=105)	N	p-value
PI-RAD score <3	54	9	63	<0.001*	57	6	63	<0.001*
PI-RAD score 3-5	21	96	117		18	99	117	
Sensitivity	91.40%				94.30%			
Specificity	72.00%				76.00%			
PVP	82.10%				84.60%			
PVN	85.70%				90.50%			
Accuracy	83.30%				86.60%			

Table 3: shows the validity of the bi-parametric and multi-parametric PI-RADs scoring system regarding the nature of the lesion by histopathology when the score-three lesions were regarded as benign.

	Bi-parametric PI-RADs scoring system				multi-parametric PI-RADs scoring system			
	Benign (n=75)	Malignant (n=105)		p-value	Benign (n=75)	Malignant (n=105)		p-value
PI-RAD score 1-3	69	45	114	<0.001*	72	12	84	<0.001*
PI-RAD score 4-5 (n=)	6	60	66		3	93	96	
Sensitivity	57.14%				88.57%			
Specificity	92.00%				96.00%			
PVP	90.90%				96.80%			
PVN	60.50%				85.70.00%			
Accuracy	71.70%				91.70%			

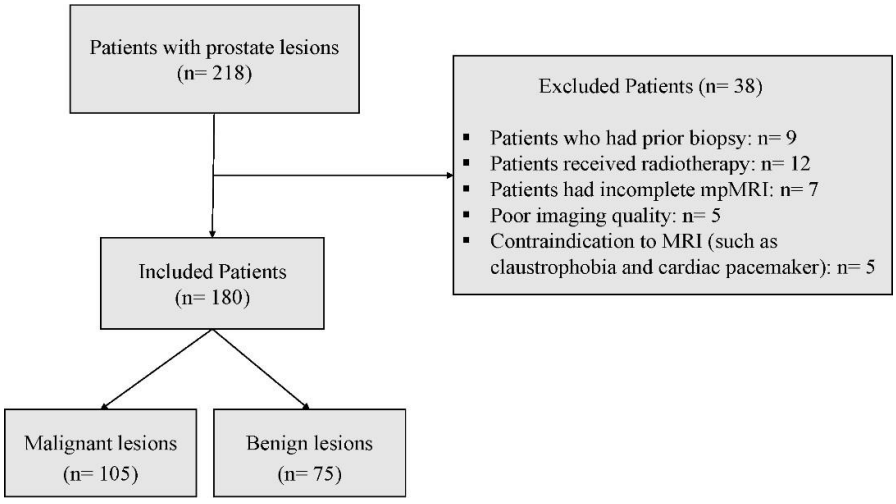

Figure (1) Illustrating the number and reason for excluded patients

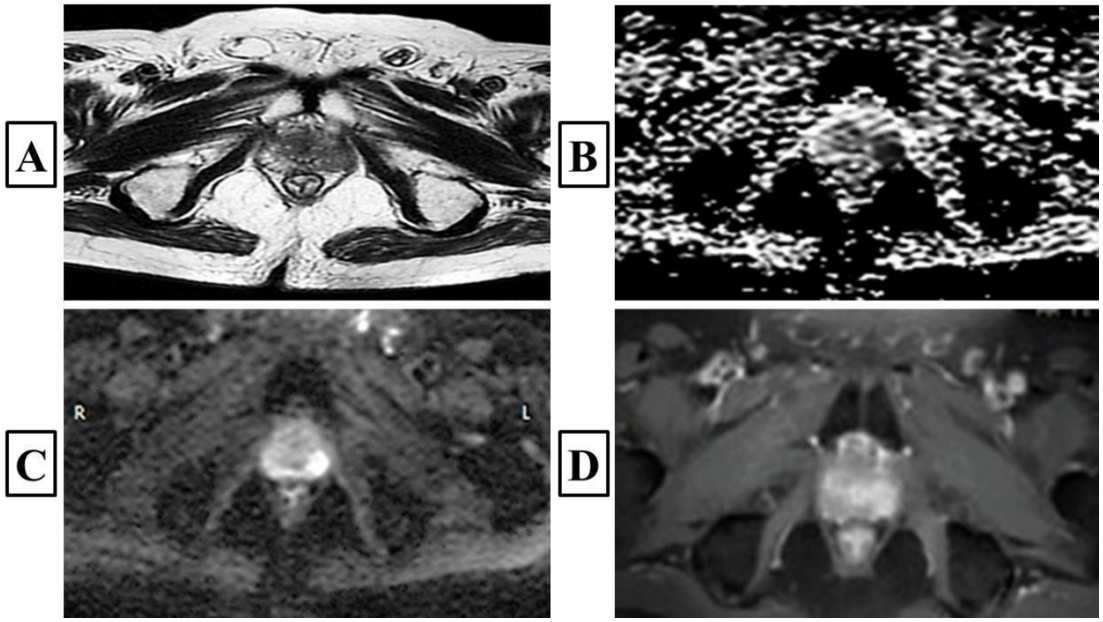

Figure (2) shows prostatic adenocarcinoma with Gleason score 4 + 4 in a 65- year-old male patient with serum PSA >30 ng/ml. (A) Axial T2WI shows circumscribed homogeneous moderate hypointense mass less than 1.5 cm seen involving the LT posterolateral peripheral zone of the prostate. (B) Axial ADC shows focal markedly hypo intense mass less than 1.5 cm. (C) Axial high b value DWI shows focal markedly hyper intense mass less than 1.5 cm (the final PI-RADS score on basis bpMRI was score 4). (D) Axial DCE shows +ve contrast enhancement. The final PI-RADS score based on mpMRI was score 4, DCE did not aid in the diagnosis of this case, and it was already diagnosed by bpMRI.

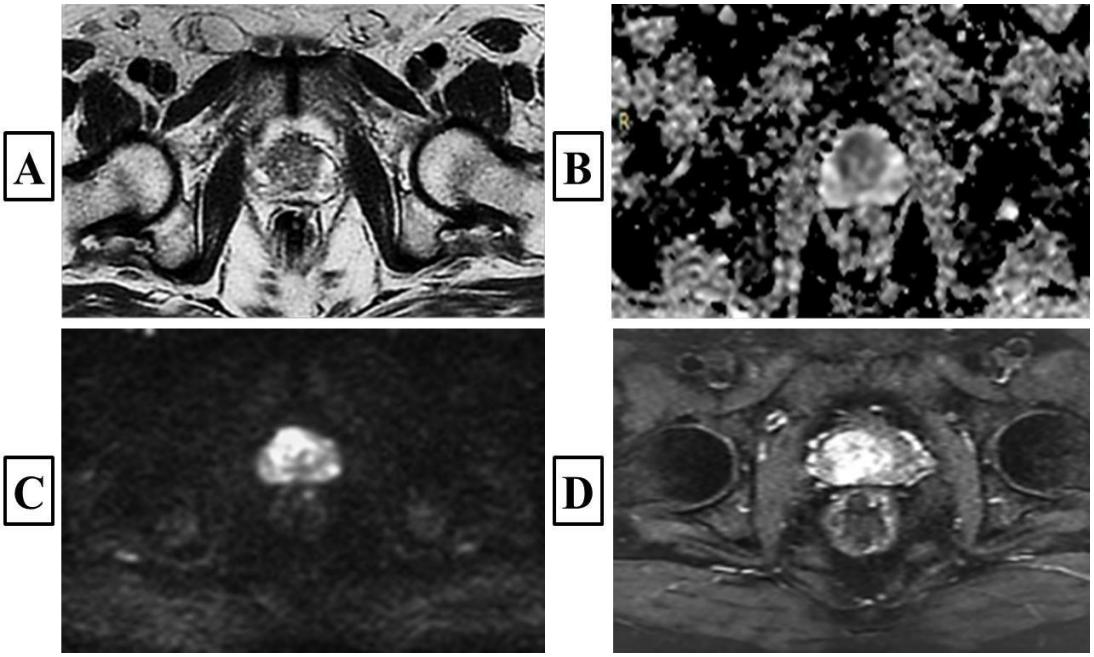

Figure (3) shows prostatic adenocarcinoma with Gleason score 4 + 3 in a 68-year-old male patient with serum PSA = 60 ng/ml. (A) Axial T2WI shows circumscribed homogeneous moderate hypointense mass > 1.5 cm seen involving the transitional zone. (B) Axial ADC shows focal markedly hypointense mass >1.5 cm. (C) Axial high b value DWI shows focal markedly hyperintense mass >1.5 cm (the final PI-RADS score on basis bpMRI was score 5). (D) Axial DCE shows +ve contrast enhancement. The final PI-RADS score based on mpMRI was score 5, DCE did not aid in the diagnosis of this case, and it was already diagnosed by bpMRI.

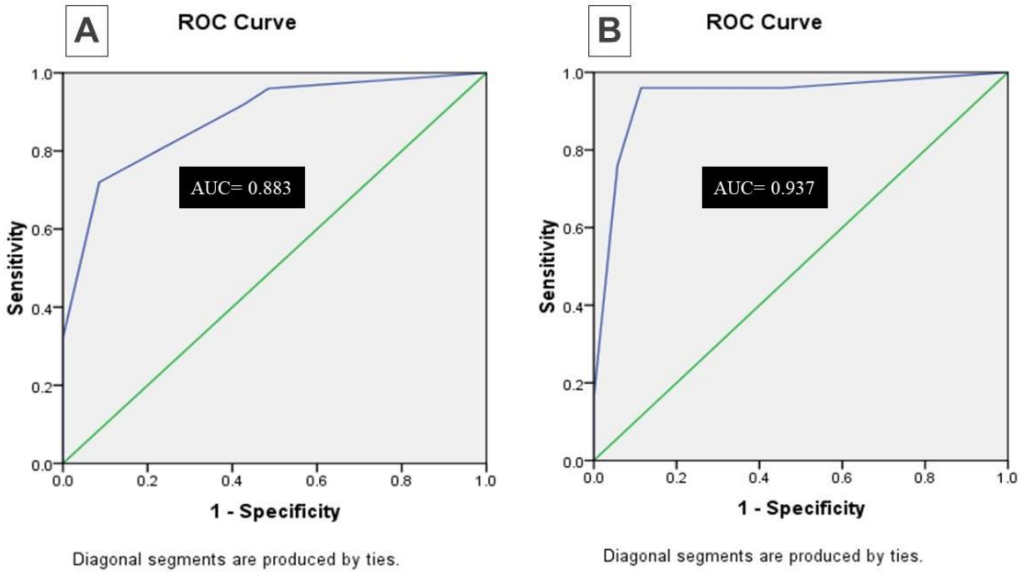

Figure (4) shows the ROC curve for the sensitivity and specificity for discrimination between benign and malignant prostatic lesions of (a) bp MRI (AUC= 0.883) and (b) mp-MRI (AUC= 0.937).

DISCUSSION

In this study, we examined the potential applicability of the abbreviated bpMRI protocol in detecting PC lesions and the consequential outcomes of omitting the use of a contrast agent during the procedure. The quest for a reduced form of prostatic MRI examination can be ascribed to the growing number of workups in patients with abnormal PSA levels, thereby stressing the need for a readily accessible method for a larger population within a much shorter duration (approximately 15-20 minutes), and conveniently **[26]**. First introduced in 2014, the concept of utilizing an abridged screening method that saves time and increases patients' accessibility was tested for breast cancer. Interestingly, a shortened MRI examination was sufficient to exclude negative cases and had a comparable accuracy to the complete protocol **[27]**.

The current results are in dispute with a vast portion of the literature, where bpMRI has been found inferior to mpMRI regarding their diagnostic reliabilities and performances. Recently, the role of the DCE component has been more controversially discussed. Since released in 2017, the PI-RADS v2.1 has witnessed substantial marginalization of the role of DCE-MRI in PC identification. In an attempt to investigate the different accuracies of various MRI protocols, Delongchamps et al. first had the observation that adding DCE-MRI significantly reduced the diagnostic accuracy of the procedure than when T2WI and DWI were used alone **[28]**.

A recent systematic review and meta-analysis that involved ten observational studies found similar efficacies among the two imaging modalities, bpMRI, and mpMRI, in PC diagnosis (29). Another investigation by Di Campli et al. found that the diagnostic accuracy of bpMRI was comparable to that of the standard protocol **[30]**.

An important finding in our study was that despite the significant difference in diagnostic accuracies between the two techniques; however when considering PI-RADS three-scored lesions as malignant, bpMRI had comparable results to the full protocol. Such an observation has been reported previously, where a 5.93% increase in false-negative results was noticed by Junker et al., only when the score-three lesions were regarded as benign **[31]**.

Similarly, Scialpi et al., who concluded the applicability of bpMRI as an alternative to mpMRI for PC detection, found a 3.3% rise in the false-negative outcome under the same settings **[16]**.

Moreover, it was stated by EL-Adalany et al. that mpMRI had higher sensitivity and specificity outcomes than the abbreviated method, only when viewing PI-RADS 3 lesions as benign **[32]**.

Although there are currently no clear justifications to this phenomenon, it strongly emphasizes the potential role of DCE-MRI in discovering lesions with a PI-RADS category equal to or more than three on bpMRI examination. This effect was also found to be more prominent amongst PZ lesions, and to a lesser extent, in the TZ **[22]**. Druskin et al. suggested that a possible explanation

for the gradually diminishing role of the DCE-MRI component in the clinical research of PC is how out-of-context the role of the procedure is discussed concerning the PI-RADS v2.1 recommendations **[33]**. The current study had some limitations in terms of design, patient selection, sample size, and the measures of classification employed. First, although unaware of the outcomes of any subsequent images obtained during the confirmatory biopsy, the reader, however, was knowledgeable of other clinical features of the patients, including past and family history, PSA levels, and characteristics. This might have introduced a source of bias during the decision-making process. Second, in the study conducted by Druskin et al., in 2017, when the chosen sample was based on patients with prior negative biopsies, the role of DCE-MRI was more beneficial **[33]**. On the other, another study by Rais-Bahrami et al., which included biopsy-naïve patients, found that omitting the contrast-agent factor did not significantly alter the diagnostic performance of the approach **[34]**.

Third, the inclusion of a larger sample size in our analysis would have allowed for more reliable results. Moreover, a multicentered study with multiple readers would have better assessed inter-reader reliability. Further investigation is mandatory for evaluating the feasibility of bpMRI as an acceptable alternative for mpMRI in clinical practice when dealing with PC.

CONCLUSIONS

we observed a significant difference in PC detection rates among the two procedures. Our results come in dispute with a vast majority of the published literature regarding PC workup. Although this could be ascribed to multiple factors, one potentially fundamental contribution to the current findings is regarding PI-RADS $\leq$ 3 lesions as benign, a phenomenon that should be taken into consideration in future work

Conflicts of interests: *None*
Financial disclosure: *None*

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To cite:

Emara, E., Ebaid, N., Eladl, I., Foda, H. Applicability of abbreviated biparametric MRI for detection of suspected prostate cancer: Comparative study to standard multiparametric MRI using PI-RADS V2.1. *Zagazig University Medical Journal*, 2024; (129-137): -. doi: 10.21608/zumj.2022.118671.2463