



Multiparametric MRI Fusion-guided Biopsy for the Diagnosis of Prostate Cancer: Results of the First 100 Consecutive Patients

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Abstract

Objective: Our aim was to compare prostate cancer detection rates according to International Society of Urological Pathology (ISUP) grade group (GG) among magnetic resonance imaging (MRI)-targeted biopsies (TBx), systematic biopsies (SBx) and a combination of both (TBx + SBx).

Materials and Methods: Between July 2018 and Nov 2020, 100 patients undergoing MRI-targeted prostate biopsy and SB were analysed retrospectively. Men with MRI-visible prostate lesions underwent both MRI-targeted (UroNav®) and systematic 12-core biopsy. The primary outcome was cancer detection according to ISUP GG. The secondary outcome were detection of cancers of GG 2 or higher.

Results: The overall cancer detection rate in the study was 43%. Among these, a histopathological ISUP grade of 1 was detected in 44.2%, ISUP grade 2 in 32.5% and higher-grade groups in 23.2% of patients. MRI-TB detected 38 and SBx biopsy detected 30 of the overall study cohort. Combined biopsy led to a cancer diagnoses in 18 more men than with either method alone. Significant cancer detection was 53.4% for TBx, 39.5% for SBx, and highest 55.8% for combination TBx + SBx ($p=0.038$). Most of the cancers missed by SBx were clinically significant. No significant side effects were recorded. The overall cancer detection rate was 20.4%/46.6% and 90.2% for prostate imaging reporting and data system 3/4/5, respectively.

Conclusion: Our results have shown that among patients with lesions visible on MRI, combined biopsy led to greater detection of all prostate cancers, providing increased detection of clinically significant tumours.

Keywords: Prostate cancer, detection, targeted biopsy, MRI US Fusion, prostate biopsy

Introduction

Prostate cancer (PCa) is the most common cancer among Northern and Western European men (1). To further improve survival in patients with PCa, it is necessary to differentiate between clinically insignificant and clinically significant cancer. In current clinical practice, Transrectal Ultrasound-guided prostate Biopsy (TRUS Bx) is the commonly used technique to further evaluate a suspected PCa diagnosis. The current diagnostic approach including PSA testing and digital rectal examination followed by transrectal ultrasound biopsies lacks both sensitivity and specificity in PCa detection and offers limited information about the aggressiveness and stage of the cancer (2,3,4). Recent scientific work supports the rapidly growing use of multiparametric magnetic resonance imaging (mpMRI) as a promising tool of growing importance in PCa evaluation. With the introduction of mpMRI, the accuracy for the localisation and detection of PCa is improved (3,5,6). Its use may improve

many aspects of PCa management, from initial detection of significant tumours using mpMRI-guided biopsies to evaluation of biological aggressiveness and accurate staging, which can facilitate appropriate treatment selection. The use of mpMRI and MRI-targeted biopsy (TB) has been shown to improve PCa detection by increasing the overall PCa detection rate and reducing the detection of insignificant tumours (3,4,5,6,7). However, experience with MRI-targeted biopsies in PCa diagnosis in Turkey has been very limited. Therefore, we carried out this study to evaluate the use of mpMRI in disease detection and the assessment of histopathological aggressiveness.

Materials and Methods

Based on our prospective database, 100 consecutive biopsy-naive patients who underwent MRI-TB combined with systematic 12-core prostate biopsy (TBx + SBx) during the period between July 2018 and November 2020 were identified and included in the

Cite this article as: Güven Aslan. Multiparametric MRI Fusion-guided Biopsy for the Diagnosis of Prostate Cancer: Results of the First 100 Consecutive Patients. Bull Urooncol 2021;20(1):11-14

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Received: 18.05.2020 **Accepted:** 04.06.2020

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analysis. Patients with firm palpable prostate nodules suggestive of cancer, any patient who had previously undergone prostate biopsy and patients with known urinary tract infections were excluded from the study. All patients gave informed consent. Patients for whom had complete pathological data were available for each Bx scheme were investigated. The patient's age and PSA level and the highest GS of each Bx scheme were evaluated. Since the study was a retrospective case-control study, IRB approval was not required.

All mpMRI for targeted biopsies were reviewed by the specified radiologist. In patients with a prostate imaging reporting and data system (PI-RADS) lesion ≥ 3 (according to the PI-RADS[®]-v2 classification) (8), software-based MRI-targeted ultrasound fusion biopsies using UroNav® (Invivo Corp, Philips, USA) were conducted. All biopsies were performed using a transrectal approach under IV sedation anaesthesia and antibiotic prophylaxis with a single dose of Fosfomycin the night before and IV Gentamycin 120 mg + third Generation Cephalosporin 1 hour before the procedure. MRI image- fusion-targeted biopsies were taken from each target, and at least 2 core samples were taken from each target lesion. In addition to targeted biopsies, SBx were performed using a 12-core approach. The biopsy cores were evaluated by dedicated uro-pathologists. The biopsy Gleason score was defined as the highest Gleason score in at least one core and was reported using the International Society of Urological Pathology (ISUP) Consensus Conference 2014 grading system (9).

Statistical Analysis

Descriptive statistics included continuous variables and frequencies and proportions for categorical variables. Differences were analysed with the use of a chi-square test using SPSS software. Differences were considered statistically significant at $p \leq 0.05$.

Results

Patient demographics of the study cohort stratified by biopsy approach are depicted in Table 1. The median number of TB cores sampled per region of interest was 4 (2,3,4,5,6,7).

The overall cancer detection rate in the study was 43%. Among these 43 patients, a histopathological ISUP grade of 1 was detected in 19 (44.2%) patients, ISUP grade 2 in 14 (32.5%) patients and higher-grade groups in 10 patients (23.2%). Cancer was detected by MRI/US-TB in 38 and by SB in 30 of the overall study cohort of 100 patients. Combined biopsy led to cancer diagnoses in 18 more men than with either method alone. There was a significant difference in the missed cancer ratio between TBx and SBx (11.6% vs 30.2%, $p=0.01$), in that any grade of cancer detection by SBx alone was significantly lower than by TBx alone.

Many patients had different PI-RADS scores registered by target lesion in the same patient. When the results were divided according to PIRAD grade, the positivity rates were 20.4%, 46.6% and 90.2% for PIRAD 3, PIRAD 4 and PIRAD 5 scores, respectively.

The rate of significant cancer detection was 53.4% for TBx, 39.5% for SBx and 55.8% for combination TBx+SBx, indicating that more significant cancer (ISUP grade 2 or higher) is detected by MRI fusion biopsy. If only SBx biopsies had been performed, 13.9% of clinically significant cancers would have been misclassified. Most of the cancers missed by SBx were clinically significant (Figure 1).

No significant side effects such as fever, urinary retention, urosepsis, and hospitalisation were recorded in any patient, except mild haematuria and hematospermia.

Discussion

In modern times, mpMRI of the prostate is becoming an integrative part of the diagnostic workup of PCa. Several prospective trials demonstrated that TBx can increase PCa

Variables		Combined MRI-TBx + SBx method (n=100)			
Age (year)		58.6±4.1 (48-75)			
PSA (ng/dL)		6.1±3.9 (2.2-27)			
Cancer Detected n=43		MRI-TBx	SBx	Combined MRI-TBx + SBx	-
	Missed Cancer	5	13	0	-
Biopsy ISUP Grades	1	15	13	19	
	2	13	9	14	
	3	8	6	8	
	4	1	1	1	
	5	1	1	1	
PI-RADS 3				20.4 %	
PI-RADS 4				46.6%	
PI-RADS 5				90.2%	
MRI: Magnetic resonance imaging, TBx: Targeted biopsies, SBx: Systematic biopsies, ISUP: International Society of Urological Pathology, PI-RADS: Prostate imaging reporting and data system, PSA: Prostate-specific antigen					

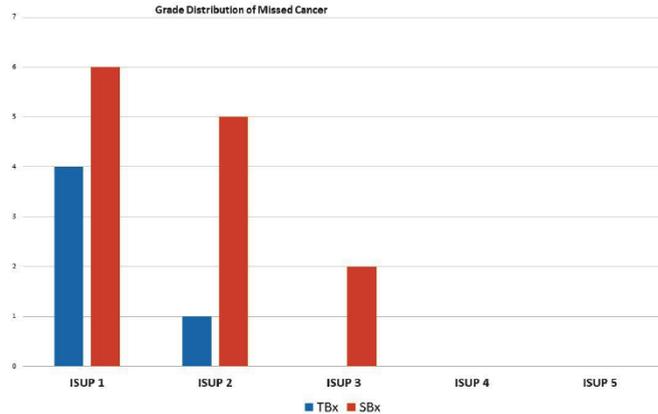


Figure 1. Distributions of ISUP grades of missed cancer according to the biopsy method

ISUP: International Society of Urological Pathology

detection rates, especially that of clinically significant PCa (GGG ≥ 2), while lowering the detection rate of low-risk PCa (2,10,11,12,13,14).

In this cohort of patients, combined TBx + SBx biopsy provided a more accurate diagnosis than MRI-targeted or SB alone. Consistent with earlier studies, we found higher cancer detection rates on TBx when compared with SBx (7,10). However, 5 out of 43 prostate cancers (11.6 %) went undetected by TBx alone. Missed cancers by TBx may reflect the underlying limitation of mpMRI, which is the possibility of invisible PCa on mpMRI, varying inter-reader agreement on the mpMRI results and missing the target lesion in biopsy.

The combination of TB and SB was superior to either method alone for the detection of clinically significant PCa (ISUP 2 or higher). When TBx alone to SBx alone are compared for the detection rate of significant PCa diagnosis, overall TB alone tends to detect more significant PCa but this superiority does not reach statistical significance. Our result complements previous results favouring MRI-targeted biopsies (15,16). Several other studies have compared MRI fusion-TB with SB with diverging results depending on the type of SB used or number of cores taken. Some found that MRI-TB led to increased detection of high-risk cancer and decreased detection of low-risk cancer but missed up to 6% of higher-risk tumours. On the other hand, others found similar detection rates in systematic and targeted transrectal biopsies (10,16,17). In the present study, SBx had inferior yet important performance to TBx in determining high-grade cancers. This may be a result of the cognitive fusion bias within the SBx that occurred when the urologist performing the SBx was aware of the localisation of the suspicious lesion on mpMRI. In our study, if a pure TBx strategy omitting SBx were to be applied, this would lead to missing up to 5 patients with cancer. Our results support that to obtain the most accurate assessment of the entire prostate gland, SBx remains necessary, in addition to TBx, due to limitations of mpMRI performance/reading and of precision during lesion targeting.

In the current study, we report our experience of biopsied PI-RADS 3,4,5 lesions. We found our detection rate of prostatic adenocarcinoma amongst these lesions to be 20.42%, 46.6%

and 90.2% respectively. The results of the current study demonstrate a good correlation between PI-RADS scores and positive biopsy. The cancer detection rate stratified by PI-RADS score is similar to that reported in the published literature (18). However, there are different cancer detection rates according to PI-RADS score. Previous studies reported overall cancer detection rates of PI-RADS v2 categories 3, 4 and 5 of 39%, 72% and 91%, respectively, for all prostate cancers. On the other hand, several studies reported lower detection rates (19). The DWI PI-RADS score alone correlates well with positive biopsies in the peripheral zone, but not the transition zone (20). PI-RADS v2 uses a simplified approach but shows a lower diagnostic accuracy. This could lead to a higher rate of false-negative results with the risk of missing tumours within low PI-RADS score levels. When performing a TB, combination with a SB still provides the highest detection rate of prostate cancer.

Study Limitations

The present study has several limitations. First and foremost, our manuscript was based on a retrospective analysis of only one centre. Our study was limited to a rather small cohort of 100 patients. In all our patients, MRI-TBx was performed by using the transrectal approach. We could not measure the potential positive or negative effects of other platforms on detection rates using transperineally biopsy systems. Moreover, failure of mpMRI fusion biopsy due to incorrect mpMRI image registration or mismatching of image planes, inaccurate sampling and intralesion Gleason score heterogeneity may have impacted on our results. However, our data reflect the real-life picture.

Conclusion

Our study shows that MRI-targeted biopsies in patients with suspected PCa result in a high detection rate and clinical significance of diagnosed tumours. These results suggest that MRI-based diagnosis and subsequent targeted biopsies fulfil an important role in increasing the detection rate and accuracy in the diagnosis of PCa. Since multiparametric MRI still has some risk of missing tumours; additional systematic 12 core biopsies should not currently be omitted.

Acknowledgements

Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as author.

Conflict of Interest: No conflict of interest was declared by the author.

Financial Disclosure: The author declared that this study received no financial support.

Ethics

Ethics Committee Approval: Since the study was a retrospective case-control study, IRB approval was not required.

Informed Consent: All patients gave informed consent.

Peer-review: Externally peer-reviewed.

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