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Characteristics of missed prostate cancer lesions on 3T multiparametric-MRI in 518 patients: based on PI-RADSv2 and using whole-mount histopathology reference

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Abstract

Purpose To determine the characteristics of missed prostate cancer (PCa) lesions on 3T multiparametric-MRI (mpMRI) based on PI-RADSv2 with whole-mount histopathology (WMHP) correlation.

Materials and methods This IRB-approved, HIPAA-compliant study, included 614 consecutive men with 3T mpMRI prior to prostatectomy at a single tertiary center between 12/2009 and 4/2017. Clinical, mpMRI, and pathologic features were obtained. PI-RADSv2-based MRI detected lesions were matched with previously finalized WMHP by a genitourinary (GU) radiologist and a GU pathologist. Patients with no mpMRI detected PCa lesion, but with at least one lesion $\geq$ 1 cm on WMHP, were reviewed retrospectively and assigned a PI-RADSv2 score. Tumor characteristics were compared between missed and detected lesions.

Result The final cohort included 518 patients with 1085 WMHP lesions. 51.9% (563/1085) of lesions were missed on 3T mpMRI. 71.4% (402/563), 21.7% (122/563), 4.4% (25/563), and 2.5% (14/563) of the missed lesions were Gleason scores (GS) $3 + 3$, $3 + 4$, $4 + 3$, and $8 - 10$, respectively. Missed PCa lesions had significantly lower proportion of GS ≥ 7 ($p < 0.001$) and smaller size for overall ($p < 0.001$) and index subcohorts ($p < 0.001$), as compared to detected lesions. 34.5% (194) of overall and 71.2% (79) index missed lesions were larger than 1 cm. In 13.7% (71/518) of patients without MR detected PCa, 149 lesions were detected on WMHP, with 70 (47%) lesions $\geq$ 1 cm. In retrospective review of these lesions, 42.9% (30), 18.6% (13), 21.5% (15), 10% (7), and 7% (5) were PI-RADSv2 1, 2, 3, 4, and 5, respectively.

Conclusion 3T mpMRI has an excellent per patients diagnostic performance for PCa and majority of missed lesions are clinically nonsignificant.

Keywords Magnetic resonance imaging · Prostate · Neoplasm

Introduction

A digital rectal exam followed by systematic transrectal ultrasound (TRUS) biopsy sampling of posterior prostate peripheral gland sextants is considered standard for detection of suspected prostate cancer (PCa) by the American Urological Association [1]. However, this technique has significant limitations including overdiagnosis of clinically insignificant lesions, underdiagnosis of clinically significant index lesions, and poor correlation of PCa aggressiveness and staging in correlation with final pathology [2]. Over the past decade, 3-Tesla multiparametric magnetic resonance imaging (3T mpMRI) has been established as the most sensitive and specific noninvasive technique for early detection, localization, grading, and

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staging of PCa [2–4]. 3T mpMRI has also significantly improved targeted biopsy yields for detection of clinically significant prostate cancer (csPCa) with overall detection reported between 71 and 92% [5–7]. However, 3T mpMRI fails to detect csPCa in up to 20–30% of patients. In order to improve the sensitivity and specificity of 3T mpMRI for detection of PCa as well as excluding indolent lesions, understanding the imaging features of missed csPCa is important. The purpose of this study is to determine the PI-RADS v2 and histological characteristics of missed PCa lesions on 3T mpMR imaging in a large cohort using whole-mount histopathology (WMHP) as the reference standard.

Materials and methods

Study population and design

In this Health Insurance Portability and Accountability Act (HIPAA)-compliant, Institutional Review Board-approved retrospective study, we evaluate 614 men with biopsy-proven prostate adenocarcinoma who underwent 3T mpMRI between Dec 2009 and May 2017 before robotic-assisted laparoscopic radical prostatectomy (RALP). Exclusion criteria were prior radiotherapy and more than a 6-month interval between 3T mpMRI and RALP. A total of 518 patients with 1085 individual PCa lesions fulfilled the inclusion criteria and comprised the final study cohort (Fig. 1).

3T mpMRI

3T mpMRI was performed on one of several systems (Siemens Magnetom Trio, Skyra or Verio scanners (Siemens Medical Systems, Malvern, Pennsylvania, USA) using a pelvic external phased-array coil, with (n = 263) or without (n = 255) an endorectal coil. An anti-peristaltic agent (1 mg of glucagon (Glucagen, Lilly, In, USA)) was administered intramuscularly to reduce bowel peristalsis. All MRI examinations included T2-weighted turbo spin-echo (TSE) imaging, dynamic contrast-enhanced (DCE) imaging and DWI, and Apparent Diffusion Coefficient (ADC) maps. 3T mpMRIs are performed according to a standardized protocol which is provided in the supplementary table.

MRI and histopathologic interpretation, analysis, and correlation

An abdominal imaging fellow (postgraduate year 6) with one of three fellowship-trained genitourinary (GU) radiologists each of whom have interpreted > 1000 prostate mpMRIs, prospectively, identified lesions suspicious for PCa on preoperative 3T mpMRI. 313 (60.4%) patients had one or more prostate biopsies before mpMRI but the radiologists were blinded to the result at the time of reporting. During the initial interpretation of MRI, the radiologist was blinded to any medical records. However, final diagnosis was made based on some clinical information, when available. Suspicious regions of interest (ROIs) were scored using a previously published institutional scoring system similar to Prostate Imaging-Reporting and Data System version 1 (PI-RADSv1) (2010–2015) [8, 9]. For studies performed after December 2015 (n = 218), each lesion was prospectively assigned a Prostate Imaging-Reporting and Data System version 2 (PI-RADSv2) score. Studies performed prior to December 2015 (n = 300) were retrospectively reviewed and assigned a PI-RADSv2 score by a fourth fellowship-trained genitourinary radiologist who had interpreted more than 500 prostate MRI examinations and was blinded to pathology and previous radiology report at the time of image interpretation. PI-RADSv2 score ≥ 3 was considered as a positive for malignancy for an ROIs on mpMRI (Fig. 2).

Two dedicated GU pathologists with 4 and 12 years of experience in interpreting WMHP, evaluated each WMHP slice, detecting individual PCa lesions and categorizing them by size, location, and primary and secondary Gleason pattern, independent of MRI findings. Later, in a series of multidisciplinary sessions at 4–8-week intervals, a GU radiologist and a GU pathologist retrospectively reviewed each case to match each previously detected lesion on 3T mpMRI ROIs to the corresponding previously detected PCa lesion on WMHP, categorizing each 3T mpMRI detected lesion as true or false positive and missed MR lesions as false negative. 3T mpMRI lesions were classified as true positive if the location of the lesion was in the same sextant as the WMHP detected tumor (right/left; apex/midgland/base). Part of images corresponding to the histologically confirmed tumors which were not previously identified on mpMRI were considered false negative, and ROIs without corresponding histopathologic correlates were considered as false positives. After the multidisciplinary sessions, patients without any detected prostate cancer lesion in 3T mpMRI, but with at least one lesion larger than 1 cm on WMHP, were retrospectively reviewed and assigned a PI-RADSv2 score by a radiologist. WMHP was used to obtain knowledge of missed tumor location and size.

The index tumor was defined as the tumor with the highest Gleason score (GS). When multiple PCa lesions had the same GS, the lesion with the largest diameter was considered as the index lesion. Lesions located on multiple WMHP slices were checked for contiguity to ensure that a

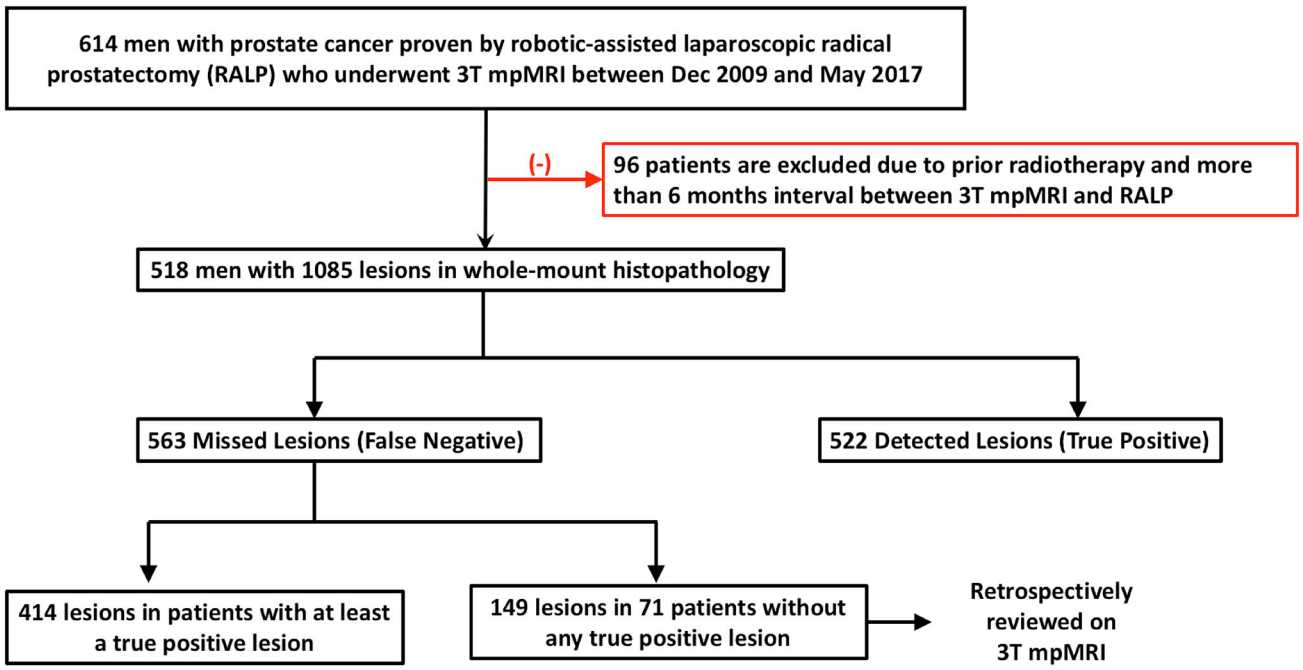


Fig. 1 Flowchart for study population and design

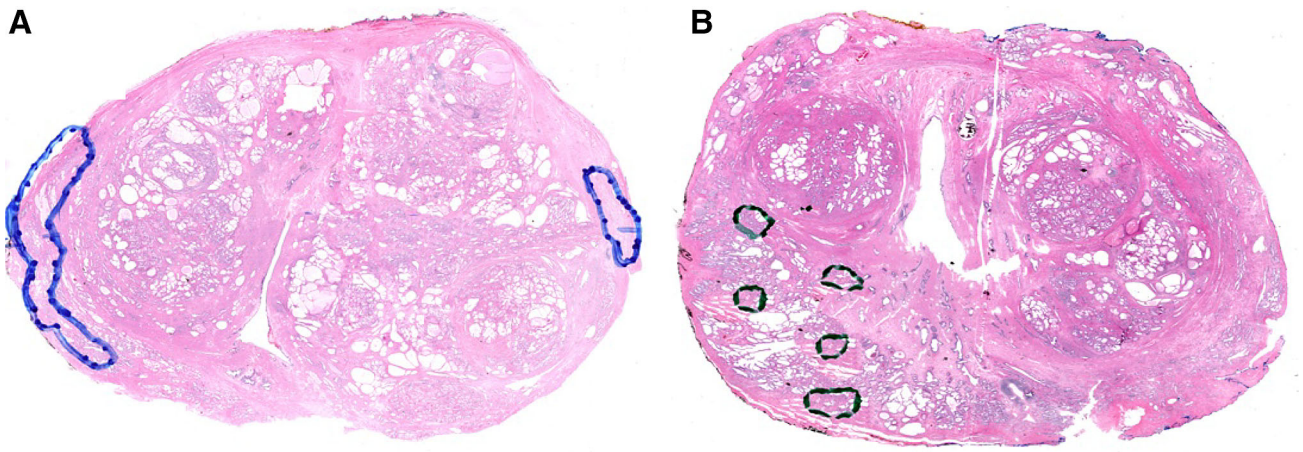


Fig. 2 Whole-mount histopathology slide of two patients with PCa lesion. **a** Lesion on the right was considered as a large tumor (2.3 cm), although it is long and narrow in shape but it is less likely to be visible on 3T mpMRI. **b** These multiple small lesions were considered as a lesion with 2.5 cm diameter

single tumor spanning multiple segments was not duplicated in the analysis.

Since there are different definitions for clinically significant prostate cancer (csPCa), the two most common were used. Definition 1(csPCa[1]) is any lesions with GS $\geq 3 + 4$, regardless of size, and lesions with GS = 3 + 3 larger than 1 cm diameter (i.e., tumor volume ≥ 0.5 mL) on WMHP and definition 2 (csPCa[2]) is any lesion with GS $\geq 3 + 4$.

Statistical analysis

Descriptive statistics for patients, mpMRI, and histopathologic characteristics were calculated for the entire study sample of 518 men. Patient's age, PSA, PSA density, pathology prostate weight, mpMRI prostate volume, pathology lesion size, GS, and tumor focality between detected and missed tumors were then compared among the 1085 histologically unique tumors. Univariate and multivariate logistic regression analyses were used to predict the odds of missing a tumor on 3T mpMRI based on the clinical and histopathology

characteristics. For multivariate logistic analysis, potential covariates were screened with univariate logistic analysis, in which any covariate with $p \leq 0.20$ was included in the forward stepwise model selection process. Pathology lesion size, GS, index status, and lesion zone were chosen for inclusion in the multivariate model regardless of univariate analysis results based on previous knowledge of these as potential confounders of detection. To account clustering effect within patients, mixed effects logistic regression was used in both univariate and multivariate analyses.

For all statistical analyses, Stata v12.1 (StataCorp LP, College Station, Texas) was used. $p < 0.05$ was considered statistically significant and all confidence intervals (CI) were computed to 95%.

Results

Patients characteristics

The final study cohort included 518 patients with 1085 PCa foci identified on WMHP with a mean interval of 63 days (range 0–177) between 3T mpMRI and prostatectomy. The mean patient age was 61.7 ± 6.9 years (range 41–82). The median PSA, median PSA density, and median prostate weight after resection were 6.0 ng/mL (range 1–139 ng/mL,), 0.13 ng/mL/cc (range 0.02–3.3 ng/mL/cc), and 44 g (range 12–151 g), respectively (more information is provided in Table 1).

Histologic findings

The mean tumor diameters on WMHP for overall and index lesions were 1.48 ± 1.0 cm and 2.15 ± 0.94, respectively. A total of 59.6% (647/1085) PCa foci were 1 cm or larger on WMHP. Of 1085 PCa lesions, 46.8% (507), 34.0% (369), 12.2% (132), and 0.7% (77) had Gleason Scores (GS) of 3 + 3, 3 + 4, 4 + 3 an,d 8 − 10. Multifocal and unifocal PCa index lesions were present in 76.5% (396/518) and 23.5% (122/518) of the overall patient cohort on WMHP, respectively (Table 1). The majority of lesions was in patients with stage pT2 disease (761 lesions (70.2%)) and remainder was in patients with pT3a (265 (24.4%)), pT3b (57 (5.2%)), and pT4, (2 (0.2%)) disease.

3T mpMRI missed and detected PCa lesion characteristics

On 3T mpMRI, of the entire 1085 PCa lesion cohort in 518 patients, 51.9% (563/1085) were missed and 48.1% (522/1085) were detected. Considering only the index lesions, the percentage of missed lesions decreased significantly to 21.4% (111/518), and detected lesions increased significantly to 78.6% (407/518) ($p < 0.001$) compared to the overall lesions. Detected lesions were assigned a PI-RADS v2 score of 3, 4, and 5 in 30.3% (158/522), 44.4% (232/522), and 25.3% (132/522) of instances, respectively.

Of the 563 missed PCa lesions, 71.4% (402/563), 21.7% (122/563), 4.4% (25/563), and 2.5% (14/563)) were graded as GS = 3 + 3, GS = 3 + 4, GS = 4 + 3, and GS = 8 − 10, respectively (Table 2). The proportion of PCa lesions with GS ≥ 3 + 4 was significantly lower in missed tumors compared to detected tumors ($p < 0.001$).

Missed PCa lesions were significantly smaller than detected lesions in both overall (0.94 ± 0.7 cm vs. 2.05 ± 0.9 cm, ($p < 0.001$)) and index (1.58 ± 0.8 cm vs 2.3 ± 0.9 cm, ($p < 0.001$)) lesion subcohorts. Missed overall and index lesions were larger than 1 cm in 34.5% (194) and 71.2% (79), respectively (Table 2).

On univariate analysis, the sensitivity for detection of index PCa was significantly higher (p value < 0.001) in patients with solitary PCa (90.5% (114/126)) than in those with multifocal PCa (73.9% (323/437)). PCa was more likely to be missed in the transition zone (TZ) compared to peripheral zone (PZ) (57.5% vs 49.7%, $p = 0.03$). Compared to the detected lesion subcohort, the missed lesion subcohort had significantly larger median prostate size (52 g vs 44 g, $p < 0.001$) and had significantly lower median PSA and PSA density ($p < 0.001$) (Table 1).

All factors except PSA and stage remained significant predictors of PCa detection in the multi-factor model. In Table 4, the odds ratio, confidence interval, and p-values for univariate and multivariate analyses are presented. PCa lesion size, Index status, and GS were the strongest factors after adjustment for stage, zone, and PSA in multivariate analysis. In comparison to lesions ≥ 1 cm in diameter, index lesions, and GS ≥ 3 + 4, the odds of missing lesions < 1 cm, not-index lesions, and GS = 3+3 were 2.5 ×, 4.3 × , and 4.25 ×, respectively (Table 3).

Characteristics of patients without true-positive lesion

Most patients with an undetected PCa lesion (86.3%, 447/518) had one or more additional PCa lesion(s) detected by 3T mpMRI. A total of 149 PCa lesions were detected in 71 men without a lesion on MRI, of which 47% (70/149) lesions were larger than 1 cm (Table 4). On retrospective review of these lesions, 42.9% (30/70), 18.6% (13/70), 21.5% (15/70), 10% (7/70), and 7% (5/70) were PI-RADSv2 1, 2, 3, 4, and 5, respectively (Fig. 3). 48% (20/41) of PI-RADSv2 score 1 or 2 lesions had ≥ 3 + 4, and 68% (28/41) were located in peripheral zone.

Of the total 518 patients, 7.7% (40/518) and 5% (26/518) had csPCa[1] and csPCa[2], respectively, which were

Table 1 Comparison of missed and detected lesions

	Total				Index			
	Detected (%)	Missed (%)	Total	*p* value	Detected (%)	Missed (%)	Total	*p* value
Total	522 (48.1)	563 (51.9)	1085		407 (78.6)	111 (21.4)	518	
Gleason score								
3 + 3	105 (20.7)	402 (79.3)	507	< 0.001*	39 (56.5)	30 (43.5)	69	< 0.001*
3 + 4	247 (66.9)	122 (33.1)	369		206 (78.3)	57 (21.7)	263	
4 + 3	107 (81.1)	25 (18.9)	132		102 (85.7)	17 (14.3)	119	
8 − 10	63 (81.8)	14 (19.2)	77		60 (89.5)	7 (10.5)	68	
Size (cm)								
Mean ± SD	2.05 ± 0.96	0.94 ± 0.72	1.48 ± 1.02	< 0.001*	2.31 ± 0.90	1.58 ± 0.88	2.15 ± 0.94	< 0.001*
1 < cm	70 (15.9)	369 (84.1)	439	< 0.001*	22 (40.7)	32 (59.3)	54	< 0.001*
1 ≥ cm	453 (70.0)	194 (30.0)	647		385 (83.0)	79 (17.0)	464	
Clinically significant 1	479 (64.8)	260 (35.2)	739	< 0.001*	401 (80.8)	95 (19.2)	496	< 0.001*
Clinically significant 2	417 (72.15)	161 (27.85)	578	< 0.001*	368 (82)	81 (18)	449	< 0.001*
Zone								
Peripheral	390 (50.3)	385 (49.7)	775	0.03*	307 (79.3)	80 (20.7)	387	0.05*
Transitional	132 (42.5)	178 (57.5)	310		96 (73.2)	35 (26.8)	131	
Endorectal coil								
Yes	263 (48.7)	276 (51.3)	539	0.29	212 (80.6)	51 (19.4)	263	0.33
No	259 (47.4)	287 (52.6)	546		198 (77.6)	57 (22.4)	255	
T stage, no. (%) of patients								
T2					251 (72.1)	97 (27.9)	348	< 0.001*
T3,T4					156 (91.7)	14 (8.3)	170	
Solitary					111 (91)	11 (9)	122	< 0.001*
Multifocal					296 (74.7)	100 (25.3)	396	
Prostate weight (g)								
Median (IQR)					44 (34–52)	52 (36–64)	46 (34–54)	< 0.001*
PSA (ng/mL)								
Median (IQR)					8.5 (4.7–9)	5.9 (4.2–6.7)	7.9 (4.9–8.3)	0.003*
PSA density (ng/mL/CC)								
Median (IQR)					0.20 (0.12–0.22)	0.12 (0.7–0.14)	0.18 (0.12–0.21)	0.002*

ECE extra capsular extension, *PSA* prostate-specific antigen, *IQR* interquartile range

entirely undetected on 3T mpMRI (Table 4). On pathological review, 20% of these missed lesions were long and narrow in shape (height was five times larger than width) and 8% were sparse (multiple < 4 mm foci) and the rest were round, oval, or geographic. 46.2% (260) and 28.6% (161) of missed lesions were csPCa[1] and csPCa[2], respectively.

Discussion

In this study, we analyzed the 3T mpMRI characteristics of missed PCa lesions with WMHP correlation in the largest reported PCa cohort to date to our knowledge. Lesions that are missed on 3T mpMRI had smaller diameter and lower aggressiveness (GS 3 + 3).

Although 13.7% of patients were missed, missing rate was only 7.7% and 5% patients with csPCa[1] and csPCa[2] lesions on 3T mpMRI. These results are important since excluding clinically insignificant cancer should limit the number of patients undergoing radical treatments with their related complications, reduce patient anxiety of having cancer, and limit the costs resulting from overtreatment [10]. Moreover, a failure to identify csPCa in males being considered for or treated with active surveillance could result in suboptimal patient outcomes [11]. As expected, the per-lesion performance of 3T mpMRI was less accurate

Table 2 Characteristics of missed lesions in 3T mpMRI based on WMHP

	Missed (%)	
	Total	Index
Total	563	111
Gleason score		
3 + 3	402 (71.4)	30 (27)
3 + 4	122 (21.7)	57 (51.4)
4 + 3	25 (4.4)	17 (15.3)
8 − 10	14 (2.5)	7 (6.3)
Size (cm)		
Mean ± SD (min–max)	0.94 ± 0.7 (0.1–4.3)	1.58 ± 0.88 (0.15–4.3)
≤ 0.5 cm	199 (35.3)	13 (11.7)
0.5–1 cm	170 (30.2)	19 (17.1)
1 ≥ cm	194 (34.5)	79 (71.2)
Clinically significant 1	260 (46.2)	95 (85.5)
Clinically significant 2	161 (28.6)	81 (72.9)

Table 3 Odds ratios for missed tumor detection by 3T mpMRI

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Gleason score						
≥ 3 + 4*	1	–	< 0.001*	1	–	< 0.001*
3 + 3	10.02	7.07–14.20		2.5	1.54–4.65	
Size						
1 ≥ cm*	1	–	< 0.001*	1	–	< 0.001*
1 < cm	12.3	9.11–16.80		4.3	2.45–7.2	
Index lesion						
Yes*	1	–	< 0.001*	1	–	< 0.001*
No	14.25	10.63–19.1		4.25	2.78–6.49	
T stage, no. (%) of patients						
T3,T4*	1	–	< 0.001*	1	–	0.19
T2	1.6	1.27–2.16		1.0	0.97–1.06	
Zone						
Peripheral*	1	–	0.02*	1	–	0.046*
Transitional	1.4	1.04–1.88		1.3	1.00–2.08	
Tumor focality						
Solitary*	1	–	< 0.001*	1	–	0.004*
Multifocal	13.4	7.16–25.40		2.7	1.22–5.45	
PSA (ng/mL)	1.04	1.01–1.06	0.003*	1.0	0.99–1.07	0.115
Prostate weight	1.02	0.982–0.988	< 0.001*	1.01	1.01–1.03	0.001*

Univariate ORs for PSA, and prostate weight as continuous variables are given for each increasing increment (ng/ml, g) were tumor focality, multifocal versus solitary (reference); Gleason score ≥ 3+4 (reference); tumor stage, T2 versus T3,T4 (reference); and tumor size > 1 cm (reference); ECE negative versus positive (reference)

OR odds ratio, *CI* confidence interval, *PSA* prostate-specific antigen, *ECE* extracapsular extension

than the per-patient sensitivity, concordant with Borofsky el al. and Ahmed el al. studies [12, 13].

The results of our study clarify results suggested by several prior studies with smaller study cohorts. Krishna et al. in a study of 47 patients reported sensitivities of 64.5 and 77.4% for csPCa lesions for two readers using PI-RADSv2 on 3T mpMRI with WMHP [14]. Using a nonPI-RADSv2 scoring system, Costa et al. in a 49 patient cohort

Table 4 Characteristics of lesions in patients without any true-positive lesion in 3T mpMRI

Total lesions no.	149
Total patients no.	71
Gleason score (%)	
3 + 3	89 (59.7)
3 + 4	43 (28.9)
4 + 3	11 (7.4)
8 − 10	6 (4)
Size (%) cm	
1 < cm	79 (53)
1 ≥ cm	70 (47)
Clinically significant (%) (per lesion)	
csPCa[1]	86/149 (57.7)
csPCa[2]	60/149 (40.2)
Clinically significant (%) (per patients)	
Missed patients subcohort	
csPCa[1]	40/71 (56.3)
csPCa[2]	26/71 (36.6)
Clinically significant (%) (per patients)	
Overall	
csPCa[1]	40/518 (7.7)
csPCa[2]	26/518 (5)
PI-RADS scoring for lesions > 1 cm	
1	30 (42.9%)
2	13 (18.6%)
3	15 (21.5%)
4	7 (10%)
5	5 (7%)

csPCa[1] or csPCa[2] clinically significant prostate cancer(definition 1 or 2)

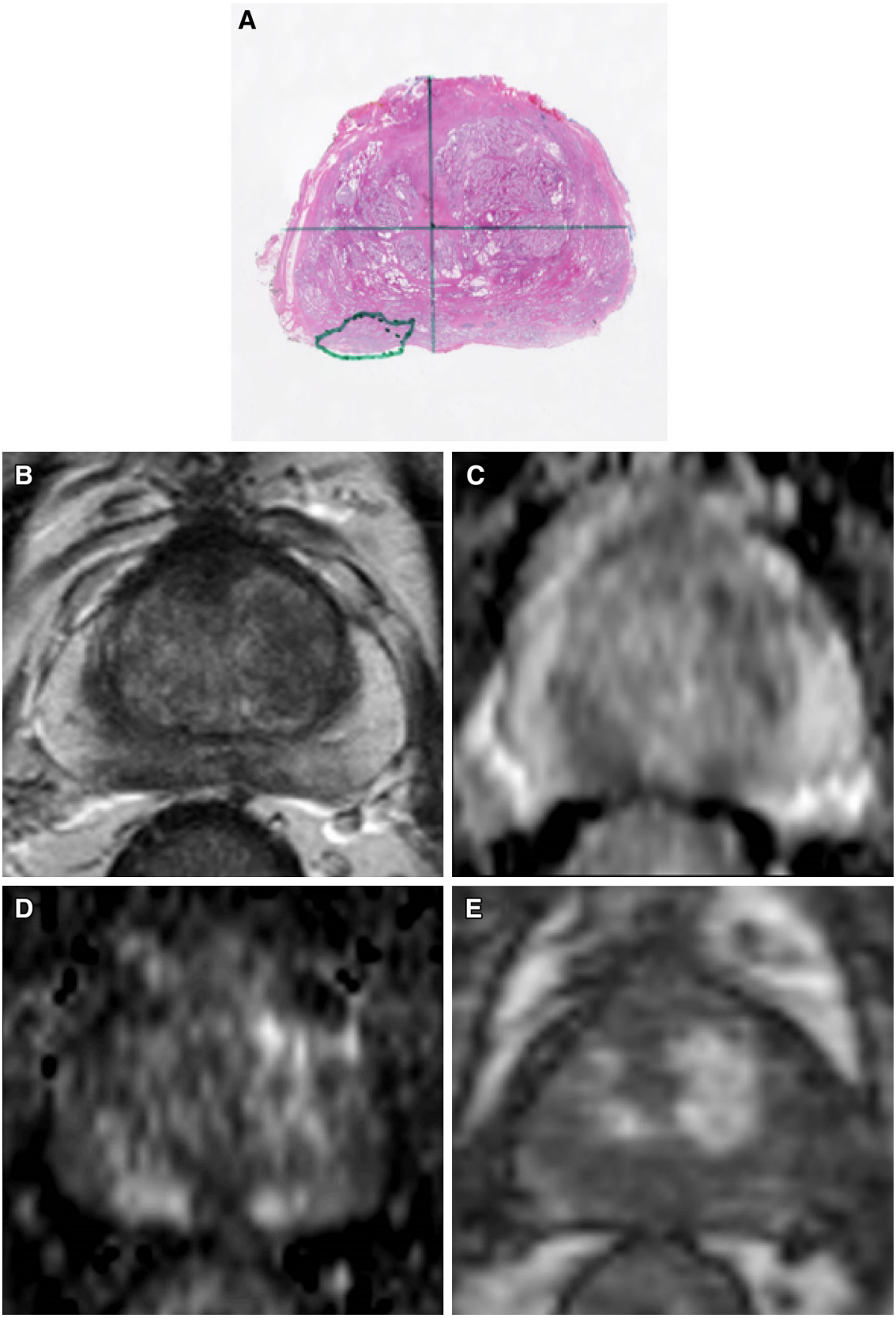
and Le et al. in a 122 patient cohort reported PCa detection sensitivity of 74% and 80% for index lesions on 3TmpMRI, respectively [15]. Using 1.5T mpMRI, Russo et al., reported a very high sensitivity of 90% for index PCa lesion detection, defined as the largest overall lesion, using WMHP as the reference standard [16]. Ahmed el al [13] in a multicentric study with 572 patients using template prostate mapping biopsy as the reference reported per-patient sensitivity of 93% for 1.5 mpMRI which was confirmed by our study.

In our study, lesion size was one of the strongest predictor for PCa detection as previously reported by Tan et al. in a study of 122 patients [7]. Borofsky et al. reported a 84% sensitivity for clinically important PCa lesions in 100 patients on 3T MRI, but included only the two largest PCa lesions for each patient in their analysis, likely overestimating MRI performance. In their series, missed PCa lesions were 2–3 times smaller in size [12]. Our study confirmed that lesions that are missed tend to be smaller and the average size of overall missed PCa lesions and missed index PCa lesions were 50% and 75% smaller than detected overall and index lesions, respectively. However, 34% of our missed PCa lesions were larger than 1 cm. On re-review of missed lesions, most lesions (61.5%) had lower PI-RADSv2 scores of 1 and 2, also reported previously by Borofsky et al. [12]. Small tumor size is an important factor in the prediction of insignificant prostate cancer which tend to have excellent oncogenic outcomes and are ideal candidates for active surveillance rather than radical treatments [17].

We found that most missed index PCa lesions were in prostate glands with multifocal PCa lesions and the detection rate was better in patients with solitary PCa lesions. This finding may be explained in part by satisfaction of search (SOS) errors that Berbaum et al. introduced in 2011 [18]. They reported that detection of one lesion decreased detection of subsequent lesions. This result needs more analysis and a multi-reader study to be verified.

Missed lesions had a significantly lower median GS than lesions detected on MRI. This finding corroborates those reported by Tan et al. and Le et al. [6, 17] and other studies [7, 16]. However, we showed that 28.8% of the missed PCa lesions had high-grade PCa (21.7% GS = 3 + 4 and 7.1% GS ≥ 4 + 3). This result has important implication on the management of men with prostate cancer for the use of imaging for focal therapy and active surveillance. De Visschere evaluated 124 patients with negative mpMRI after 2 years of follow-up calculating patient-based performance of mpMRI [19]. Although their detection rate of 75.3% was similar to ours (78.6%), their missed high-grade (GS ≥ 3 + 4) index lesion rate of 14.5% was less than our study. They did not mention the frequency of high-grade lesions in detected tumors, therefore we could not evaluate the distribution of the lesions in their whole population. Borofsky reported that 16% of clinically important lesions were not detected at initial mpMRI [12].

In our study, PCa lesions were significantly more likely to be missed in the transition zone (TZ) compared to the peripheral zones (PZ), although the lesion mean size and grade distribution were similar between TZ and PZ PCa lesions. De Visschere et al. reported that all of their missed PCa lesions were in the peripheral zone [19]. They did not mention the frequency of tumor location in detected tumors, we could not assess the difference between the result. Since TZ lesions have overlapping imaging features with benign lesions such as benign prostatic hyperplasia (BPH) and they have reportedly different pathological and clinical characteristics from PZ lesions, detection of tumor can be more challenging in this zone [20]. This may in part also explain why we missed more PCa lesions in larger


A
B
C
D
E

◀**Fig. 3** Images of a 62-year-old patient with a serum PSA level of 5.9 ng/mL. **a** Whole-mount pathologic specimen obtained at robotic-assisted prostatectomy shows a lesion with Gleason score 3 + 4 in the right peripheral zone. This lesion was not detected on the first review of mpMRI, and on the retrospective review: **b** Axial T2-weighted MR image shows an area of hypointense signal in right peripheral zone. **c** Axial apparent diffusion coefficient (ADC) map shows areas of focal hypointensity in the right peripheral zone. **d** DW (b = 1400 s/mm^2) shows areas of focal hypointensity in the same location. **e** Dynamic contrast-enhanced MR images do not show any clinically important abnormality. This lesion was assigned a PI-RADSv2 score 4

prostate glands, where these benign conditions mostly increase the size of the prostate.

There are limitations to this study. First, this study was retrospective and thus has intrinsic selection bias to surgical patients based on the study design, we evaluated men who underwent RALP and excluded men who underwent active surveillance or radiation therapy. As a result, our findings may not reflect the population of men with prostate cancer who did not undergo surgery. Second, the study population contained patients referred to one high-volume tertiary care academic institution with subspecialty prostate cancer expertise. Therefore, these results may not be broadly or generally applicable to centers without expertise. Third, since no repeat 3T mpMRI examinations were performed, the test–retest reproducibility of the MRI examinations is unknown. Fourth, we did not regularly scan the ex vivo prostate after prostatectomy and we did not use a prostate mold for all patients; therefore, the MR Images and the WMHP slices were not directly overlaid and despite all the care taken to confirm a match, mismatches might have occurred.

In conclusion, on 3T mpMRI, most missed PCa lesions were smaller and were lower grade than detected lesions. Only 5% and 7.7% of patients were missed who had csPCa[1] and csPCa[2] lesions, respectively. The majority of csPCa missed lesions in missed patients had score 1 or 2 based on PI-RADSv2 in the retrospective review.

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Compliance with ethical standards

Ethical approval This study was performed in accordance with the 1996 Health Information Portability and Accountability Act (HIPAA) and under waiver of informed consent by the institutional review board (IRB).

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