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Feasibility of multi-parametric magnetic resonance imaging in detection and local staging of prostatic carcinoma

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Abstract

Background: The objective of this study was to assess the feasibility of multi-parametric magnetic resonance imaging (mpMRI) in detection, localization and local staging of prostate cancer (Pca).

Methods: The study included 58 patients with Pca who underwent mpMRI before radical prostatectomy (RP) at two university hospitals, during the period June 2014 to April 2018. All prostatectomies were performed on the basis of preoperative transrectal ultrasound-guided prostatic biopsies. For tumor localization, the prostate in each patient was divided into six segmental regions. Biopsy specimens, for each segmental region, were evaluated for the presence of cancer. The diagnostic performance of mpMRI in tumor localization as well as extracapsular extension (ECE) and seminal vesicle (SV) invasion of the tumor was evaluated, by using the histopathological findings of RP specimens as reference standard.

Results: The mean age of patients was 63.45 ± 7.45 years. Of the total number of 348 segmental regions, tumor was detected in 143. From them, cancer was detected in 142 regions by mpMRI. The sensitivity and specificity of mpMRI for cancer localization were 99.30% and 97.56%. On RP specimen, nine cases had ECE and five had SV invasion. All of them were detected preoperatively by mpMRI. The sensitivity and specificity of mpMRI for detection of ECE were 100% and 97.96%. For detection of SV invasion, the sensitivity and specificity were 100% and 98.11%.

Conclusions: mpMRI enables localization and staging of cancer prostate with reasonable accuracy. Its combination with ultrasound should be counted on for improvement in efficacy of the prostatic biopsy procedure.

Keywords: Prostatic carcinoma, Multi-parametric magnetic resonance imaging, Transrectal ultrasound, Prostatic biopsy

1 Background

Most of prostate cancer (PCa) cases are first found during screening with digital rectal examination (DRE) or serum prostatic-specific antigen (PSA) [1, 2]. The actual diagnosis of PCa is based only on prostatic biopsies. In 1989, Hodge et al. introduced transrectal ultrasound (TRUS)-guided biopsy which became the core of the standard care in diagnosis of PCa [3]. However, its role in local staging is limited.

Magnetic resonance imaging (MRI) was introduced in 1990s as a tool to aid the locoregional staging of PCa. This traditional technique is based on anatomical sequences only, and its resolution is allowed for only assessment of T3 disease [4]. The recent advent of multiparametric MRI (mpMRI), based on the anatomic T1- and T2-weighted imaging (WI) and functional imaging of alteration caused by neoplastic tissue, expanded the scope of MRI in diagnosis and local staging of PCa [5, 6].

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The aim of the present study was to get a better understanding the value of mpMRI in detection, localization, and local staging of PCa, using radical prostatectomy (RP) specimens as reference standard.

2 Methods

The study included patients with PCa who underwent mpMRI before RP during the period from June 2014 to April 2018 at our university hospitals. Patients with incomplete medical record, previous prostatic biopsies within 3 months of mpMRI and those with known diagnosis of or non-PCa before mpMRI were excluded. The study protocol was approved by our local ethical committee. The patients' demographic data, clinical characteristics, presenting PSA level, TRUS findings and TRUS biopsy and RP specimen histopathology reports were reviewed and recorded.

All patients underwent mpMRI 3–10 days before undergoing the prostate biopsy. The mpMRI was comprised of T2WI, diffusion WI (DWI), magnetic resonance spectroscopy (MRS) and axial dynamic contrast enhancement (DCE) imaging. Examinations were performed using a 3.0 Tesla scanner, (Achiva, 3T; Philips Healthcare Best, Netherlands) equipped with a pelvic phased array surface coil with the patient in supine position. The guidelines of prostate imaging–reporting and data system (PI-RADS) v2™ [7] were followed in patient preparation, MRI technical specifications, lesion assessment, staging and reporting.

Ultrasound-guided transrectal prostate biopsies were performed under local anesthesia by the guidance of ultrasound [BK-medical, Denmark; supplied with a biplanar transrectal probe (5–7.5 MHz)]. A tru-cut 18-gauge needle was used, and a systematic 12-core biopsy was employed.

The prostatic biopsies and RP specimens were examined by an expert histopathologist. For tumor localization, prostate was divided into right and left halves and each half was divided into three segments (base, midgland and apex). Biopsy specimens for each segmental region were evaluated for the presence of cancer.

Data were analyzed using MedCalc statistical software program. Continuous data were expressed as mean ± standard deviation (SD), median and range. Categorical data were expressed as frequency and percentage. Mann–Whitney *U* test was used to compare continuous variables, and Chi-square or Fisher exact test was used to compare the categorical variables. The diagnostic accuracy of different diagnostic tools was evaluated by measuring the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios. Also the area under the curve (AUC) was measured and presented with its 95% confidence interval (CI). An alpha error of ≤ 0.05 was considered statistically significant.

3 Results

Fifty-eight patients were eligible for the study. The age of study subjects ranged from 51 to 78 years (mean 63.45 ± 7.45 years). The patients' median presenting the PSA level was 17.60 ng/mL. Tumor staging on DRE was cT1 in 32.76% ($n=19$) of cases and cT2 in 67.24% ($n=39$). The patients' age, presenting the PSA level and prostate size, is shown in Table 1.

The pathological examination of RP specimen revealed that: 46.55% ($n=27$) were pT2b, 39.65% ($n=23$) were pT2c, 6.90% ($n=4$) were pT3a, and 6.90% ($n=4$) were pT3b. No regional lymph node involvement or positive surgical margins were detected in any of the RP specimens. Six cases (10.34%) had Gleason score: 3 + 3, 21 (36.21%): 3 + 4, 29 (50.00%): 4 + 3 and 2 (3.45%): 4 + 5.

Of the total number of 348 ROIs, cancer was detected in 89 regions (25.57%) in TRUS-guided biopsies, in 147 regions (42.24%) in mpMRI, and in 143 regions (41.09%) in RP specimens. Using the histopathological findings of RP specimens as reference standard, the diagnostic performance of preoperative TRUS and mpMRI in tumor localization was as follows: sensitivity (57.34% and 99.30%); specificity (96.59% and 97.56%); PPV (92.13% and 96.60%); and NPV (76.45% and 99.50%) (Table 2).

On RP specimens, ECE was observed in nine (15.52%) patients. All cases were detected on preoperative mpMRI compared to three on TRUS scan. The diagnostic performance of preoperative TRUS and mpMRI for ECE was as follows: sensitivity (33.33% and 100%); specificity (83.67% and 97.96%); PPV (2.04% and 49.00%); and NPV (87.23% and 100%) (Table 3).

Regarding SV invasion, five (8.62%) patients had SV invasion on RP specimen and all were detected by preoperative mpMRI. From those five cases, only two were detected by TRUS scan. The diagnostic performance of preoperative TRUS and mpMRI for SV

Table 1 Patients' age, presenting serum PSA level and prostate size in study subjects

	Minimum	Maximum	Median	Mean	SD
Age (years)	51.00	74.00	64.00	63.77	7.21
Total serum PSA (ng/mL)	2.60	170.00	17.40	22.55	24.27
Prostate size by TRUS (cc)	20.00	194.00	50.00	58.69	38.60
Prostate size by MRI (cc)	17.00	190.00	50.00	58.57	37.90

MRI magnetic resonance imaging, *PSA* prostatic-specific antigen, *TRUS* transrectal ultrasonography

Table 2 Diagnostic performance of preoperative TRUS and mpMRI for localization of prostate cancer in the 348 segmental regions in the studied 58 patients

	TRUS		mpMRI		Histopathology	
Cancer site (number)						
Right base	40		49		47	
Right mid-zonal	31		43		43	
Right apex	1		6		4	
Left base	12		27		27	
Left mid-zonal	7		18		18	
Left apex	0		4		4	
Total	89		147		143	
	Test + ve	Test − ve	Test + ve	Test − ve		
	82	61	142	1	143	True + ve
	7	198	5	200	205	True − ve
Sensitivity (%)	57.34 (95% CI 48.81–65.57)		99.30 (95% CI 96.17–99.98)			
Specificity (%)	96.59 (95% CI 93.09–98.62)		97.56 (95% CI 94.40–99.20)			
Positive PV (%)	92.13 (95% CI 84.46–96.78)		96.60 (95% CI 92.24–98.89)			
Negative PV (%)	76.45 (95% CI 70.80–81.48)		99.50 (95% CI 97.26–99.99)			
Positive LHR	16.79 (95% CI 08.00–35.26)		40.71 (95% CI 17.13–96.78)			
Negative LHR	00.44 (95% CI 00.36–00.54)		00.01 (95% CI 00.00–00.05)			
AUC	00.77 (95% CI 00.72–00.81)		00.98 (95% CI 00.96–00.99)			

AUC area under the curve, *LHR* likelihood ratio, *mpMRI* multi-parametric magnetic resonance imaging, *PV* predictive value

Table 3 Diagnostic performance of preoperative TRUS and mpMRI for detection of extracapsular extension in the studied 58 patients

Cancer site (number)	TRUS		mpMRI		Histopathology	
	Test + ve	Test − ve	Test + ve	Test − ve		
	3	6	9	0	9	True + ve
	8	41	1	48	49	True − ve
Sensitivity (%)	33.33 (95% CI 07.49–70.07)		100 (95% CI 66.37–100)			
Specificity (%)	83.67 (95% CI 70.34–92.86)		97.96 (95% CI 89.15–99.95)			
Positive predictive value (%)	27.27 (95% CI 06.02–60.97)		90.00 (95% CI 55.50–99.75)			
Negative predictive value (%)	87.23 (95% CI 74.26–95.17)		100 (95% CI 92.60–100)			
Positive likelihood ratio	02.04 (95% CI 00.67–06.26)		49.00 (95% CI 07.04–340.94)			
Negative likelihood ratio	00.80 (95% CI 00.49–01.29)		0.00			
AUC	00.59 (95% CI 00.45–00.71)		00.99 (95% CI 00.92–1.00)			

AUC area under the curve, *LHR* likelihood ratio, *mpMRI* multi-parametric magnetic resonance imaging, *PV* predictive value

invasion was as follows: sensitivity (40.00% and 100%); specificity (92.45% and 98.11%); PPV (33.33% and 83.33%); and NPV (94.23% and 100%) (Table 4).

The ADC values were significantly higher in tumors with low grade. The apparent diffusion coefficient (ADC) values were 1 ± 0.23 mm^2/s for low-grade tumors, 0.7 ± 0.17 mm^2/s for intermediate-grade tumors and 0.5 ± 0.13 mm^2/s for high-grade tumors ($p < 0.001$).

4 Discussion

Currently, risk stratification and decision-making in PCa are largely dependent on probability tables and nomograms which are based on preoperative evaluation parameters as the serum PSA level, clinical staging by DRE and TRUS-guided prostatic biopsies. These parameters already have their pitfalls [8–10]. Therefore, there is a real need for clinicians to base therapeutic

Table 4 Diagnostic performance of preoperative TRUS and mpMRI for detection of seminal vesicle invasion in the studied 58 patients

Cancer site (number)	TRUS		mpMRI		Histopathology	
	Test + ve	Test − ve	Test + ve	Test − ve		
	2	3	5	0	5	True + ve
	4	49	1	52	53	True − ve
Sensitivity (%)	40.00 (95% CI 05.27–85.34)		100 (95% CI 47.82–100)			
Specificity (%)	92.45 (95% CI 81.79–97.91)		98.11 (95% CI 89.93–99.95)			
Positive predictive value (%)	33.33 (95% CI 04.33–77.72)		83.33 (95% CI 35.88–99.58)			
Negative predictive value (%)	94.23 (95% CI 84.05–98.79)		100 (95% CI 93.15–100)			
Positive likelihood ratio	05.30 (95% CI 01.27–22.11)		53.00 (95% CI 7.61–369.34)			
Negative likelihood ratio	00.65 (95% CI 00.32–01.33)		0.00			
AUC	00.66 (95% CI 00.53–00.78)		0.99 (95% CI 0.92–1.00)			

AUC area under the curve, *LHR* likelihood ratio, *mpMRI* multi-parametric magnetic resonance imaging, *PV* predictive value

decisions on not only nomograms but also advanced imaging technique.

There is a great interest in mpMRI, being a combination of the anatomical T2W imaging and functional sequences like DWI and DCE. The addition of these functional sequences which are based on special aspects of tumor cells like angiogenesis, proliferation and metabolism give the mpMRI superiority when compared with the traditional MRI that based on the anatomical sequences only [11, 12].

As validated by the results of the present study and most of previous studies, mpMRI has a high sensitivity and specificity in local staging and localization of PCa. With higher sensitivity and specificity, mpMRI is increasingly used in guiding biopsies in biopsy-negative and previously negative cases. Also, it is used for proper staging, risk stratification and decision-making and is being incorporated in clinical nomograms [5, 8, 9, 13–16]. Moreover, MR tractography helps visualizing the prostatic nerve bundles guiding the nerve-sparing surgery to reserve the erectile function [17].

Furthermore, there is a potential role for mpMRI in not only localizing tumor but also in identifying the areas of more aggressive cancer that could be selectively targeted by biopsy or for focal ablation therapy. Several studies have shown that both DWI and spectroscopic imaging are correlated with the Gleason grade [5, 18–20]. As confirmed by our pathologic–radiologic comparison, low ADC values are associated with an increasing Gleason score.

Lastly, the higher accuracy of mpMRI for diagnosis of prostate cancer makes it a proper imaging modality for identifying patients who would benefit from an active surveillance program by ruling out the presence of clinically significant disease and avoiding unnecessary prostate biopsies [16].

The major limitations of our study is the use of RP specimens as the reference standard because prostatectomy specimens are highly selected since men must be test positive for cancer on TRUS biopsy and choose to have surgery. In addition, in our study the cost-effectiveness aspect was not taken into account as the costs of mpMRI/biopsy and those of TRUS-guided biopsy were not compared.

5 Conclusions

The mpMRI enables the detection, localization and staging of PCa with reasonable sensitivity and specificity. Its combination with ultrasound should be counted on for future improvement in safety and efficacy of the prostatic biopsy procedure.

Abbreviations

AUC: area under the curve; CI: confidence interval; DCE: dynamic contrast enhancement; DRE: digital rectal examination; DWI: diffusion-weighted imaging; mp: multi-parametric; MRI: magnetic resonance imaging; MRS: magnetic resonance spectroscopy; NPV: negative predictive value; PCa: prostate cancer; PI-RADS: prostate imaging–reporting and data system; PPV: positive predictive value; PSA: prostatic-specific antigen; RP: radical prostatectomy; SD: standard deviation; TRUS: transrectal ultrasound.

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Authors' contributions

AA contributed to data collection and analysis and manuscript writing. HH contributed to performing radical prostatectomies and data collection; SE contributed to protocol development and data collection; TE contributed to MRI scanning; GA contributed to histopathologic examination of specimens; MMA contributed to performing radical prostatectomies, TRUS scanning and TRUS-guided prostatic biopsies; AF contributed to protocol development and revision and edited the final version of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This study was approved by the Research Ethics Committee of the Urology Department, Al-Azhar University, Cairo, Reference Number of approval: Uro_Azhar_7_016. Informed consent: not applicable. (It is a retrospective diagnostic test accuracy study.)

Consent for publication
Not applicable. (No photographs or patients' personal information were included in this retrospective diagnostic test accuracy study.)

Competing interests
The authors declare that they have no competing interests.

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