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Research Article

Effectiveness of magnetic resonance imaging–targeted biopsy for detection of prostate cancer in comparison with systematic biopsy in our countries with low prevalence of prostate cancer: our first experience after 3 years

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ABSTRACT

Background: Some men are subjected to multiple repeated biopsies because of ongoing suspicion of prostate cancer, which might subject them to complications. The aim of the study was to determine the diagnostic accuracy of magnetic resonance imaging (MRI)/target fusion–guided biopsy in comparison with systematic biopsy in our low prevalence prostate cancer population, in terms of validity measure, case detection rate, and detection of clinically significant cancer.

Methods: This is a retrospective cohort study. All consecutive patients who met the inclusion criteria (all men with persistent high prostate-specific antigen levels >4 ng/ml and/or subnormal finding in direct rectal examination, with suspicious regions identified on prebiopsy MRI) were subjected to transrectal MRI/ultrasound fusion–guided biopsy.

Results: A total of 165 cases met the inclusion criteria and were included in the study. The cancer detection rate (CDR) of target biopsy was significantly higher than that of standard biopsy (27.9% vs 14%, respectively), and 25 cases (52%) were missed by standard strategy and correctly classified by multiparametric MRI with targeted biopsy (MRI-TB). On the other hand, only 2 cases (4.3%) were misclassified by MRI-TB, and one of them was clinically significant. There was an exact agreement between the 2 strategies in 15 (31%) cases. Targeted biopsy diagnosed 41.5% more high-risk cancers vs systematic biopsy (41.6% vs 6.2%, $P < .001$). The difference between sensitivity, specificity, and negative predictive value of MRI-TG varies between 80% and 98%.

Conclusion: The CDR of prostate cancer in general and clinically significant cancer, in specific, is significantly higher with MRI-TG modality than with systematic modality. Yet, MRI-TG biopsy still misses some men with clinically significant prostate cancer. Hence, the addition of a 12-core biopsy is required to evade missing cases of clinically significant and insignificant cancer.

1. Introduction

Prostate cancer (PCa) is considered the most commonly diagnosed cancer among men in many countries of the world. New cases are anticipated to increase to 1.7 million new cases and 499000 deaths are likely to be reported by 2030.[1]

In our region, PCa is not quite prevalent as compared with figures reported from Western countries, while the age-standardized incidence rate reported from the USA, Canada, and the UK, for instance, was 126.1, 122, and 112.8, and it ranged from 5.5 (Saudi Arabia) to 39.5 (Lebanon) in our Arab area.[2]

When PCa is localized, early detection and treatment provides the highest chance of cure. The threshold of the total prostate-specific antigen (PSA) level for prostate biopsy is associated with

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the increased number of localized cancers detected, but it leads to higher number of unnecessary biopsies and morbidities associated with the procedure.[3]

Transrectal ultrasound (TRUS)-guided prostate biopsy is considered the gold standard for diagnosis of PCa. The sensitivity and specificity of sextant biopsy in patients with a total PSA value ranging from 4–10 ng/mL ranged from 39 to 52% and 81 to 82%, respectively. However, about 20% of PCas are not distinguished at the first procedure, and a repeat biopsy may be suggested.[4]

In case of systematic 12-core biopsy, some men are exposed to repeat biopsies because of continuing suspicion of PCa, which might subject them to minor complications.[5] In addition, it is associated with high rates of false-positive results and increase in odds of repeated procedures.[6]

After the development of the technology of magnetic resonance imaging (MRI), it has considerably been improved in the last few years, and some professionals believe it may be time to reassess its use in management decisions and guiding treatment.[7,8]

In Brisbane, the Wesley Hospital, where the first clinical trial was conducted, demonstrated that a MRI-guided technique improved significantly detection of life-threatening PCa and reduced overdiagnosis of non–life-threatening cases. The study declared that use of multiparametric MRI (mpMRI) decreased the number of patients needing prostate biopsies by 51% and decreased the problem of overdiagnosis of non–life-threatening disease by about 90%. Its sensitivity for diagnosis of clinically significant PCa was 92%, in comparison with TRUS biopsy, which had a lower sensitivity (70%).[9]

MRI-guided biopsy technique for PCa diagnosis was introduced for the first time in our region in Saudi Arabia in 2015. The aim of the study was to determine the diagnostic accuracy of MRI/target fusion–guided biopsy in comparison with systematic biopsy in our population with low prevalence of PCa, in terms of validity measure, case detection rate, and detection of clinically significant cancer.

2. Subjects and methods

It was a retrospective cohort study, in which men suspected to have PCa due to persistent high PSA levels (>4 ng/ml) and/or abnormal direct rectal examination (DRE) findings were referred to urology. They were offered prebiopsy mpMRI with targeted biopsies (MRI-TB). The patients would undergo TRUS immediately, followed by fusion with MRI on the profuse software of the artemis platform; after that, the regions of interest (ROIs) would be targeted with 2–4 cores, each using the Artemis system, and after all ROIs were properly sampled with 2 to 4 biopsies, each systematic 12-core biopsy would be obtained. Ethics approval was obtained from our faculty board as part of a large study.

2.1. Study population

Over the period of the study, all consecutive patients who met the inclusion criteria (all men with persistent high levels of PSA >4 ng/ml and/or subnormal finding in DRE, no past host history of PCa, with suspicious regions identified on prebiopsy 3T MRI consisting of T2-weighted (T2W), diffusion-weighted, and dynamic contrast-enhanced [DCE] sequences) were subjected to biopsy.

2.2. Conduct and reporting of MRI

Patients underwent an mpMRI of the prostate on a 3 Tesla magnet Skyra system (Siemens A.G., Erlangen, Germany) using an external multichannel body phased-array coil. MRI examination was conducted as follows: (i) axial and coronal T2W fast spin echo (TSE, ETL 25) sequences, 3-mm-thick slices, TR/TE: 5540/107; (ii) axial diffusion-weighted (DWI) high-resolution sequence, readout-segmented EPI (RESOLVE), 3-mm-thick slices, and ADC maps (with quantitative ADC evaluation), TR/TE: 5250/62; (iii) axial T1-weighted 3D gradient echo sequence for DCE-MRI, 3.5-mm-thick slices, 1922 matrix, TR/TE/FA: 4.9/6.7/150, 10-sec time resolution, 40 time points, bolus injection of 0.1 mM/kg of Gd-DOTA; and (iv) axial T1-weighted, fat-suppressed sequence for late postcontrast imaging of the pelvis and node, 3.5-mm-thick slices, gradient echo sequence, TR/TE: 3.5/1.5, FOV = 240 mm.

A trained radiologist was responsible for reporting and interpreting MRI findings. Reporting was carried out using a combination of parameters within priority order: morphology on T2W images, DWI (ADC maps), DCE-MRI, CSI, and suspicious ROIs contoured on T2W axial slices for subsequent processing on a biopsy US device. Interpretation criteria for the positivity of parameters conformed to European Society of Urogenital Radiology recommendations in the Prostate Imaging Reporting and Data System (PI-RADS). ROIs were delineated and graded 1–5 using a scoring system established before the PI-RADS was described.

Patients with abnormal findings on MRI (PI-RADS 2 and higher) underwent a standard 12-core TRUS-guided biopsy, with the addition of at least two additional cores using MRI-US fusion for each lesion identified on MRI. Positive biopsy results were classified as clinically significant disease, high-grade ($\geq$7 [3 + 4] or [4 + 3]) disease, or clinically insignificant, low-grade disease (Gleason score [GS] = 3 + 3).

2.3. Conduct of transrectal MRI/US fusion–guided biopsy

The biopsy was performed with an 18G biopsy needle under local anesthesia. The ROIs identified on MRI were electronically loaded into the Artemis/profuse system and software (Eigen, CA, USA). A systematic 12-core technique was performed in each patient after a minimum of 2–3 cores up to 6 cores were taken from the targeted lesion, depending on the size of the lesion.

2.4. Statistical analysis

McNemar's chi-square test was used to compare the two biopsy strategies and detection of low-risk PCa (i.e., GS = [3 + 3] 6) and high-risk PCa (i.e., GS $\geq$ 7). A 2 × 2 table was designed to compare different parameters, i.e., sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), of MRI-targeted biopsy.

3. Results

During the study period, 165 cases met the inclusion criteria and were included in the study.

Table 1
Description of biological parameters of the study sample.

Parameter	Range
Age	51–81 years
PSA	3.5–26 ng/ml
Prostate volume	31–170 cc
Prior prostate biopsy with negative findings	23 (14%) patients
DRE positive	15 (9%) patients
DRE negative	150 (91%) patients

PSA = prostate-specific antigen; DRE = direct rectal examination.

Table 2
Comparison of positive and negative cases detected by both strategies.

MRI-targeted biopsy	Standard 12-core biopsy		Total
	Positive	Negative	
Positive	21 (12.7%)	25 (15.1%)	46
Negative	2 (1.2%)	117 (71%)	119
Total	23	142	165

MRI = magnetic resonance imaging.

Table 1 describes the biological variables of patients in the study. Their age ranged from 51 to 82 years, and the PSA level ranges from 3.5 to 26 ng/ml. Most of them (91%) had a negative finding on DRE examination. Only 23 patients (14%) had a prior history of prostate biopsy, and it was negative.

Table 2 compares detected cases across the 2 strategies and validity measures for MRI-TB. A total of 25 cases (52%) were missed by standard strategy and correctly classified by MRI-TB. On the other hand, only 2 cases (4.3%) were misclassified by MRI-TB. The sensitivity was 91.3% (71.96–98.93%), the specificity was 82.39% (75.12–88.27%), the PPV was 45.65% (36.54–55.06%), and the NPV was 98.32% (93.95–99.53%). The cancer detection rate (CDR) of target biopsy was significantly higher than that of standard biopsy (27.9% vs 14%, respectively, chi-square = 9.59, and p = 0.00).

Based on International Society of Urological Pathology (ISUP) grading, 17 cases were classified as low-risk grade 1, 10 cases were classified as intermediate favorable grade 2, 6 cases were classified as intermediate unfavorable grade 3, and the number of cases in high-risk grade 4 and 5 was 8 and 7 cases, respectively.

Table 3 compares the GS between the 2 biopsy techniques. Among cases detected by both strategies, 15 (31.2%) patients demonstrated concordance between the two biopsy strategies for the presence of low- or high-risk cancer. Clinically significant PCa was distinguished in 20 cases (41.6%) detected by MRI-targeted biopsy. The difference between clinically significant cases detected by MRI fusion biopsy compared and those detected by systematic biopsy was statistically significant (41.6% vs 6.2%, p = 0.000). A total of 2 cases (4.3%) were missed by MRI-TB and detected by systematic biopsy, and one of them was clinically significant.

Of 1980 systematic cores, 76 (3.8%) were positive, and the positive cores in target biopsy were 85 (21.1%) of 402 total cores (p = 0.0002). As per the PI-RADS, the CDR as per PI-RADS 2 was 9.5% (4 cancer-positive cases/42 total cases), as per PI-RADS 3 was 10.3% (6 cancer-positive cases/58 total cases), as per PI-RADS 4 was 46.6% (21 cancer-positive cases/45 total cases), and as per PI-RADS 5 was 85% (17 cancer-positive cases/20 total cases).

It is worth mentioning that no major complications have been encountered after biopsy, and only 4 patients went into acute retention.

4. Discussion

The efficacy of mpMRI of the prostate has been assessed in numerous studies for choosing men for prostate biopsy, including men undergoing repeat prostate biopsies. The study by Engehausen et al,[10] which was conducted on patients with prior negative TRUS-guided biopsy sessions, indicated a CDR of 40.6% using MRI-guided targeted biopsy.

The cancer detection rate (CDR) for MRI-targeted biopsy in the present study was significantly higher than that for standard biopsy (27.9% vs 14%), yet it was lower than other studies, which could be due to lower prevalence of PCa and great numbers of negative cases, which could be ascribed to misclassification of positive cases in reading mpMRI as having a prostate lesion (PI-RADS 3 or higher). Detection of clinically significant PCa was significantly higher with MRI-targeted biopsy than with systematic biopsy.

Peltier et al[11] reported a CDR of 62.7% for MRI-targeted biopsy and that mpMRI enhanced clinically significant PCa detection rate in comparison with standard protocol only, with less tissue sampling and a higher GS. A recent systematic review published in 2019 reported that MRI-TB had a higher and significant rate of detection of clinically significant cancer in men than systematic biopsy (detection ratio [DR] = 1.16 [95% confidence interval {CI} = 1.09–1.24], p < 0.0001), and MRI-TB detected fewer men with clinically insignificant cancer than systematic biopsy (DR = 0.66 [95% CI = 0.57–0.76], p < 0.0001). However, 13% of patients with clinically significant cancer were missed by MRI-TB but detected by addition of systematic biopsy.[12]

On the other hand, Salami et al[13] reported no significant difference between MRI/TRUS fusion-guided and standard 12-core biopsy protocol with regard to the CDR (52.1% and 48.6%, respectively, P = 0.435). However, fusion biopsy was more likely to detect clinically significant PCa than 12-core biopsy (47.9% vs 30.7%; P < 0.001). Using mpMRI and the subsequent MRI/TRUS fusion-guided biopsy platform may improve detection of clinically significant PCa in men with previous negative biopsies.[13] The clinical trial (PROFUS Trial) by Wysock et al[14] concluded that fusion biopsy was more histologically revealing than visual targeting but did not upsurge cancer detection. Its use may lessen the learning curve needed for visual targeting and progress community acceptance of MRI-targeted biopsy.

The present study revealed high sensitivity, high specificity, and a high NPV of MRI-targeted biopsy expect for its PPV, which is very low (45.6%). It is well documented that prevalence influences the PPV and NPV of tests. As the prevalence decreases, like in Saudi Arabia, the PPV decreases while the NPV increases.[15,16] In 2015, Siddiqui et al[17] reported in a subset analysis of 70 patients, who underwent radical prostatectomy biopsy, the results with whole-gland pathology and that the overall sensitivity of targeted-only biopsy was 77% compared with 53% for standard biopsy, when

Table 3
Comparison of positive cases detected by the 2 techniques with regard to the Gleason score.

Positive cases detected mutually by both strategies mutually	
Gleason score = 6	7 (14.6%)
Gleason score ≥7	8 (16.7%)
Gleason score ≥7 for MRI biopsy and Gleason score of 6 for systematic biopsy	4 (8.3%)
Gleason score = 6 for MRI biopsy and ≥7 for systematic biopsy	2 (4.2%)
Positive cases detected by MRI-targeted biopsy only	
Gleason score = 6	9 (18.7%)
Gleason score ≥7	16 (33.3%)
Positive cases detected by systematic biopsy only	
Gleason score = 6	1 (2.15%)
Gleason score ≥7	1 (2.15)

MRI = magnetic resonance imaging.

compared with final prostatectomy pathology. Specificity was similar for both techniques (68% vs 66%).[17]

Our results showed that a higher percentage of positive cores were found in target biopsy than in systematic biopsy, resulting in target biopsy having a higher risk attribution relative to systematic biopsy, and our results showed that MRI-TB biopsy correctly identified 20 cases (41.6%) with clinically significant cancer and missed 3 cases diagnosed correctly by systematic biopsy. A review published in Cochrane, 2019, which compared multiple procedures (MRI alone, MRI together with a biopsy, and a pathway that uses MRI to help decide whether to conduct a biopsy or not with the standard ultrasound-guided biopsy), revealed that of 300 men, the MRI pathway can correctly identify 216 (72%) as having clinically significant PCa, but the pathway missed the remaining 84 men. As for the 700 men who do not have clinically significant PCa, the MRI pathway can correctly classify 672 (96%) as not having PCa, while it misclassifies 4% of men as having clinically significant PCa.[18] There is an argument concerning the point of conducting only target biopsy in men with positive MRI scans.[19] Although it has been recommended that MRI-positive patients undergo only MRI-targeted biopsy, without additional systematic biopsies,[20,21] this opinion was disputed by the reliable study findings of cancers, with higher GSs not being distinguished on MRI-directed biopsy cores but on supplementary TRUS biopsy cores (nearly 21% of cases), which might have led to undertreatment due to risk misclassification if TRUS biopsy was eliminated.[22–26]

The first limitation of the study is that the two biopsy modalities were compared with each other, unlike other studies using template mapping biopsy or radical prostatectomy specimens as the gold standard. Second, not all sample sizes were biopsy naive, a small proportion had previous negative prostate biopsy results, so additional validation is necessary in a larger population of men without prior biopsy. Third, the small sample size due to very low prevalence and the single-institution study could have introduced selection bias. Finally, patients with no visible lesions on MRI were excluded from the study, so it was not possible to compare the results of biopsy for these patients.

5. Conclusion

MRI-TG biopsy has higher sensitivity, higher specificity, and a higher NPV. The CDR of PCa in general and clinically significant cancer, in specific, is significantly higher with MRI-TG modality than with systematic modality. However, MRI-TG biopsy still misses some men with clinically significant PCa, and the addition of 12-core biopsy is needed to avoid missing some cases of clinically significant and insignificant cancer.

Ethical approval

The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010. The fieldwork was conducted after approval from the ethics committee of the Faculty of Medicine, King Saud University (approval no. 10/2597/IRB).

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Conflict of interest

The authors declare that they have no conflict of interest.

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