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Role of MRI in diagnosis of prostate cancer and correlation of results with transrectal ultrasound guided biopsy "TRUS"

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Abstract

Background: Prostate cancer is the most common cancer in elderly men, and the second leading cause of cancer-related death in developed countries. For a long time, TRUS is used in screening, diagnosis of prostate lesions. Recently the implementation of multi parametric MRI into a screening program currently seems to be the most promising technique to improve the early detection of prostate cancer.

Results: Thirty Patients were referred from urological outpatient clinics complaining of urological symptoms (dysuria, frequency and urine retention). The study was carried, and the patients were submitted to Ultrasonography, conventional magnetic resonance, diffusion weighted images and MR spectroscopy techniques, these results were correlated with histopathological data. In this study Conventional MRI has moderate sensitivity 81.8% and low specificity 37.3% in diagnosing prostate malignancy. Using of mpMRI combination of diffusion-weighted, Dynamic contrast enhanced and MR spectroscopic imaging is a promising approach for discriminating between benign and malignant lesions in the PZ and increase sensitivity 100% and specificity 96.6% in diagnosing prostate malignancy.

Conclusions: The standard for the definitive diagnosis of prostate cancer is trans-rectal ultrasound biopsy. However, TRUS guided biopsy has a significant sampling error and can miss up to 30% of cancers and may show underestimation of Gleason grade, especially in anteriorly located tumors. It may lead to an increase in complications. MRI has an essential role to play in making safer in diagnosis. It can aid in staging also and surgery or radiation treatment planning. Although T2W MRI has been used widely for diagnosis on the basis of its excellent soft tissue resolution, but its accuracy for the detection and localization of cancer prostate is unsatisfactory. The implementation of multi parametric MRI: MR spectroscopy, Dynamic contrast enhanced and diffusion weighted imaging into a diagnosis program improve the diagnostic performance. These advances are beginning to translate into better treatment selection and more accurate image-guided therapies. In addition, early detection of local recurrence.

Keywords: Prostatic cancer, Transrectal ultrasound, MR spectroscopic imaging, T2-weighted

Background

The prostate is an exocrine gland composed of both glandular and non-glandular tissue. It is encircling the neck of the bladder and urethra with the apex located above the urogenital diaphragm and the broad base below the bladder [1].

Worldwide, diseases of Prostate gland are responsible for significant morbidity and mortality among adult males. Most frequently encountered diseases affecting prostate are Prostatitis, Benign prostatic hyperplasia and Prostatic cancer [2].

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Prostate cancer is one of the most common malignancies in elderly men and it is one of the leading causes of cancer-related mortality [3].

By 1990, Transrectal ultrasound (TRUS) has emerged as the best imaging modality of the prostate. Its use led to an improved understanding and demonstration of intra glandular anatomy. For a long time, TRUS is used screening, diagnosis and monitoring of benign disease, prostatic cancer and for guiding biopsy from the suspicious lesions [4].

The implementation of multi-parametric MRI (mpMRI) into a screening program currently seems to be the most promising technique to improve the early detection of clinically significant PC [5].

Recently, great interest has been shown in mpMRI, which combines anatomic T2-weighted (T2W) imaging and T1W with MR spectroscopic imaging (MRSI), diffusion-weighted imaging (DWI) and/or dynamic contrast-enhanced MRI (DCE-MRI) [6].

The combination of anatomical, biologic and functional dynamic information offered by mpMRI improve many aspects of PC management. There is a real need for clinicians to base therapeutic decisions not only on predictive methods and nomograms that include PSA, digital rectal examination (DRE) findings, and TRUS biopsy findings, but also on imaging [6].

Traditionally, prostate cancer detection and local staging depend on a combination of different tests, such as serum prostate-specific antigen (PSA) and digital rectal examination (DRE).

Transrectal ultrasound (TRUS)–guided biopsy, a standardized but untargeted method [7]. Because of the limitations of these available diagnostic tools, much effort is being put into improving the accuracy of prostate cancer detection. Advances in MRI techniques show potential for improving the diagnostic accuracy of MRI for prostate cancer detection. A recently developed A Multi-parametric MRI approach that combines anatomic T2-weighted imaging with functional data appears to be one of the most promising techniques for prostate cancer detection [8].

The addition of functional MRI techniques can provide metabolic information, display altered cellularity, and aid in noninvasive characterization of tissue and tumor vascularity [9]. Although these techniques have not been implemented broadly in daily clinical practice yet, they are increasingly mentioned in prostate cancer guidelines [10]. The latest diagnostic consensus statement by the European Society of Urogenital Radiology (ESUR) recommends anatomic T2-weighted imaging combined with at least two functional techniques: diffusion-weighted imaging (DWI), dynamic contrast-enhanced MRI (DCE-MRI), and optionally MR spectroscopy. The accuracy of this method has, however, not been studied systematically [7].

Prostate cancer diagnosis is accounted if PSA is elevated (>4 ng/mL) or DRE detect suspected cancer. However, PSA has low specificity (36%), so it doesn't correspond to the presence of cancer. Even normal PSA does not exclude cancer [7].

In clinical practice, reliable detection and localization of often small regions of prostate cancer is of increasing therapeutic importance due to the emergence of "active surveillance" and focal ablative therapy.

In addition, tumor localization has been related to the risk of post prostatectomy tumor recurrence, with a higher risk when surgical margins are positive at the base than at the apex.

Materials and methods

Aim of the work

The aim of this study is to highlight diagnostic efficiency of MRI with different parameters in evaluating the prostatic tumors in form of differentiation of benign from malignant prostatic lesions.

This study was conducted during the period from October 2019 to June 2021. Thirty consecutive male patients age ranged between 54 and 80 years (77 years mean) were initially enrolled in this prospective study, these patients were either presented by different prostatic lesions or with raised PSA > 4 ng/dl or with a hard nodule by digital rectal examination were assessed by magnetic resonance imaging and then these imaging findings were correlated with histopathological results TRUS guided biopsy.

The patients who have the following criteria will be included in the study: Men at least 18 years or over at risk of prostate lesions. Fit to undergo all protocol procedures. Elevated PSA.

The patients who have the following criteria will be excluded from the study: Previous history of prostate surgery. General contraindications to MRI as metal implant, pacemaker implant, claustrophobia and renal impairment estimated GFR < 50. General contraindications to TRUS as piles and acute painful perianal disorders. Finally total 30 patients were included in this current study.

The following data will be collected from each patient

Demographic data: Name, age, residence and occupation.

Medical history: Any urinary symptoms (urinary frequency, dysuria, weak stream, hesitancy, urgency,

nocturia, incomplete emptying, terminal dribbling, overflow or urge incontinence, complete urinary retention, body aches and sometimes fever and problems during sexual intercourse).

Investigations: Abdominal sonography. TRUS color Doppler. Prostate—specific antigen (PSA). Histopathology of TRUS guided prostatic biopsy.

Methods

All patients will be subjected to TRUS as screening of different prostatic pathologies by APLIO 500 TOSHIB Devicea.

All the MRI procedures and multi-voxel spectroscopic analysis were carried out with a 16-channel 1.5 T MR scanner (Philips Achieva) by using a 16-channel standard pelvic-phased array coil.

Whole prostate and seminal vesicles were visualized in every patient, then the acquired images were transferred to off line work station (extended work station space).

Patient preparation

Reassurance of the patient from the entrance to the scanning room must be a rule, including an appropriate knowledge of the whole process.

Parameters of prostate imaging in this study were

T2W sequence: First we started with Axial T2weighted turbo spin-echo sequence (TR 3000, TE 90, ACQ matrix 260×259, slice thickness 3.5 mm and 24 slice). Followed by sagittal T2- weighted turbo spin-echo sequences (TR 4990, TE 120, ACQ matrix 268×233, slice thickness 1.5 mm and 20 slice). Followed by cronal T2- weighted turbo spin-echo sequence (TR 438, TE 10, ACQ matrix 260×252, slice thickness 3.5 and 24 slice).

T1W sequence: Axial T1-weighted turbo spin-echo sequence (TR 438, TE 10, ACQ matrix 260×250, slice thickness 3.5 and 24 slice).

DW sequense: The prostate is then imaged with a multi shot echoplanner DW sequences and three orthogonal diffusion gradient (TR 1294, TE 85, ACQ matrix 88×84, slice thickness 5 mm and 20 slice) with b value 0, 250, 500, 1000, 2000s/mm2.

3D HMR Spectroscopy: Multi-voxel H-MR Spectroscopy imaging is followed with application of an automatic shimming algorithm and adding manual post shimming optimizing field homogeneity followed by frequency selective fat and water suppression using a box adjusted to prostate for quantitative detection of choline, citrate and creatinine. (TR 1132 and 1500, TE 110 and 120, SPIR1500, ACQ matrix 4×5, slices $55 \times 55 \times 55$ and 5 slice).

Analysis of data set

T2WI was first examined to assess tumor localization and tumor extension with the criteria for cancer by the presence of a mass or nodule homogenously low-signal intensity with ill-defined margins 2;4;5;17.

The prostate was divided into 2 halves: Right (R) and Left (L), then to 3 zones: central (C) zone, transitional (T) zone, and peripheral (P) zone. Thus, in each case we had 6 regions of interest (ROI) within the whole prostate of each patient. In order to avoid discordance of exact localizations for image evaluations and the biopsy site through whole prostate, multiple ROI's were placed through each half, zones and compartments of each prostate. We graded the ROI positive if cancer was found out in any compartment of R and L, C-T and P.

Second, DWI-ADC mapping was interpreted, diagnostic criteria were the focal or conglomerated areas or lesions, hyper- intense in DWI and hypointense in ADC mapping, relative to surrounding prostate.

Third, H-MRS was evaluated: Multivoxel approach with PRESS voxel excitation by band-selective inversion with gradient dephasing, water–lipid suppression and spatial encoding by chemical shift imaging with high resolution at all three dimensions via 3D-TE: 135 acquisition 127;135;136.,spectral data were analyzed to provide standard deviation and peak estimates of choline(Cho), citrate(Cit) and creatine(Cre) resonances, Cit resonance was found at 2.6 ppm, Cre at 3.0 and Cho resonance at 3.2 ppm, respectively 138–140.

For further analysis, Cho/ Cit and Cho + Cre/Cit ratios were used for the tumor depiction; Voxels with more than 30% tumor, were taken as positive ROI for the presence of cancer.

Statistical analysis

Data were statistically described in terms of range, mean, standard deviation, frequencies (number of cases) and percentages when appropriate. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of conventional T2WI, diffusion weighted imaging, MR spectroscopy were calculated separately for each parameter and were calculated for multi-parametric MRI. Difference between variables was done using Mann–Whitney test. Statistical significance was set at ($P < 0.05$) and all reported P values were two sided. Receiver operating characteristic (ROC) curve analysis was used to evaluate ADC and

Table 1 Age and clinical presentation among the studied cases

Characteristics	Mean ± SD	Range
Age (years)	57.3 ± 8.9	42.0 – 74.0
	N	**%**
Retention	20	66.7
Dysuria	16	53.3
Hematuria	13	43.3
Frequency	9	30.0
Hematosperia	4	13.3
Bone pain	2	6.7

Total = 30

Table 2 Conventional MRI compared with histopathology results

Histopathology	MRI findings	No	Percent (%)
Cyst	Cystic lesion (high T2, low T1)	3	100
BPH	Enlarged transitional zone with normal peripheral zone	4	100
Malignant	Enlarged transitional zone with abnormal SI at peripheral zone (BPH + cancer)	14	86.7
	Abnormal SI at peripheral zone and transitional zone (sarcoma	2	13.35
	Total	16	100
Infarction	Enlarged transitional zone with abnormal SI at peripheral & transitional zones	2	100
Atrophy	Normal transitional zone with abnormal SI at peripheral zone	3	100
Granulomatous prostatitis	Enlarged transitional zone with abnormal SI at peripheral & transitional zones	2	100

H-MRS cut off values. All statistical calculations were done using SPSS (Statistical Package for the Social Science, version 19).

Results

The study included 30 male patients; their age varies from 42 to 74 Y (Mean ± SD 57.3 ± 8.9) with different urological symptoms.

Conventional MRI (T2W)

T2W image findings among the studied cases (Total cases 30) about 23 has abnormal signal in T2W image with percent about 76.7% and about 7 cases show no abnormalities in T2W with percent about 23.3%

The above Tables 1, 2 shows that using conventional MRI and compared with histopathology. sixteen cases are malignant with 13 enlarged transitional zone with abnormal SI peripheral zone and 2 cases with abnormal SI at peripheral zone and transitional zone (sarcoma).

Diffusion-weighted imaging (DWI)

MRI DWI findings among the studied cases (Total 30 Cases) revealed about 20 cases show restricted diffusion at (b0, b500 and b1000 values) with percent about 66.7% and 10 cases have free Diffusion with percent about 33.3%

Table 3 Showing biopsy results compared to DWI results

DWI	Biopsy			
	Adenocarcinoma	**BPH**	**Mets**	**Lymphoma**
Restricted	14	1	4	0
Facilitated	2	7	0	2
Total	16	8	4	2

MRI DWI/ADC findings compared with hitopathological results

In this Table 3 showing biopsy results compared to DWI results.

MR-Spectroscopy (MRS)

Seventeen cases of total 30 patient show MRS spectral curve positive for malignancy high (Cho + Cr)/Cit ratio with percent about 56.7%, about 7 cases show negative spectral curve for malignancy low Cho + Cr)/Cit ratio with percent about 23.3% & 6 cases with percent 20% have non-specific spectral.

Table 4 Agreement between biopsy (reference) and MRI T2W findings

MRI T2W	Biopsy		Total
	Malignant	Benign	
Lesion	18 (60.0%) [TP]	5 (16.7%) [FP]	23 (76.7%)
No lesion	4 (13.3%) [FN]	3 (10.0%) [TN]	7 (23.3%)
Total	22 (73.3%)	8 (26.7%)	30 (100.0%)
Kappa (95% CI)	0.201 (0.000–0.584)	P	0.269

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

MRI DCE (dynamic contrast enhanced)

Among the studied cases we find 17 cases have Positive curve for malignancy (Early contrast-enhanced T1-weighted and early uptake and early washout curve). Their percent 56.7%. About 2 cases have Negative curve for malignancy (No enhancement or persistent increase curve) with percent 6.7%. 11 cases have non-specific curve (plateau, delayed uptake and decline) with percent 36.7%

Histopathological results

Twenty-two cases were pathologically proved by Biopsy among the studied cases as malignant lesions, their percent 73.3% another 8 cases were proved by biopsy as benign lesion 26.7%.

Histopathological results of the 30 patients in our study after TRUS biopsy we found

Fifteen cases diagnosed as adenocarcinoma with percent 52% of total cases, 11 cases diagnosed BPH with percent 36% of total cases, one case diagnosed as lymphoma with percent 1% and 3 cases histopathologically proved as metastatic deposit lesions with percent 8%. This study was conducted during the period from October 2019 to June 2021.

Agreement between biopsy (reference) and MRI T2W findings

Table 4.

MRI T2W had moderate sensitivity (81.8%) & PPV (78.3%) and low specificity (37.5%) & NPV (42.9%) in diagnosing prostate malignancy with Diagnostic accuracy (DA) (70%) and Youden's index (19.3%) (Tables 5, 6, 7).

MRI MRS (non-specific considered positive) high sensitivity (90.9%) & PPV (82.4%) and low specificity (62.5%) & moderate NPV (71.4%) in diagnosing prostate malignancy with Diagnostic accuracy (DA) (83.3%) and Youden's index (53.4%) (Table 8).

MRI MRS (non-specific considered negative) moderate sensitivity (63.6%) & PPV (82.4%) and low specificity (62.5%) & NPV (38.5%) in diagnosing prostate malignancy with Diagnostic accuracy (DA) (73.3%) and Youden's index (8%) (Table 9).

MRI DCE (non-specific considered positive) had very high sensitivity (95.5%) & high PPV (75.0%) and very low specificity (12.5%) & NPV (50.0%) in diagnosing prostate malignancy (Table 10).

Table 5 Diagnostic characteristics of MRI T2W findings in diagnosing prostate malignancy

Characters	Value (%)	95% CI
Sensitivity	81.8	59.7–94.8
Specificity	37.5	8.5–75.5
Diagnostic accuracy (DA)	70.0	50.6–85.3
Youden's index	19.3	0.0–56.5
Positive predictive value (PPV)	78.3	56.3–92.5
Negative predictive value (NPV)	42.9	9.9–81.6
Positive likelihood ratio (LR+)	1.31	0.74–2.32
Negative likelihood ratio (LR-)	0.48	0.14–1.71
Diagnostic odd ratio (LR)	2.70	0.45–16.25

CI: Confidence interval

Table 6 Agreement between biopsy (reference) and MRI DWI/ADC findings

MRI DCW/ADC	Biopsy		Total
	Malignant	Benign	
Restricted	19 (63.3%) **TP**	1 (3.3%) **FP**	**1 (3.3%)**
Free	3 (10.0%) **FN**	7 (23.3%) **TN**	**10 (33.3%)**
Total	**22 (73.3%)**	**8 (26.7%)**	**30 (100.0%)**
Kappa (95% CI)	**0.684 (0.402–0.967)**	**P**	**< 0.001***

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Bold values are referred to as significant value and better results than other filtering methods

Table 7 Diagnostic characteristics of MRI DWI/ADC findings in diagnosing prostate malignancy

Characters	Value (%)	95% CI
Sensitivity	86.4	65.1–97.1
Specificity	87.5	47.3–99.7
Diagnostic accuracy (DA)	86.7	69.3–96.2
Youden's index	73.9	46.8–100.9
Positive predictive value (PPV)	95.0	75.1–99.9
Negative predictive value (NPV)	70.0	34.8–93.3
Positive likelihood ratio (LR+)	6.91	1.10–43.54
Negative likelihood ratio (LR-)	0.16	0.05–0.46
Diagnostic odd ratio (LR)	44.33	3.93–500.27

Table 8 Agreement between biopsy (reference) and MRI MRS findings (non-specific considered positive)

MRI MRS	Biopsy		Total
	Malignant	Benign	
Positive/ non-specific	20 (66.7%) [TP]	3 (10.0%) [FP]	**23 (76.7%)**
Negative	2 (6.6%) [FN]	5 (16.7%) [TN]	**7 (23.3%)**
Total	**22 (73.3%)**	**8 (26.7%)**	**30 (100.0%)**
Kappa (95% CI)	**0.556 (0.213–0.900)**	**P**	**0.002***

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Bold values are referred to as significant value and better results than other filtering methods

Table 9 Diagnostic characteristics of MRI MRS findings (non-specific considered positive) in diagnosing prostate malignancy

Characters	Value (%)	95% CI
Sensitivity	90.9	70.8–98.9
Specificity	62.5	24.5–91.5
Diagnostic accuracy (DA)	83.3	65.3–94.4
Youden's index	53.4	17.8–89.0
Positive Predictive value (PPV)	87.0	66.4–97.2
Negative Predictive value (NPV)	71.4	29.0–96.3
Positive likelihood ratio (LR +)	2.42	0.98–5.99
Negative likelihood ratio (LR-)	0.15	0.03–0.61
Diagnostic odd ratio (LR)	16.67	2.17–128.18

CI: Confidence interval

Table 10 Agreement between biopsy (reference) and MRI MRS findings (non-specific considered negative)

MRI MRS	Biopsy		Total
	Malignant	Benign	
Positive	14 (46.7%) [TP]	3 (10.0%) [FP]	**14 (56.7%)**
Negative/ non-specific	8 (26.7%) [FN]	5 (16.7%) [TN]	**13 (43.3%)**
Total	**22 (73.3%)**	**8 (26.7%)**	**30 (100.0%)**
Kappa (95% CI)	**0.218 (0.000–0.552)**	**P**	0.201

Percentages are from the total (30), **TP**: True positive, **TN**: True negative, **FP**: False positive, **FN**: False negative

Bold values are referred to as significant value and better results than other filtering methods

MRI DCE (non-specific considered negative) had low sensitivity (59.1%) & moderate PPV (76.5%) and low specificity (50.0%) & low NPV (30.8%) in diagnosing prostate malignancy (Table 11).

Table 11 Diagnostic charactersitcis of MRI MRS findings (non-specific considered negative) in diagnosing prostate malignancy

Characters	Value (%)	95% CI
Sensitivity	63.6	40.7–82.8
Specificity	62.5	24.5–91.5
Diagnostic accuracy (DA)	63.3	43.9–80.1
Youden's index	26.1	0.0–65.2
Positive Predictive value (PPV)	82.4	56.6–96.2
Negative Predictive value (NPV)	38.5	13.9–68.4
Positive likelihood ratio (LR +)	1.70	0.66–4.38
Negative likelihood ratio (LR-)	0.58	0.27–1.26
Diagnostic odd ratio (LR)	2.92	0.55–15.56

CI: Confidence interval

Table 12 Agreement between biopsy (reference) and MRI DCE findings (non-specific considered positive)

MRI	Biopsy		Total
	Malignant	Benign	
Positive/ non-specific	21 (70.0%) [TP]	7 (23.4%) [FP]	**28 (93.3%)**
Negative	1 (3.3%) [FN]	1 (3.3%) [TN]	**2 (6.7%)**
Total	**22 (73.3%)**	**8 (26.7%)**	**30 (100.0%)**
Kappa (95% CI)	**0.104 (0.000–0.421)**	**P**	0.440

Percentages are from the total (30), **TP**: True positive, **TN**: True negative, **FP**: False positive, **FN**: False negative

Bold values are referred to as significant value and better results than other filtering methods

Table 13 Diagnostic characteristics of MRI DCE findings (non-specific considered positive) in diagnosing prostate malignancy

Characters	Value (%)	95% CI
Sensitivity	95.5	77.2–99.9
Specificity	12.5	0.3–52.7
Diagnostic accuracy (DA)	73.3	54.1–87.7
Youden's index	8.0	0.0–32.5
Positive predictive value (PPV)	75.0	55.1–89.3
Negative predictive value (NPV)	50.0	1.3–98.7
Positive likelihood ratio (LR +)	1.09	0.83–1.44
Negative likelihood ratio (LR-)	0.36	0.03–5.15
Diagnostic odd ratio (LR)	3.00	0.16–54.57

CI: Confidence interval

For multiparametric MRI

Multi-parametric MRI reaches 96.67% specificity and 100% sensitivity in our study with + PV of 95.8%, -PV of 100% and accuracy 98.1 compared to biopsy proved pathological results this shown in Tables 11, 12, 13, 14, 15, 16.

Table 14 Agreement between biopsy (reference) and MRI DCE findings (non-specific considered negative)

MRI	Biopsy		Total
	Malignant	Benign	
Positive	13 (43.4%) **TP**	4 (13.3%) **FP**	**17 (56.7%)**
Negative/ non-specific	9 (30.0%) **FN**	4 (13.3%) **TN**	**13 (43.3%)**
Total	**22 (73.3%)**	**8 (26.7%)**	**30 (100.0%)**
Kappa (95% CI)	**0.076 (0.000–0.413)**	**P**	0.657

Percentages are from the total (30), **TP**: True positive, **TN**: True negative, **FP**: False positive, **FN**: False negative

Bold values are referred to as significant value and better results than other filtering methods

Table 15 Diagnostic characteristics of MRI DCE findings (non-specific considered negative) in diagnosing prostate malignancy

Characters	Value (%)	95% CI
Sensitivity	59.1	36.4–79.3
Specificity	50.0	15.7–84.3
Diagnostic accuracy (DA)	56.7	37.4–74.5
Youden's index	9.1	0.00–49.4
Positive Predictive value (PPV)	76.5	50.1–93.2
Negative Predictive value (NPV)	30.8	9.1–61.4
Positive likelihood ratio (LR+)	1.18	0.54–2.57
Negative likelihood ratio (LR-)	0.82	0.35–1.93
Diagnostic odd ratio (LR)	1.44	0.28–7.34

CI: Confidence interval

Table 16 Showing results of multi-parametric MRI with biopsy results

Sensitivity	Specificity	+PV	-PV	Accuracy
100.00	96.67	95.8	100.0	98.1

Diagnosis: benign prostatic hyperplasia (BPH).
Figure 1.

Diagnosis by biopsy: Adenocarcinoma Gleason scores 4 + 5
Figure 2.

Discussion

Prostate cancer is the most common cancer in men, and the second leading cause of cancer-related death in developed countries.

Although most types of prostate cancer grow slowly and may need minimal or no treatment, other types are aggressive and can spread quickly. Prostate cancer that is detected early has a better chance of successful treatment. Therefore, detection of prostate cancer in an early stage is important but remains challenging [11].

The aim of our study was to evaluate the diagnostic accuracy of MRI techniques in detection and characterization of different prostatic lesions in comparison with TRUS, and to highlight the value of the advanced MRI techniques in accurate detection, localization and staging of cancer prostate.

The mean of the age of patients was 57.3 ± 8.9 years with minimum age 42 years and maximum 74 years old. It also shows the mean of the PSA level was 64.2 ± 34.4 ng/dl with minimum 7 ng/dl and maximum 123 ng/dl, however in study of [12] mean age of their patients was 49 years.

To date, most studies have reported various sensitivity and specificity values for the accuracy of anatomic T2-weighted imaging with one or more additional functional techniques for the detection of prostate cancer. Recently, a systematic review and meta-analysis was published on the diagnostic accuracy of T2-weighted imaging combined with DWI compared with T2-weighted imaging alone [13].

In our study, by using conventional MRI almost two third of the cases 23 (76.7%) had abnormal signal in the prostate, by MR diffusion there was restriction in 20 (66.7%) cases, however MRI spectroscopy showed 23 (76.7%) cases were abnormal, 17 cases were showing results suggesting cancer with percentage of 56.7%, 6 cases were abnormal with percentage of 20% and only 7 cases were normal with percentage of 23.3%.

By Contrast enhanced MRI, we found that only 17 cases with percentage of 56.7% were with enhanced curve Positive curve for malignancy, while 11 show nonspecific curve with percentage of 36.7% and 2 cases with curve negative for malignancy with percentage of 6.7%.

In our study a combined positive result from mpMRI indicated the presence of tumor with high specificity (96.67%), while high sensitivity (98%) was attained with + PV of 95.8%,-PV of 100% and accuracy 98.1 compared to biopsy proved pathological results.

Similar to our results, conducted study from Singapore was performed on 24 men, the cancer detection rate 59.2% [12]. *Zangos* et al. [14] reported their preliminary results regarding MRI-guided transgluteal biopsies in a cohort of 25 individuals and a median PSA of 11.8 ng/ml. Their cancer detection rate was 40% (10 of 25). It has to be considered, however, that (1) the men were not examined consecutively (i.e., selection bias in unclear) and (2) not all individuals had prior negative TRUS-guided biopsies and, therefore, a subset of men underwent their biopsy for the first time. A transgluteal approach also is not considered state of the art for prostate biopsy because of its invasive nature. Also in 2005, *Beyersdorff* et

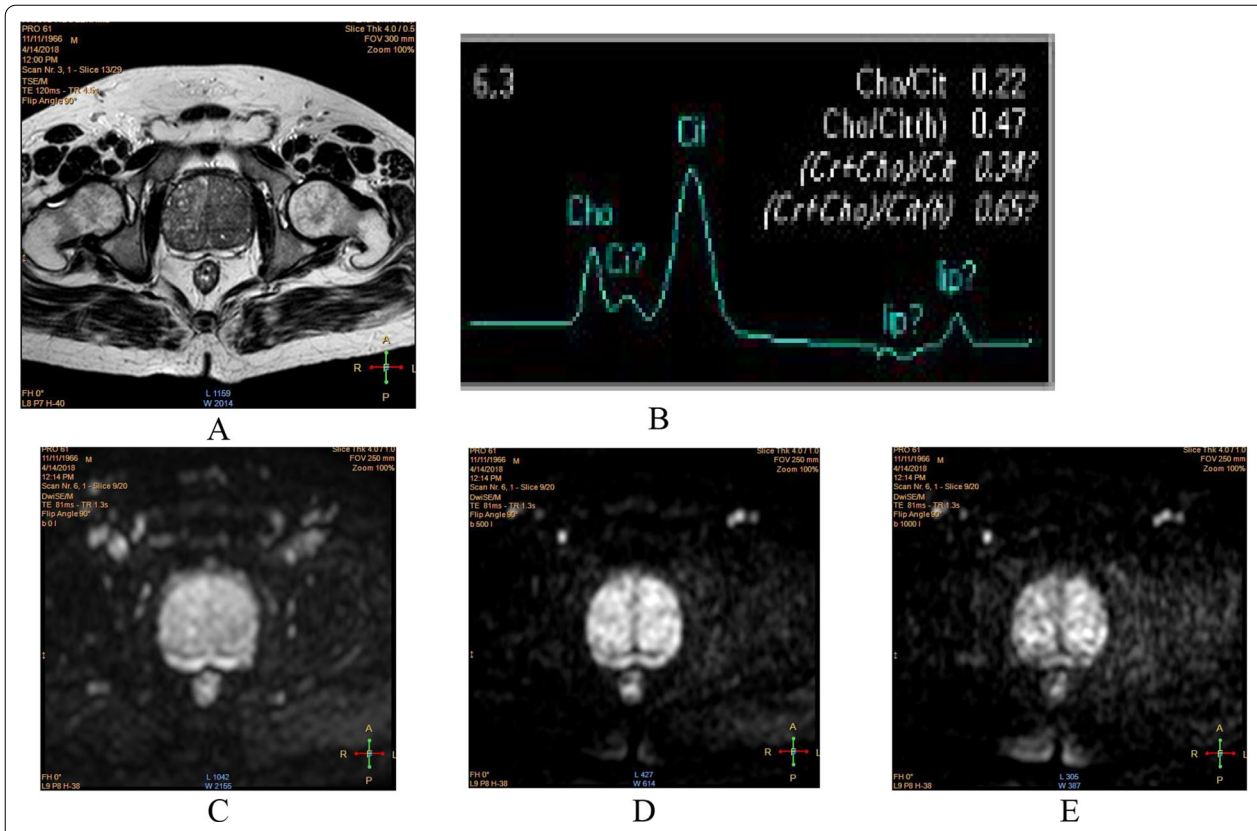

Fig. 1 61-year-old male patient presented with dysuria, A: Axial T2WI reveals hyperintense signal of both peripheral zones. B: MRS reveals spectral wave negative for malignancy. C, D and E: Diffusion weighted images at (b0, b500 and b1000 values) shows facilitated diffusion

al. [15] described their initial experience of MRI-guided transrectal prostate biopsies using a closed MR unit at 1.5 Tesla in 12 consecutive patients and a median PSA of 10 ng/ml (range, 6–60). Cancer was detected in five of 12 men.

The sensitivity of MRI diagnosis in this study with 15 cases are true positive with percentage of 50%, 8 cases are true negative with percentage of 26.7% and 7 cases are false positive with percentage of 23.3%. Our results support the findings of systematic reviews that assess the diagnostic accuracy of MP-MRI [16, 17]. The reviews declared sensitivities of 58–96%, negative predictive value of 63–98% and specificity of 23–87%. The ranges were broad because of the single center nature of the studies, each of which invoked different target conditions on different reference standards. Most studies were limited by retrospective analysis, non-blinding of imaging findings (incorporation and reporting biases), and MP-MRI comparison with inaccurate (TRUS-biopsy) or inappropriate (radical prostatectomy) reference tests. One other prospective study compared MP-MRI with TPM-biopsy that reported interim32 and then final results [17]. Their study reported 96% sensitivity, 36% specificity, 92% negative predictive value and 52% positive predictive value for detection of clinically significant cancer (defined as Gleason score 7–10 with more than 5% Gleason grade 4, 20% or more positive cores, or 7 mm or larger tumor). This Australian study was not blinded, was single-center, permitted two magnetic field strength scanners, used a TPM-biopsy protocol that sampled the prostate with fewer cores and did not include the standard test, TRUS-biopsy [18].

The meta-analysis of the 10 included studies showed a higher diagnostic accuracy for T2-weighted imaging combined with DWI (sensitivity and specificity of 0.72 and 0.81, respectively) than for T2-weighted imaging alone (0.62 and 0.77). The major strength of this diagnostic meta-analysis is that this study is the first meta-analysis to investigate the accuracy of the combination of anatomic T2-weighted imaging and two functional techniques, DWI and DCE-MRI, as recommended by the ESUR guidelines [7]. This diagnostic meta-analysis showed that the accuracy of multiparametric MRI shows potential for the detection of prostate cancer. Although the FN rate of 26% still might be too high, TRUS-guided biopsy tends to miss tumors as well, with detection rates

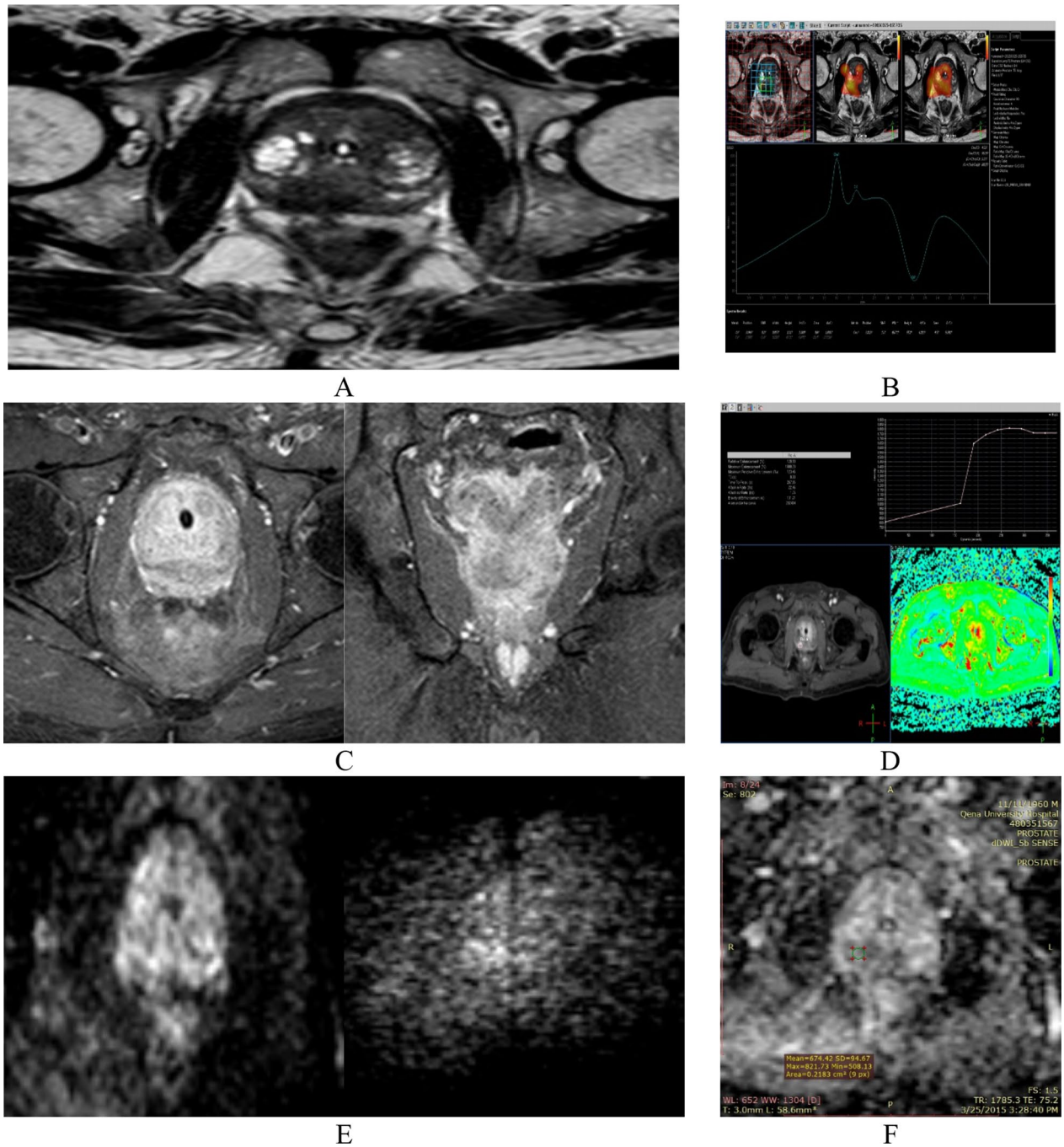

Fig. 2 67-year-old male patient presented with haemospermia and dysuria. A: Axial T2 Hypointense focal lesion in the PZ of Rt lobe with NV infiltration. B: MRS reveals Cho + Cr/Cit ratio is high 86 (+ ve for malignancy). C: Post GD contrast: shows Heterogeneous enhancement. D: DCE shows plateau curve. E and F: DWI Restricted at (at b500 and b1000 values free at b 1500) and (ADC mean 0.6)

of 10–19% on repeat TRUS-guided biopsy [19] and up to 59% on MRI-guided biopsy after two negative TRUS-guided biopsy sessions [20].

The recommendation of the ESUR of using T2-weighted imaging, DWI, and DCE-MRI for prostate cancer detection is based on expert opinion, and the question remains about whether this strategy is the best multiparametric combination because prospective validation studies have not yet been performed [20]. Of the seven included studies, four studies [21, 22] recommend

using both DWI and DCE-MRI as additional techniques and show significant differences in performance compared with the use of DWI or DCE-MRI alone. The other three studies [23–25] show no change in performance or worse results when comparing the combination of T2-weighted imaging, DWI, and DCE-MRI with T2-weighted imaging and DWI.

By using TRUS in our study, we found that about 13 cases have enlargement with nodule with percentage of 43.3%, 13 cases have enlargement without nodule with percentage of 43.3% and 4 cases have cystic lesion with percentage of 13.3%. 19 of the cases were diagnosed as malignancy with percentage of 64%, 11 cases were diagnosed as BPH with percentage of 36%.

In this study, the sensitivity of TRUS diagnosis with 6 cases are true positive with percentage of 20%, 8 cases are true negative with percentage of 26.7%, 9 cases are false positive with percentage of 30% and 7 cases are false negative with percentage of 23.3%, [16] said that MP-MRI was more accurate than TRUS-biopsy in terms of both sensitivity (98% vs 48%) and negative predictive value (89% vs 74%). TRUS-biopsy showed better specificity in their study (41% vs 96%) and positive predictive value (51% vs 90%).

Ohori et al. [26] found a sensitivity of 91% and positive predictive value of 79% for transrectal ultrasound combined with digital rectal examination in predicting extra capsular tumor extension. Another study done by [27], he found an overall sensitivity of only 68% and a specificity of 63% for transrectal ultrasound in prostate cancer staging. *Carter* et al. [28] also showed a sensitivity of 52% and specifity of 68% positive predictive value of 54% and negative predictive value of 66% for detecting of prostate cancer by transrectal ultrasound, *Maričić* et al. [29] also reported that sensitivity of transrectal sonography in the first period sensitivity was 62.57%, specificity 94.2%, accuracy 86.2%, positive predictive value 80.45% and negative predictive value 87.72%. In the second period sensitivity was 50.87%, specificity 91.93%, accuracy 73.84%, positive predictive value 83.24% and negative predictive value 70.39%. Studies performed with a sampling of up to 21 cores by TRUS-guided biopsy yielded higher detection rates than biopsy regimens involving the removal of fewer cores [30].

In study of *Siddiqui* et al. [31], no cancer was found in 95% of lesions classified a slow suspicious lesion on MRI, while a clinically significant cancer was diagnosed in 65 of the 71 high suspicious lesions. A good correlation between the level of radiologic suspicion on multiparametric MRI and the D'Amico risk stratification were already demonstrated in their study. Another study published by *Yerram* et al. [32], showed that low suspicion lesions on MRI were associated with 88% of either negative biopsies or clinically significant disease.

In study *Djavan* et al. [33], they detailed the detection rates of prostate cancer in relation to the number of prior negative TRUS-guided biopsies, which is the first study of its kind. They found no significant effect from the number of prior negative TRUS-guided biopsies on the prostate cancer detection by MRI-guided biopsy. For TRUS-guided biopsies, the detection rate decreases with the number of biopsies performed; detection rates of 10%, 5%, and 4% have been reported for the first, second, and third rebiopsies, respectively.

Djavan et al.[33] concluded that the detection rates of MRI-guided biopsy in their study were 29%, 40.0%, 66.7%, and 35.0% in the first, second, third, and fourth or more re-biopsies, respectively. Only four 1.5 T MRI-guided biopsy studies, with a total of 176 patients, have been previously published [15, 34–36]. The reported overall detection rates ranged between 42 and 55% with a high proportion of transition zone cancers, accounting for 35% of removed cores.

Results of *Park* et al. [37], *Deliveliotis* et al. [38] confirm these findings, demonstrating a high proportion of transition zone cancers (43% on a core basis and 42% on a patient basis). The high fraction of transition zone cancers detected by MRI and MRI-guided biopsy is likely due to a selection bias because cancers localized in the anterior part of the prostate are more likely to be missed using systematic TRUS-guided biopsy approaches.

In study of *Djavan* et al. [33], they demonstrated that pre-biopsy mp-MRI for detection of PCa in patients with prior negative TRUS-bx findings can improve the overall detection rate by adding mp-MRI-bx under visual TRUS-guidance to standard TRUS-bx even without preceding experience of doing this. They found an overall PCa-detection rate of 47% (39/83) in patients with a median of 2 prior negative TRUS-bx sessions among which 26% (10/39) harbored high-grade PCa (GS $\geq$ 8). According to the literature, the detection rate at first TRUS re-biopsy is 10–22%, depending on the initial biopsy technique with decreasing rates at repeated procedures [33]. *Labanaris* et al. [39] found in their study that only two patients had insignificant PCa providing an overall detection rate of clinically significant PCa of 45% (37/83 patients). They concluded that suspicious lesions seen on MP-MRI can be targeted by biopsies and improve the detection rate of clinically significant PCa, which is in line with previous studies [40]. The location of the PCa lesion affects the sensitivity and specificity of MP-MRI. Transitional-zone tumors are more difficult to identify, as reported by *Delongchamps* et al. [23] where sensitivity and specificity decreased from 80 to 97% in the peripheral zone, to 53% and 83% in the transition zone. In addition, sparse

tumors where PCa growth is intermixed with normal tissue can also limit the diagnostic performance of mp-MRI in detection of PCa.

Recent studies [41, 42] which have found that MRI-US fusion targeted biopsies detect more clinically significant cancers (median: 33.3% vs 23.6%) using fewer cores (median: 9.2 vs 37.1) and 17% fewer low-risk cancers compared with standard biopsy techniques, respectively [31]. This is also confirmed by a recent meta-analysis in which MRI-TBx had a higher rate of detection of significant prostate cancer compared to TRUS-Bx with a sensitivity as high as 91% and a lower rate of detection of insignificant prostate cancer [43]. Another study from 2009 showed that a non-suspicious MRI has a 94% specificity for identification of significant cancer [44].

Conclusions

Currently, the clinical standard for the definitive diagnosis of prostate cancer is trans-rectal ultrasound (TRUS)-biopsy. However, this type of TRUS guided biopsy has a significant sampling error and can miss up to 30% of cancers and may show underestimation of Gleason grade, especially in anteriorly located tumors. It may lead to an increase in complications.

MRI has an essential role to play in making safer in diagnosis. It can aid in staging also and surgery or radiation treatment planning.

Although T2W MRI has been used widely for diagnosis on the basis of its excellent soft tissue resolution, but its accuracy for the detection and localization of cancer prostate is unsatisfactory.

The implementation of multi-parametric MRI (mp MRI) MR spectroscopy (MRS), Dynamic contrast enhanced (DCE MRI) and diffusion weighted imaging (DWI) into a diagnosis program improve the diagnostic performance.

In this study Conventional MRI has moderate sensitivity 81.8% and low specificity 37.3% in diagnosing prostate malignancy.

Using of mpMRI combination of diffusion-weighted, Dynamic contrast enhanced and 3D 1H MR spectroscopic imaging is a promising approach for discriminating between benign and malignant lesions in the PZ and increase sensitivity 100% and specificity 96.6% in diagnosing prostate malignancy.

Abbreviations

2D US: Two-dimension Ultrasound; ADC: Apparent Diffusion Coefficients; CT: Computed tomography; CZ: Central zone; DCE-MRI: Dynamic contrast enhanced MRI; DWI: Diffusion weighted imaging; EPE: Extra-prostatic extension; GD: Gradient echo; IMRT: Intensity-Modulated Radio-Therapy; LSN–MRI: Lymphotrophic super paramagnetic nanoparticle–enhanced MRI; MPG: Motion probing gradients; MR: Magnetic resonance; MRS: MR Spectroscopy; NPP: Negative Predictive value; NVBs: Bilateral neurovascular bundles; PPV: Positive predictive value; PSA: Prostate-specific antigen; PZ: Peripheral zone; RF: Radiofrequency; ROI: Regions of interest; ROC: Receiver's operating curve; SD: Standard deviation; SNR: Signal-to-noise ratio; STIR: Short TI inversion recovery; SV: Seminal vesicle; TRU: Transrectal ultrasound.

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Author contributions

I.H. and S.E. conceived of the presented idea. I.H., H.G and M.E.A. developed the theory and performed the computations I.H. collected the data. I.H. and H.G. contributed data or analysis tools. M.E.A and I.H. verified the analytical methods. I.H, S.E. and M.E.A. wrote the paper. M.E.A. supervise and encouraged writing the manuscript.M.E.A. and H.G. performed the analysis. I.H and S.E. contributed data or analysis tools. M.E.A. encouraged I.H. and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript. All authors provided critical feedback and helped to shape the research, analysis and manuscript. S.E. and I.H. designed the model and the computational framework and analyzed the data. All authors read and approved the final manuscript.

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Availability of data and materials

All data and material available upon request.

Declarations

Ethical and consent to participate

The study has been approved from The Ethical Committee of the Department of radiology, Faculty of Medicine, Ain Shams University. Written consent was taken from all participants before recruitment in the study after explanation of the purpose and procedures of the study.

Consent for publication

Written consent was taken from all participants before recruitment in the study after explanation of the purpose and procedures of the study. Patient personal data were hidden and not published.

Competing interests

No competing interests between authors.

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