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Prostate cancer detection rate according to lesion visibility using ultrasound and MRI

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AIM: To evaluate the difference in prostate cancer detection rates according to lesion visibility using transrectal ultrasound (TRUS) and magnetic resonance imaging (MRI) before biopsy.

MATERIALS AND METHODS: Patients who underwent TRUS-guided prostate biopsy in 2016 and 2017 (n=1,022) were divided into three groups: (1) patients who did not undergo a prebiopsy MRI (group 1, n=622); (2) patients without visible lesions on the prebiopsy MRI (group 2, n=77); and (3) patients with visible lesions on the prebiopsy MRI (group 3, n=323). Biopsy results were compared using chi-square tests or independent t-tests between patients with and without TRUS-visible lesions in each group. A logistic regression test was used to determine the variables independently associated with the detection of clinically significant cancer.

RESULTS: Focal lesions were visible on TRUS in 710 patients. Clinically significant cancers were detected in 39.4% and 13.1% of patients with and without TRUS-visible lesions, respectively (p<0.001). The cancer detection rate was significantly higher in patients with TRUS-visible lesions in groups 1 and 3 (p<0.001). Within group 1, the Gleason scores, number of positive cores, and the cancer involvement ratios were significantly greater in patients with TRUS-visible lesions than in patients without TRUS-visible lesions. MRI- and TRUS visibility were positively associated with the detection of clinically significant prostate cancer (p=0.002 and p<0.001, respectively).

CONCLUSION: TRUS- and MRI-visible focal lesions in the prostate were significantly associated with the detection of clinically significant cancer.

Introduction

For patients with elevated prostate specific antigen (PSA), transrectal ultrasound (TRUS)-guided biopsy is

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performed to determine the presence of prostate cancer. Today, magnetic resonance imaging (MRI) has become more popular for patients with elevated prostate-specific antigen (PSA) as a diagnostic examination to identify focal prostate lesions. Many studies have shown the importance and clinical usefulness of prebiopsy prostate MRI to detect clinically significant cancer and to select patients who can avoid an unnecessary biopsy.[1] TRUS-guided targeted biopsy is performed on prostate focal lesions detected by prebiopsy MRI using real-time MRI–ultrasound (US) fusion or cognitive fusion. TRUS-guided targeted biopsy is based on US images even when a fusion technique is used. Therefore, the visibility of focal lesions via TRUS may be important for enhancing the cancer detection rate.

There have been a few reports that have shown that TRUS visibility could improve the detection and targeting of prostate cancer and cancer detection rate for TRUS highly suspicious lesion and TRUS unlikely lesions were 82% and 0%, respectively in an article.[2,3] Another previous study had shown that almost half of the MRI lesions were visible on TRUS. The study had also shown that TRUS-visible lesions were more aggressive than TRUS-invisible lesions.[4] Therefore, TRUS visibility may be helpful for stratifying prostate cancer risk during TRUS-guided biopsy regardless of a prebiopsy MRI; however, previous studies included a small number of patients. Moreover, other studies have shown the impracticality of TRUS for characterizing focal lesions.[5–7] Therefore, the importance of TRUS visibility of prostate focal lesions is not widely accepted.

The purpose of this study was to evaluate the difference in prostate cancer detection rates according to lesion visibility using TRUS and MRI before biopsy.

Materials and methods

Patients

The institutional review board of Seoul St Mary's Hospital approved this study and waived the informed consent requirement due to the retrospective study design. Consecutive patients who underwent TRUS-guided prostate biopsy between January 2016 and December 2017 were included in the study (n=1,022). The mean age of patients was 67.8±8.5 (range, 40–92) years old. Patients were divided into three groups: (1) group 1, which included patients who did not undergo prebiopsy MRI (n=622); (2) group 2, which included patients without visible lesions on the prebiopsy MRI (n=77); and (3) group 3, which included patients with visible lesions on the prebiopsy MRI (n=323). Performing prebiopsy MRI was determined by the urologists' preference and many urologists had a very different stance on prebiopsy MRI. As the patients were not assigned to each urologist depending on the clinical condition, the different clinical practice patterns among urologists were similar to the randomized selection of patients. TRUS-guided biopsy was performed in group 2 patients even with a negative prebiopsy MRI due to rising PSA or prostatic intraepithelial neoplasia on the previous biopsy. The prebiopsy PSA level and history of a prior negative prostate biopsy were recorded. Prior biopsy history did not affect the selection of patients. Lesion detection via MRI was recorded based on the reports already made in clinical practice by one of seven abdominal radiologists with >5 years of experience in prostate MRI. If the radiologist noted a focal lesion with high or equivocal suspicion in the prostate gland, the patient was classified as having a MRI-visible lesion: focal lesions that radiologists considered to be prostate cancer were defined as lesions with high suspicion and lesions with equivocal suspicion were those with indeterminate findings that could not be discriminated between prostate cancer and benign findings. Focal lesions reported as definitely benign, such as inflammation or benign prostate hyperplasia, were classified as non-MRI-visible lesions. The size and location of focal lesions were described in the MRI reports.

Pathology reports of prostate biopsies were reviewed. The Gleason score of the prostate cancers, the number of positive cores, and the cancer involvement ratio in the cores were recorded. Gleason grade groups that were based on prognosis were recorded as follows: grade group 1 (Gleason score 6), grade group 2 (Gleason score 3 + 4 = 7), grade group 3 (Gleason score 4 + 3 = 7), grade group 4 (Gleason score 8), and grade group 5 (Gleason score 9–10).[8]

MRI protocol

MRI examinations were performed using various MRI machines: 3-T MRI systems (Magnetom Verio, Siemens, Erlangen, Germany and Ingenia, Phillips, Best, The Netherlands) or 1.5-T MRI systems (Magnetom Avanto, Siemens, Erlangen, Germany and Achieva, Phillips, Best, The Netherlands) with a pelvic-phased array coil. An intramuscular injection of 20 mg scopolamine butylbromide (Buscopan; Boehringer Ingelheim, Ingelheim, Germany) was performed to reduce bowel movements for patients without absolute contraindication of the agent. Biparametric MRI was performed as prebiopsy MRI and it consisted of sagittal, coronal, and axial T2-weighted imaging (WI), axial T1WI, and axial diffusion WI. MRI parameters of two MRI scanners are summarized in Table 1.

Table 1
MRI sequences and parameters of the two MRI systems.

	1.5-T MRI		3-T MRI	
	T2WI	DWI	T2WI	DWI
TR (ms)	3,000	2,900	>3,500	>7,000
TE (ms)	103	86	101	85
Thickness (mm)	3	3	3	3
Intersection gap (mm)	0	0	0	0
Matrix size	256×256	100×100	320×320	100×90
FOV (cm)	20×20	20×20	20×20	20×20
NEX	2	8	3	4
b-Factor (s/mm^2)		0, 50, 500, 1000		0, 50, 500, 1000

TR, repetition time; TE, echo time; FOV, field of view; NEX, number of excitations; T2WI, T2-weighted image; DWI, diffusion-weighted image.

Biopsy protocol

TRUS-guided biopsies were performed by two abdominal radiologists with 4 and 14 years of TRUS-guided biopsy experience, respectively. They performed TRUS before biopsy and recorded in the radiological reports whether a focal lesion was visible at TRUS. For patients who have a visible focal lesion on the prebiopsy MRI (group 3), cognitive fusion biopsy was performed and TRUS was used to evaluate lesion visibility. On TRUS, focal lesions in the peripheral zone were defined as well-demarcated hypoechoic lesions with nodular or lenticular shape. Focal lesions in the transition zone were defined as ill-defined, iso-echoic, or subtle hypoechoic lesions without whirling heterogeneous echogenicity. Additional observations to increase the detection of focal lesions included contour-bulging and the presence of vascularity.[9] Diffusely decreased echogenicity at the peripheral zone and well-defined hypoechoic nodular lesions in the transition zone were not classified as focal lesions as they were considered benign. If a focal lesion was detected, the radiologist ensured that the lesion was targeted by at least one biopsy core. In patients with visible lesions at either TRUS or MRI, targeted biopsies were performed for focal lesions, while other areas of the prostate gland were blindly biopsied similar to a 12-core biopsy. Biopsies were performed using the Philips iU22 system (Philips Medical Systems, Bothell, WA, USA) and an 18 G, 20-mm side notch, semi-automatic core biopsy needle (Mission, Bard Biopsy Systems, Tempe, AZ, USA). A targeted biopsy report was immediately created to describe the presence and location of focal lesions and the core number that covered each focal lesion. If there were no detectable lesions in the prostate using both TRUS and MRI, a random systematic 12-core biopsy was performed. All biopsy samples were numbered separately and reviewed by an experienced pathologist. Histopathology results of the TRUS biopsy were considered reference standard in this study. Clinically significant prostate cancer was defined as prostate cancer with a Gleason score $\geq$7.

Statistical analysis

Age and PSA level of three groups were compared by analysis of variance (ANOVA) test. Baseline characteristics and outcomes of the biopsies were compared between patients with TRUS-visible lesions and without TRUS-visible lesions in each group. Patient ages and prebiopsy PSA levels were compared using independent *t*-tests. Cancer detection rates were compared using a chi-square test. The number of positive cores and the cancer involvement ratio in the cores were compared using independent *t*-tests. A binary logistic regression analysis was used to identify the factors significantly associated with detection of clinically significant prostate cancer; multivariate analysis included factors with $p<0.15$ in the univariate analysis. Statistical analyses were performed with SPSS 24.0 (IBM Corporation, Armonk, NY, USA). A p-value <0.05 was considered statistically significant.

Results

There was no significant difference in age and PSA among three groups: mean age of patients in three groups were 68±8.2, 66.4±8.1, and 68±9 ($p=0.284$) and PSA were 31.2±162.2, 8±7.6, and 32.1±174.4 ng/ml, each respectively ($p=0.465$).

In group 1, patients with TRUS-visible lesions were significantly older and had significantly higher PSA levels than patients without TRUS-visible lesions. Within group 3, the number of previous biopsies was significantly smaller in patients with TRUS-visible lesions than patients without TRUS-visible lesions. No patient underwent the previous biopsy within 6 months before MRI. Other factors were not significantly different between the subgroups within each group (Table 2).

Prostate cancer and clinically significant prostate cancer were detected more frequently in patients with TRUS-visible lesions than in patients without TRUS-visible lesions (49.9% versus 22.8%, 39.4% versus 13.1%, $p<0.001$). The detection rates of all prostate cancers and clinically significant prostate cancers were significantly higher in patients with TRUS-visible lesions than others in groups 1 and 3 (Table 3). As the PSA level was significantly different between subgroups within group 1, a further evaluation was conducted. For patients in group 1 with a PSA level <10 ng/ml, detection rates of all prostate cancers and clinically significant prostate cancers were significantly higher in patients with TRUS-visible lesions that those without TRUS-visible lesions (39.4% [106/269] versus 21.5% [40/186] and 26.4% [71/269] versus 10.8% [20/186]; $p<0.001$).

Among the three groups, detection rates of prostate cancer and clinically significant prostate cancer were higher in group 3, followed by group 1, and then group 2: the

Table 2
Patient baseline characteristics.

	No MRI			MRI, no visible lesion			MRI, visible lesion		
	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value
No. of patients	217	405	-	43	34	-	52	271	-
Age (years)	66.4±8.8	68.8±7.8	0.001	65.8±7.2	67.1±9.2	0.489	67.1±9.5	68.1±8.9	0.460
PSA (ng/ml)	7.6±8.4	43.8±199.9	<0.001	8.3±7.4	7.7±7.8	0.691	10±11.8	36.4±190	0.071
No. of previous biopsy	0.1±0.4	0.1±0.3	0.308	0.3±0.5	0.2±0.4	0.315	0.6±0.8	0.3±0.5	0.006

MRI, magnetic resonance imaging; PSA, prostate-specific antigen; TRUS, transrectal ultrasonography.

Table 3
Differences in cancer detection rates according to lesion visibility using transrectal ultrasonography and MRI.

	All cancer			Clinically significant cancer		
	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value
No MRI	54/217 (24.9)	192/405 (47.4)	<0.001	31/217 (14.3)	153/405 (37.8)	<0.001
MRI, no visible lesion	7/43 (16.7)	11/34 (32.4)	0.148	3/43 (7.0)	6/34 (17.6)	0.098
MRI, visible lesion	10/52 (19.2)	151/271 (55.7)	<0.001	7/52 (13.5)	121/271 (44.6)	<0.001

Numbers in parentheses are percentages.
MRI, magnetic resonance imaging; TRUS, transrectal ultrasonography.

prostate cancer detection rate was 49.8%, 39.5%, and 23.4%, respectively ($p<0.001$), and the clinically significant prostate cancer detection rate was 39.6%, 29.6% and 11.7%, respectively ($p<0.001$). The significant differences in cancer detection rates among the three groups were also noted for patients with TRUS-visible lesions ($p=0.012$ for all prostate cancers and $p=0.006$ for clinically significant cancers), but not for patients without TRUS-visible lesions ($p=0.377$ and 0.431; Table 3).

Within group 1, Gleason scores, Gleason grade groups, the number of positive cores, and the cancer involvement ratio in the cores were significantly different according to TRUS visibility (Table 4). In groups 2 and 3, the mean values of biopsy results were greater in patients with TRUS-visible lesions than patients without TRUS-visible lesions, but the difference was not significant.

Age, PSA, MRI visibility, TRUS visibility, and history of prior biopsy were significantly associated with the detection of clinically significant prostate cancer using univariate regression analysis as well as multivariate regression analysis (Table 5). Older age, higher PSA, MRI visibility, TRUS visibility, and no history of a previous prostate biopsy were associated with higher clinically significant cancer detection rates.

Discussion

The present study compared cancer detection rates according to TRUS and MRI visibility. Detection rates of all prostate cancers and clinically significant cancers were significantly higher in patients with visible lesions using TRUS in group 1 (no prebiopsy MRI) and group 3 (MRI-visible lesions). TRUS and MRI visibility were significant factors that were associated with cancer detection at multivariate regression analysis. Therefore, the presence of visible lesions on TRUS and the prebiopsy MRI seemed to be useful for stratifying risk of prostate cancer before pathological evaluation. Thorough TRUS for detecting visible focal lesions is important for biopsy regardless of a prebiopsy MRI.

In the present study, prostate cancer was detected with >20% higher frequency in patients who had TRUS-visible lesions than patients without TRUS-visible lesions. A previous study had shown that TRUS visibility facilitated a precisely targeted biopsy and increased accuracy.[3] This previous study had compared the diagnostic yield of systematic biopsies and targeted biopsies using a MRI–US fusion system for MRI-visible or MRI- and TRUS-visible lesions. In the present study, cognitive fusion biopsy was performed for patients who had a visible lesion on the prebiopsy MRI. Consistent with a previous study, higher cancer detection rates were found for MRI- or TRUS-visible lesions than for lesions not visible. Furthermore, the biopsy results in patients who did not undergo prebiopsy MRI were also evaluated.

Clinically significant cancers were detected most frequently in patients with lesions visible on both MRI and TRUS and least frequently in patients without visible lesions on both examinations. The detection rate of clinically significant cancers in patients who did not have a prebiopsy MRI (group 1) was similar to the patients with MRI-visible lesions (group 3); however, most of the TRUS-visible lesions in patients without MRI-visible lesions (group 2) were not clinically significant cancers. Therefore, MRI and TRUS appeared to play an independent and complementary role in stratifying the risk of prostate cancer. Within group 1, significantly higher PSA levels in patients with TRUS-visible lesions than in patients without TRUS-visible lesions could result in higher detection rates; however, further evaluation of patients with PSA levels <10 ng/ml also showed significantly higher cancer detection rates in patients with TRUS-visible lesions than patients without TRUS-visible lesions.

Table 4
Differences in biopsy results among patients with prostate cancer in each of the three groups.

	No MRI			MRI, no visible lesion			MRI, visible lesion		
	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value	TRUS, no visible lesion	TRUS, visible lesion	*p*-Value
Gleason score	6.7±0.7	7.3 ±0.9	<0.001	6.6±0.8	6.6±0.5	0.934	6.9±0.9	7.2±0.9	0.347
Gleason grade group	1.9±1	2.8±1.3	<0.001	1.3±0.5	1.8±0.9	0.750	2.4±1.3	2.7±1.2	0.444
Number of positive cores (*n*)	3.4±3.3	5.5±3.6	<0.001	1.9±1.1	2.6±3.2	0.543	3.2±3.2	5±3.2	0.083
Cancer involvement ratio in the core (%)	28.2±17.6	44.4±23.5	<0.001	19.6±0.1	30.5±21.8	0.166	32.4±25.6	41.2±20.6	0.201

MRI, magnetic resonance imaging; TRUS, transrectal ultrasonography.

Table 5
Univariate and multivariate analyses on factors associated with detection of clinically significant prostate cancer.

	Univariate analysis (95% CI)			Multivariate analysis		
	Odds ratio	95% CI	*p*-Value	Odds ratio	95% CI	*p*-Value
Age	1.060	1.042–1.078	<0.001	1.053	1.034–1.073	<0.001
PSA	1.035	1.023–1.047	<0.001	1.026	1.015–1.037	<0.001
Prebiopsy MRI (+)	1.240	0.948–1.623	0.117	0.492	0.233–1.040	0.063
MRI-visible lesion (+)	1.751	1.303–2.272	<0.001	3.351	1.553–7.232	0.002
TRUS-visible lesion (+)	4.304	2.999–6.177	<0.001	2.985	2.034–4.382	<0.001
History of prior biopsy (-)	2.118	1.371–3.273	0.001	2.351	1.462–3.781	<0.001

CI, confidence interval; PSA, prostate specific antigen; MRI, magnetic resonance imaging; TRUS, transrectal ultrasound.

These results indicate that TRUS was also useful to elevate the cancer detection rate even in patients without prebiopsy MRI. Although the cancer detection rate was higher in patients with TRUS-visible lesions than in those without TRUS-visible lesions, clinically significant cancers were detected in only 38% and 45% TRUS-visible lesions of groups 1 and 3, respectively. As focal lesions with high or equivocal suspicion were considered visible lesions and were not further stratified, it was possible that visible lesions included a large number of non-cancerous lesions.

The higher Gleason scores, greater numbers of positive cores, and the higher cancer involvement ratio in the cores of patients with TRUS-visible lesions in group 1 demonstrated the importance of TRUS itself for TRUS-guided biopsy. Although there was no significant difference in biopsy results between patients with or without TRUS-visible lesions in group 3, similar trends were noted. A previous study also had shown that higher Gleason scores and longer cancer lengths were observed in cores from TRUS-visible lesions in MRI–US fusion biopsies.[3] Another study had shown that TRUS-visible lesions had more aggressive characteristics than TRUS-invisible lesions.[4] In the past, cancer detection rates in biopsies of focal lesions detected by TRUS have been reported as approximately 21–25%.[6,7] Although a study had demonstrated that TRUS could stratify prostate cancer risk using a detailed classification of focal lesions, there is a general call to disregard TRUS results[9]; however, from the results it is evident that TRUS can help improve biopsy results in patients with and without a prebiopsy MRI.

From the multivariate regression analysis, MRI- and TRUS visibility were independently associated with the detection of clinically significant prostate cancer. The importance of a prebiopsy MRI for detecting clinically significant cancer has been reported.[1,10,11] Many studies on prostate MRI have consistently shown that low-grade cancers could not be detected via MRI.[12–15] The present study also showed that the cancer detection rate was higher in group 3 than in groups 1 or 2. As more aggressive tumours are more likely seen with MRI, lesion visibility could be a factor that predicts the presence of clinically significant cancer; however, whether or not prebiopsy MRI was performed was not significantly associated with biopsy results in this study. At Seoul St Mary's Hospital, patients whose prebiopsy MRI was negative rarely underwent TRUS-guided biopsy, and only patients with very high PSA levels or increasing PSA levels underwent TRUS-guided biopsy despite negative MRI results. A large proportion of patients who had negative MRI results were not included in this study, and the impact of performing a prebiopsy MRI on cancer detection could not be evaluated. For the same reason, the number of patients without MRI-visible lesions was very small in this study, and TRUS visibility was not significantly associated with biopsy results in group 2.

Multivariate regression analysis showed that age and PSA levels were positively correlated with the presence of clinically significant prostate cancer. The association of older age and higher PSA levels with higher incidences of prostate cancer is well known.[16–19] In this study, a history of no previous biopsies was also an independent factor related to positive cancer detection rates. Previous studies have shown lower cancer detection rates in previously biopsied men than in biopsy naive men.[18,20] A previously negative biopsy result means that the prostate gland had been examined but no cancer was detected, so the risk may be lower in patients with previously negative biopsy results than in biopsy-naive patients, even with similar PSA levels.

Generally, expert genitourinary radiologists perform retrospective image reviews in studies that investigate the correlation of imaging findings and patient's outcome or pathological results; however, the present study evaluated the real impact of lesion visibility using TRUS and MRI in daily practice. Therefore, retrospective image analysis was not performed and the Prostate Imaging Reporting and Data System could not be applied. The MRI reports in this study were made by abdominal radiologists on faculty. TRUS visibility was also based on reports made immediately after TRUS-guided biopsy. Since images were stored by radiologists who performed TRUS, there is no guarantee that the images of the entire prostate gland were stored. Therefore, retrospective analysis of TRUS images may not reflect actual results. Furthermore, by evaluating all patients who underwent TRUS-guided biopsies, selection bias resulting from the selection of patients who underwent radical prostatectomy could be avoided.

There are several limitations to this study. First, the reference standard of this study was TRUS-guided biopsy. Therefore, better biopsy results for TRUS-visible lesions could be due to better targeting. The presence of invisible, but more aggressive, cancer could not be confirmed. So, systematic biopsies were also performed with targeted biopsies to reduce the possibility of missing prostate cancer;

however, a considerable number of clinically significant cancers were missed at TRUS-guided biopsy in a previous study with approximately 60% sensitivity.[1] Although TRUS-guided systematic biopsy is the most commonly used conventional examination of the prostate gland, random systematic TRUS-guided biopsy may underestimate the cancer burden and miss significant cancers. Second, the biopsy results were not compared between systematic and targeted biopsy cores. More aggressive prostate cancers could be detected in the systematic biopsy cores than in the targeted biopsy cores; however, the aim of the present study was to investigate the role of TRUS and MRI in real clinical practice and individual patient analysis better reflected the actual clinical setting.

In conclusion, TRUS and MRI visibility of focal lesions in the prostate was significantly associated with the detection of clinically significant cancer.

Conflict of interest

The authors declare no conflict of interest.

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