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Effect of lesion diameter and prostate volume on prostate cancer detection rate of magnetic resonance imaging: Transrectal-ultrasonography-guided fusion biopsies using cognitive targeting

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ABSTRACT

Objective: This study aimed to evaluate the effect of prostate volume and lesion size on the clinically significant prostate cancer (csPCa) detection rates of transrectal ultrasonography (TRUS)-guided prostate biopsies, performed by a cognitive targeting method for sampling peripheral zone lesions.

Material and methods: We retrospectively enrolled 219 consecutive patients, who underwent multiparametric magnetic resonance imaging with a 3-T scanner and had peripheral zone lesions suspected for prostate cancer. All of these patients underwent combined cognitive targeted biopsy of suspicious lesions and TRUS-guided systematic biopsy. The detection rates of csPCa according to different lesion diameters (<5 mm, 5–9.9 mm, and ≥10 mm) and prostate volumes (<30 mL, 30–49.9 mL, 50–79.9 mL, and ≥80 mL) were calculated per lesion basis. In addition, subgroup analysis of csPCa detection rates was performed according to Prostate Imaging Reporting and Data System scores of lesions.

Results: The csPCa detection rates according to lesion diameters <5 mm, 5–9.9 mm, and ≥10 mm were 4%, 9.8%, and 33.1%, respectively, and were significantly lower for lesions <10 mm (p<0.001). The csPCa detection rates were 61.5%, 24.1%, 16.2%, and 6.9%, respectively, for prostate volumes <30 mL, 30–49.9 mL, 50–79.9 mL, and ≥80 mL, and were significantly higher for prostate volumes <30 mL (p<0.001).

Conclusions: Clinicians should be very careful when they prefer cognitive targeted prostatic biopsy in patients with periferal zone lesions less than 10 mm and with prostate volumes greater than 30 mL, because of significantly low csPCa detection rates.

Keywords: Cognitive fusion biopsy; lesion diameter; magnetic resonance imaging; prostate cancer.

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Introduction

Transrectal-ultrasonography-guided systematic biopsy (TRUS-SB) is reported to miss 30–40% of clinically significant prostate cancer (csPCa) and may also lead to high detection rates of clinically insignificant prostate cancer (cisPCa).[1,2] Multiparametric magnetic resonance imaging (mpMRI) and Prostate Imaging Reporting and Data System (PIRADSv2) offer the opportunity of locating, scoring, and targeting suspicious lesions, and targeted biopsies (TBs) from magnetic resonance imaging (MRI)-suspicious lesions have been shown to be more successful for detection of csPCa when compared with TRUS-SB.[3-7] TB can be performed in a cognitive manner or using a fusion software.[8] Cognitive targeted biopsy (COG-TB) is performed by targeting the suspicious regions of the prostate cognitively during transrectal ultrasonography (TRUS)-guided biopsy; fusion targeted biopsy (FUS-TB) is performed using a fusion device for electronically superimposing magnetic resonance (MR) images over TRUS to visualize and target the suspicious lesion.[9] Although some studies revealed no difference in csPCa detection between COG-TB and FUS-TB, others reported improved accuracy with FUS-TB, especially for smaller lesions and in larger glands.[8-12] Transition zone (TZ) is the origin of benign prostatic hyperplasia (BPH) and responsible for the increase of prostate volume, which may cause decreased accuracy of

biopsy methods reported in larger gland volumes.[9-12] However, most (80–85%) of the prostate cancers (PCas) are located in the peripheral zone (PZ), which does not enlarge significantly during the BPH process.[13] In this context, we aimed to evaluate whether increasing prostate volumes or small lesion diameters would affect the csPCa detection rate of COG-TB for lesions located at the PZ.

Material and methods

Written informed consent was obtained from all patients before mpMRI examination and TRUS-guided biopsies. All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments. The study was approved by our institutional Ankara University Ethical Committee (decision number; I3-175-20).

Study design

In this retrospective study, medical records for 410 consecutive patients were evaluated. Exclusion and patient selection criteria are shown in the flowchart (Figure 1). A total of 219 consecutive biopsy naive patients with elevated prostate-specific antigen (PSA) values (higher than 4 ng/mL) and/or positive digital rectal examinations who all had undergone mpMRI in our hospital, had PIRADSv2 lesions with scores 3, 4, or 5 located in the PZ, and undergone TRUS-guided COG-TB in our institution between March 2015 and September 2019 were enrolled in the study group.

All of the patients were scanned using a 3-T MRI scanner. A single radiologist (A.E) who is experienced on mpMRI of prostate scored every visible PZ lesion with a score of 1–5 in each patient's mpMRI on the basis of PIRADSv2.[14,15] The lesion with the highest PIRADSv2 score and the largest diameter is named as the index lesion. The sizes of lesions were measured by MRI and divided into three categories: lesion diameter <5 mm, lesion diameter between 5 and 9.9 mm, and lesion diameter ≥10 mm. Prostate volume was calculated using by elliptical volume measurement ($\pi/6 \times$ transverse diameter × anteroposterior diameter × cephalocaudal diameter) and divided into four groups according to volumes <30 mL, 30–49.9 mL, 50–79.9 mL, and ≥80 mL.

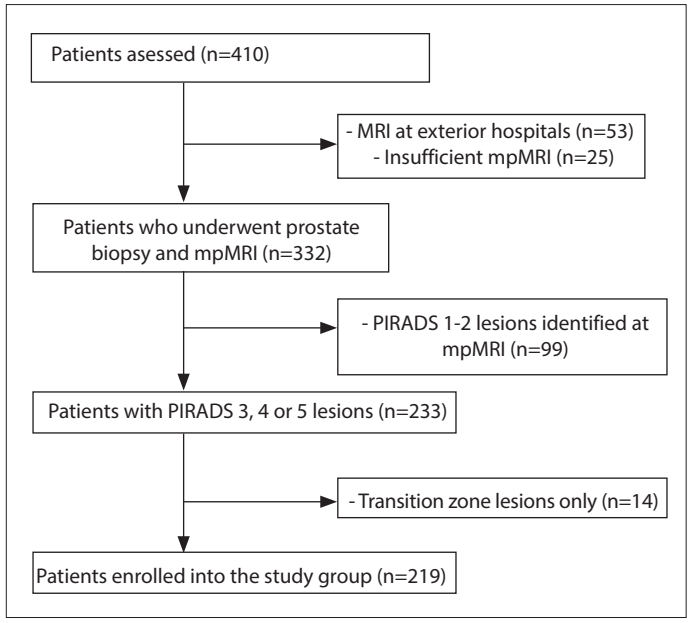

Figure 1. Flowchart illustrating the patient selection process

Prior to biopsy, the locations of suspicious lesions were also reviewed by the operator. The biopsy procedure was performed using TRUS guidance and transrectal route. After 12 core systematic biopsies (SBs), three extra cores from the region of index lesion were taken using TRUS guidance cognitively. All patients underwent equal number of biopsies (12 core SBs and three cores from the index lesion region).

MR image acquisition technique

Multiparametric MR images were obtained using a 3.0-T system (MAGNETOM Verio; Siemens Medical Solutions, Erlangen, Germany). Standard body matrix coil was used for signal reception from the patients' prostate. The sequences used in this study were as follows: sagittal TSE T2-weighted, oblique axial TSE T2-weighted, oblique axial TSE T1-weighted, oblique coronal TSE T2-weighted, axial TSE T2-weighted sequence encompassing pelvic lymph nodes to the level of the aortic bifurcation, and oblique axial diffusion weithed echo-planar imaging (DW EPI) sequence combined with spectral fat saturation with

Main Points:

- The rate of detection of csPCA with COG-TB was 4%, 9.8% and 33.1%, respectively, for lesions <5 mm, 5-9.9 mm and ≥10 mm. The csPCA detection rate was statistically higher than ≥10 mm lesions (p<0.001).
- The csPCA detection rate with COG-TB was 61.5% for prostate volume <30 ml, and decreased to 24.1% for prostate volumes of 30-49.9 mL, 16.2% for 50-79.9 ml and 6.9% for ≥80 ml prostate volumes (p<0.001).
- It is recommended that COG-TB should not be preferred as a priority for lesions with a diameter of <5 mm, which is only shown to have a detection rate of 4% csPCa.
- Significant increase in csPCa detection due to a decrease in prostate volume reveals that COG-TB performs much better in small prostate volumes.
- Clinicians should be careful when they prefer cognitive targeted prostatic biopsy in patients with periferal zone lesions less than 10 mm and with prostate volumes greater than 30 ml, due to significantly low csPCa detection rates.

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b-values of 0, 1000, and 2000 s/mm^2. After the intravenous administration of 0.2 mL/kg of gadolinium chelate compound, dynamic pre- and postcontrast-enhanced images were acquired in oblique axial plane with 3D fat-suppressed GE T1-weighted volumetric interpolated breath-hold sequence (VIBE) sequence.

TRUS biopsy procedure

TRUS was performed by using a GE P5 ultrasound scanner (GE Healthcare, Tokyo, Japan) equipped with a biplanar convex/convex transrectal probe (BE9CS). The biopsies were performed by transrectal route, using a full automatic core biopsy device with 18-gauge, 25-cm Tru-Cut-type needle. All biopsy procedures were performed by the same operator (E.O) who had a 20-year experience in TRUS-SB. All biopsy specimens were labeled according to the site of the prostate biopsied and sent for the histopathologic evaluation.

Clinical and biopsy data

Biopsy specimens were evaluated according to the International Society of Urological Pathology (ISUP) modified Gleason system.[16] The biopsy histopathology results were classified with regard to the presence /absence of PCa and csPCa. Cancer detection rates were analyzed on a per-lesion basis. csPCa is defined on histopathology as a Gleason score >3+3 (≥ISUP grade group 2), per-lesion basis.

Statistical analysis

IBM Statistical Package for the Social Sciences (IBM SPSS Corp.; Armonk, NY, USA) statistics version 25 was used for statistical analysis. The suitability of variables to normal distribution was analyzed by the Kolmogorov–Smirnov analysis. Descriptive statistics were expressed as median + interquartile range (IQR) for variables that are not normally distributed. The Chi-square test was used to assess the significance of differences, as appropriate. Subgroup analysis or which group the difference originated from was evaluated by post hoc analysis. Not normally distributed data correlation analysis was calculated using the Spearman correlation test. A p-value of less than 0.05 in the 95% confidence interval was considered to indicate statistical significance.

Results

Median age of the patients was 65 (IQR: 59–71) years, median PSA value was 6.60 (IQR: 5–9.18) ng/mL, and median TRUS volume was 56.5 (IQR: 42–78) mL. The clinical parameters and mpMRI PIRADSv2 scores of patients are shown in Table 1.

The csPCa detection rates according to lesion diameters of <5 mm, 5–9.9 mm, and ≥10 mm were 4% (1/25), 9.8% (9/91), and 33.1% (34/103), respectively; csPCa detection rates were significantly higher for lesions ≥10 mm (p<0.001). In subgroup analysis, the increase in lesion diameter for PIRADS 3 lesions did not significantly affect the rate of csPCa detection (p=0.489) (Table 2). However, for PIRADS 4 lesions, we noted a statistically significant increase in the detection rate of csPCa for lesions ≥10 mm diameter (p=0.018).

Table 1. Demographic and clinical information of patient population characteristics

Parameters	n (219)
Median age (years) (IQR)	65 (59–71)
Median PSA (ng/mL) (IQR)	6.60 (5–9.18)
Median TRUS volume (mL) (IQR)	56.5 (42–78)
Median MRI volume (IQR)	63 (47–82)
PIRADS score 3	116 (36.4%)
PIRADS score 4	62 (19.4%)
PIRADS score 5	41 (12.8%)
Median mpMRI lesion diameter (mm)	8.05 (3–25)

IQR: interquartile range; PSA: prostate-specific antigen; TRUS: transrectal ultrasonography; MRI: magnetic resonance imaging; PIRADS: Prostate Imaging Reporting and Data System; mpMRI: multiparametric magnetic resonance imaging.

Patients were divided into four groups according to the calculated prostate volume. Of these patients, 13 (5.9%) had <30 mL, 82 (37.4%) has 30–49.9 mL, 80 (36.5%) had 50–79.9 mL, and 43 (19.6%) had ≥80 mL prostate volumes (Table 3). The csPCa detection rate was 61.5% in the group with a prostate volume of <30 mL, and this was statistically significantly higher than other groups (P<0.001). csPCa detection rates for 30–49.9 mL, 50–79.9 mL, and ≥80 mL prostate volumes were 24.1%, 16.2%, and 6.9% respectively, but no statistically significant difference was observed between these groups. csPCa and cisPCa detection rates are shown graphically according to lesion size and prostate volume in Figure 2.

Cancer detection rates according to the PIRADSv2 scores of lesions are shown in Figure 3. csPCa was detected in 4.3%, 25.8%, and 56.1% of PIRADS 3, 4, and 5 lesions, respectively. There was a statistically significant difference in terms of csPCa detection rates between both PIRADS 3 and 4 (p=0.001) and PIRADS 4 and 5 lesions (p=0.002).

Discussion

The value of mpMRI in the early detection of PCa has been demonstrated by several reports.[17-20] However, targeting the mpMRI-suspicious lesions is still problematic. Existing mpMRI TB strategies are in-bore MRI-TB, FUS-TB, and COG-TB. The

Table 2. Clinically significant and insignificant cancer detection rates according to lesion diameter

	Lesion diameter (mm)			
Parameters	**<5 mm n=25 (14.1%)**	**5–9.9 mm n=91 (51.1%)**	**≥10 mm n=103 (34.8%)**	**p***
Median age (years) (IQR)	67 (61–70)	65 (60–70)	66 (61–71)	0.65
Median PSA (ng/mL) (IQR)	7 (5.48–10.5)	6.57 (4.84–9.5)	6.81(5.17–10)	0.708
PIRADS 3 (n=116)	19 (76%)	59 (64.8%)	38 (59.3%)	
cisPCa	3 (15.7%)	10 (16.9%)	8 (21%)	0.337
csPCa	1 (5.2%)	2 (3.3%)	2 (5.2%)	0.489
PIRADS 4 (n=62)	6 (24%)	32 (35.2%)	24 (38.7%)	
cisPCa	1 (16.6%)	10 (31.2%)	4 (16.6%)	0.238
csPCa		7 (21.8%)	9 (37.5%)	0.018*
PIRADS 5 (n=41)	–	–	41 (100%)	
cisPCa	–	–	9 (21.9%)	–
csPCa	–	–	23 (56.1%)	–
Total (n=219)	25	91	103	
cisPCa	4 (16%)	20 (21.9%)	21 (20.3%)	0.547
csPCa	1 (4%)	9 (9.8%)	34 (33.1%)	<0.001*

*Fisher's exact and chi-square test. IQR: interquartile range; PSA: prostate-specific antigen; PIRADS: Prostate Imaging Reporting and Data System; cisPCa: clinically insignificant prostate cancer; csPCa: clinically significant prostate cancer

in-bore MRI-TB technique is the most time-consuming and costly method; therefore, most centers around the world prefer COG-TB or FUS-TB for PCa diagnosis.[12] FUS-TB requires special software and a tracking device to perform an image fusion and allows visualization and TBs of MRI-identified lesions. For COG-TB, the operator evaluates the MR images of suspicious lesions to visually estimate the regions to take samples and then target the most appropriate areas during TRUS-guided biopsy.[8,11,21] FUS-TB has been reported to have additional costs in terms of the fusion software and time taken to plan and perform procedures.[22] The COG-TB represents the simplest TB approach, but lacks the advantage of directly visualizing the lesions on ultrasound screen and requires an experienced operator for the cognitive fusion procedure.[9] Several authors have shown that performance of COG-TB and FUS-TB for PCa diagnosis was similar.[17,23,24] Wegelin et al.[8] found no significant difference in the detection of csPCa between cognitive and software-fusion-based approaches in their meta-analysis.

One might have hypothesized that FUS-TB would have an advantage in patients with large prostates or small lesions when compared with COG-TB because of inability of directly visualizing the lesions and only sampling the suspicious areas during COG-TB. Delongchamps et al.[18] evaluated two TB techniques and stated that detection differences were higher for lesions with a diameter less than 10 mm in favor of FUS-TB. Contrarily, another study revealed no difference in PCa detection, even when stratifying by lesion volume and location.[11] In this study, we focused on the question of whether increasing prostate volumes or small lesion diameters would lead to lower cancer detection rates of lesions located at the PZ of the prostate. To the best of our knowledge, no other study specifically addressed the issue of suspicious lesion size and prostate gland volume, which may limit the csPCa detection rate of COG-TB for lesions located at the PZ of the prostate. According to our results, the csPCa detection rate of COG-TB increased from 4% to 9.8% for lesions with a diameter <5 mm and 5–9.9 mm. For lesions ≥10-mm diameter, the csPCA detection rate was 33.1%. The csPCA detection rate for lesions ≥10 mm was statistically higher than that for lesions <10 mm (p<0.001). Our results are in accordance with the current literature; in the PROFUS trial, patients underwent both FUS-TB and COG-TB, and the authors stated that despite no overall PCa detection differences, the software-based approach had performed best among smaller targets.[12] Another study determined that FUS-TB achieved an increased per patient and per-lesion cancer detection rate as compared with COG-TB especially for lesions smaller than 10

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Table 3. Clinically significant and insignificant cancer detection rates according to prostate volume

	Prostate volume (mL)				
Parameters	**<30 mL n=13 (5.9%)**	**30–49.9 mL n=82 (37.4%)**	**50–79.9 mL n=80 (36.5%)**	**≥80 mL n=44 (19.6%)**	**p***
Median age (years) (IQR)	66 (58–74)	65 (60–67)	67 (60–71.75)	69 (62–71)	0.104
Median PSA (ng/mL) (IQR)	6.1 (4.1–8.4)	6.2 (4.3–9)	7.35 (5.56–11)	6.7 (5.64–10.5)	0.158
PIRADS 3 (n=116)	4 (30.8%)	37 (45.1%)	45 (56.2%)	30 (68.1%)	
cisPCa	2 (50%)	8 (21.6%)	9 (20%)	2 (6.6%)	0.057
csPCa	1 (25%)	2 (5.4%)	–	2 (6.6%)	0.069
PIRADS 4 (n=62)	5 (38.4%)	26 (31.7%)	22 (27.5%)	9 (20.4%)	
cisPCa	2 (40%)	7 (26.9%)	5 (22.7%)	–	0.372
csPCa	3 (60%)	8 (30.7%)	4 (18.1%)	1 (11.1%)	0.172
PIRADS 5 (n=41)	4 (30.8%)	19 (23.2%)	13 (16.2%)	5 (11.3%)	
cisPCa	–	5 (26.3%)	3 (23%)	2 (40%)	0.176
csPCa	4 (100%)	10 (52.6%)	9 (69.2%)	–	0.018*
Total (n=219)	13	82	80	44	
cisPCa	4 (30.7%)	20 (24.1%)	17 (21.2%)	4 (9.9%)	0.207
csPCa	8 (61.5%)	20 (24.1%)	13 (16.2%)	3 (6.9%)	<0.001*

*Fisher's exact and chi-square test. IQR: interquartile range; PSA: prostate-specific antigen; PIRADS: Prostate Imaging Reporting and Data System; cisPCa: clinically insignificant prostate cancer; csPCa: clinically significant prostate cancer

mm.[25] They could not demonstrate a significant difference in detection of PCa for lesions ≥10 mm between two techniques.[25] Our findings also imply that COG-TB performed best for lesions larger than 10 mm. In our cohort's subgroup analysis, although csPCa detection rates were low for both PIRADS 3 (5.2%) and PIRADS 4 (0%) lesions, which are <5 mm, for lesions with a diameter of 5–9.9 mm, these rates were 3.3% and 21.8%, respectively, and we think this may imply that PIRADS 4 lesions with a diameter 5–9.9 mm may be sampled using COG-TB when FUS-TB is not available. However, we believe that especially for lesions <5-mm diameter, which we have shown to have only 4% total csPCa detection rate, COG-TB should certainly not be preferred.

We had also investigated the effect of prostate volume on cancer detection rates of PZ lesions, with regard to PIRADS categories. Detection rates were calculated separately for patients with <30 mL, 30–49.9 mL, 50–79.9 mL, and ≥80 mL prostate volumes. The decrease in prostate volume increased the detection of csPCa significantly; we have determined that the csPCA detection rate of COG-TB was 61.5% for prostates <30 mL and decreased to 24.1% for prostate volumes 30–49.9 mL, to 16.2% for prostate volumes 50–79.9 mL, and to 6.9% for prostate volumes ≥80 mL (p<0.001). The statistically significant difference shows that COG-TB performs much better in small prostate volumes. Our finding is supported by the literature; in a study that analyzed the results for prostate volumes higher or lower than 50 mL, the authors did not find any significant difference between PCa detection rates in small and large prostate groups for FUS-TB, but in the COG-TB group, the csPCA detection rate fell to 20% from 51.5% in the large prostate volumes.[26] Our 16.2% csPCA detection rate is similar to these values and implies that prostate volume ≥50 mL will also affect the performance of COG-TB inversely. In our cohort's subgroup analysis, even for the largest lesions with PIRADS score 5, the csPCA detection rate fell from 100% to 69.2% with increasing prostate volumes. We also notice the same pattern of decreasing detection rates with increasing prostate volumes for PIRADS 4 lesions (60%, 30.7%, 18.1%, and 11.1% for <30 mL, 30–49.9 mL, 50–79.9 mL, and ≥80 mL groups, respectively). These results also show a statistically significant trend for increasing csPCA detection rate with decreasing prostate volumes (Table 3).

As a secondary goal, we aimed to determine the overall and csPCA detection rates of COG-TB for different PIRADS categories. Results of our cohort are shown in Figure 3. Overall,

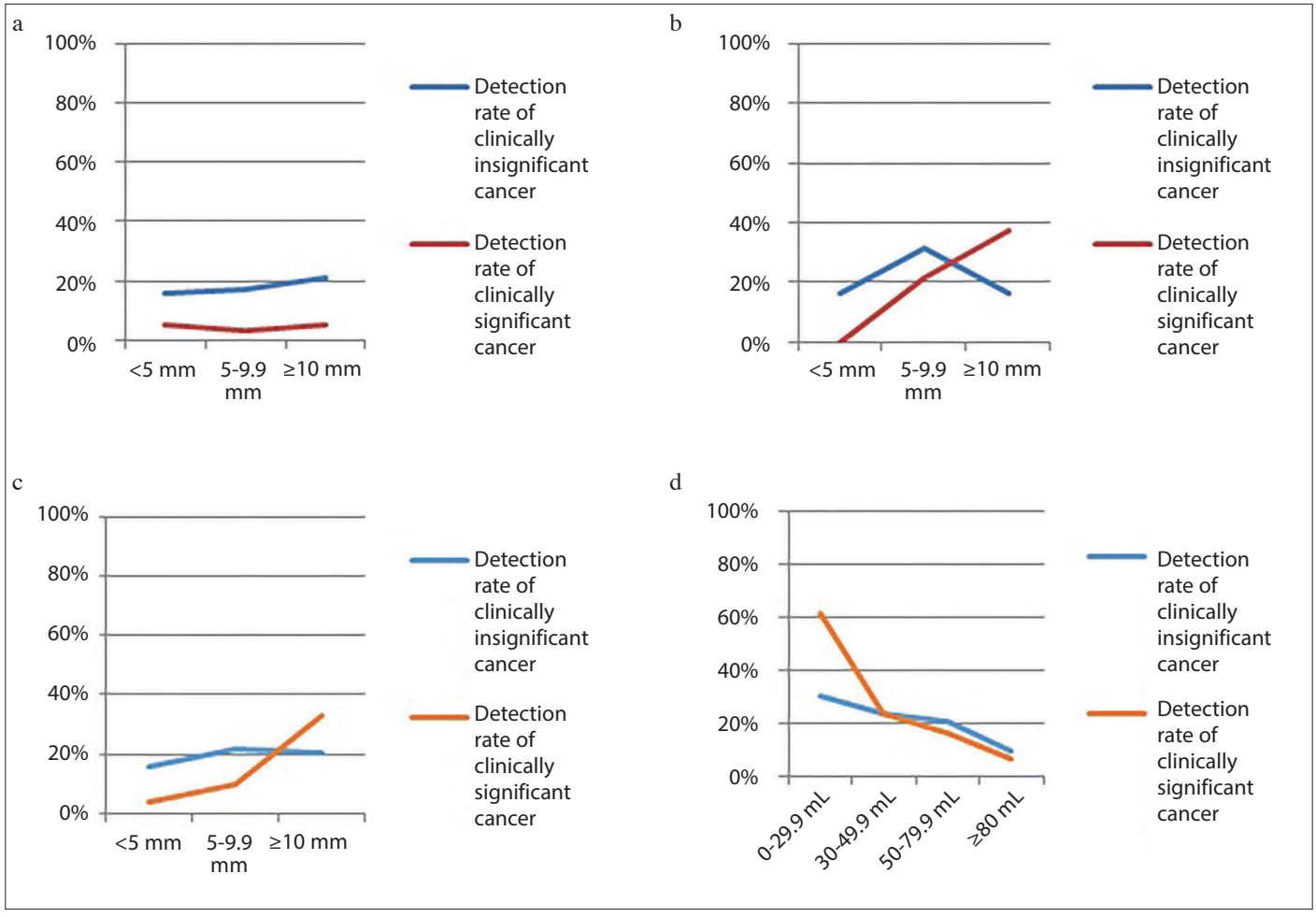

Figure 2, a-d. Graph of csPCa and cisPCa detection rates according to lesion diameters (a) PIRADS 3 lesions. (b) PIRADS 4 lesions. (c) Total (PIRADS 3, 4, and 5 lesions). (d) Graph of csPCa and cisPCa detection rates according to prostate volume

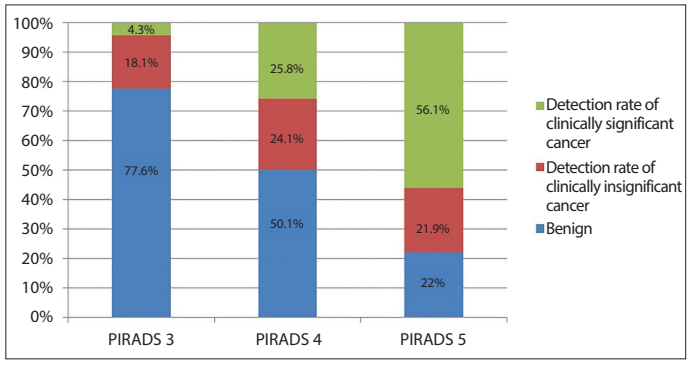

Figure 3. Cancer detection rates according to PIRADSv2 categories

csPCA detection rates are significantly increased by higher PIRADS scores ($p<0.05$). These results clearly support that higher PIRADSv2 scores are associated with increased risk of csPCa.[1,14]

What differentiates this study from previous reports is that we evaluated the csPCA detection rate of COG-TB for specifically PZ located lesions. Previous reports also stated that the csPCa detection rates decreased with increasing prostate volumes and small lesion diameters, but the suspicious lesions evaluated were located at both PZ and TZ.[10-12,25,26] During the BPH process, mainly the TZ enlarges, but our results showed that the increase in volume and the small lesion diameter also affected the detection rate of PZ-located lesions. Our study denotes values for lesion diameter and prostate volumes, allowing the operator to decide when to perform or not COG-TB in settings without access to FUS-TB. Prospective studies are necessary to evaluate the impact of these parameters on cancer detection rates of COG-TB for PZ lesions.

Our study has some limitations. First of all, this is a retrospective study. This study does not compare COG-TB and FUS-TB groups, but only evaluates a COG-TB cohort for cancer detection rates with regard to lesion size and prostate volumes. Whole

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mount histopathology results were not evaluated as a reference, because all the patients did not undergo radical prostatectomy. One of the most important issues for mpMRI analysis and TB is the operator's experience. At this point, 20 years of experience for the operator performing TB implies that our results may be attributed in part to experience level of the operator and may not be generalizable to all.

In conclusion, clinicians should be very careful when they prefer cognitive targeted prostatic biopsy in patients with periferal zone lesions less than 10 mm and with prostate volumes greater than 30 mL, because of significantly low csPCa detection rates.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara University (decision number; I3-175-20).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.Ö.; Design - E.Ö., Ç.A.; Supervision - Ö.Y.; Resources - E.Ö., Ç.A.; Materials - A.İ., E.K.; Data Collection and/or Processing - E.Ö., Ç.A.; Analysis and/or Interpretation - E.Ö., Ç.A.; Literature Search - E.Ö., Ç.A., A.İ., A.E.; Writing Manuscript - E.Ö., Ç.A., A.E.; Critical Review - E.Ö., A.E.; Other - A.Ç., A.İ., E.K.

Conflict of Interest: The authors have no conflicts of interest to declare.

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