The Efficacy of Target Biopsy of Suspected Cancer Lesions Detected by Magnetic Resonance Imaging and/or Transrectal Ultrasonography during Initial Prostate Biopsies: Comparison of Outcomes between Two Physicians

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ABSTRACT

Background The efficacy of adding target prostate biopsy (PBx) of suspected cancer lesions identified on magnetic resonance imaging (MRI) and/or transrectal ultrasonography (TRUS) to initial systematic PBx was evaluated. Moreover, the outcomes were compared between 2 physicians.

Methods We retrospectively investigated 238 patients who underwent first-time PBx in our hospital. All patients were examined with prostate MRI before PBx. Fourteen systematic biopsies were obtained in all patients. When a suspected lesion was present on MRI and/or TRUS, the lesion was the target of target PBx.

Results The overall detection rate of prostate cancer (PCa) was 45% (106/238). With target PBx, the PCa detection rate was 32% overall, while that of suspected lesions seen only on MRI was 32%, that of suspected lesions seen only on TRUS was 8% and that of suspected lesions seen on both MRI and TRUS was 52%. The same tendency was shown for each physician. Comparing systematic PBx and target PBx, the overall rate of Gleason score (GS) upgrading with target PBx was 13%. The rate of PCa detected only by systematic PBx was 95%. There was no significant difference between the 2 physicians.

Conclusion In initial PBx, the addition of target PBx of suspected cancer lesions detected by MRI and/or TRUS to systematic PBx might not be useful to improve the cancer detection rate. However, it may enable more accurate risk classification and detection of minute cancers with a high GS.

Key words magnetic resonance image; prostate cancer; target prostate biopsy; transrectal ultrasonography

The pathological diagnosis of prostate cancer (PCa) is based on the use of ultrasonography-guided prostate biopsy (PBx). Based on recent systematic reviews, 10 to 12 cores are generally taken because they show better efficacy for cancer detection than 6 cores.[1] However, the cancer detection rate of PBx has traditionally been fraught with poor sensitivity, around 50%.[2] Many methodologies, techniques and approaches are used to improve this situation. However, no dramatic improvement of the cancer detection rate has been achieved. Accordingly, the best methodology for PBx remains controversial.

On the other hand, progress in imaging modalities, for example magnetic resonance imaging (MRI) and transrectal ultrasonography (TRUS), has been remarkable in recent years. MRI has developed particularly rapidly in the past 20 years, along with the management of localized PCa. A high diagnostic accuracy has been reported using various groups of patients and protocols. Many reports have suggested that the rate of PCa detection was improved by combining MRI findings with a PBx.[3–6] However, there are also reports that deny the usefulness of MRI in PBx.[7, 8] Currently, as the methodology of PBx has progressed, the detection rate of the MRI/US fusion biopsy system has been reported.[9, 10] However, since such systems are very expensive, at the moment, use of this approach has not become widespread.

Although past studies have focused on methodologies of PBx, to the best of our knowledge, no papers have examined the difference in outcomes with different operators who performed the PBx using the same methodology and instrument. Therefore, the aim was to evaluate the efficacy of the addition of target PBx of suspected cancer lesions detected by MRI and/or TRUS to a systematic, 14-core, transrectal ultrasound-guided PBx. Moreover, the outcomes of the PBx performed by 2 physicians who used the same methodology and instruments were compared.

MATERIALS AND METHODS

Patients

This study was approved by the Ethics Committee of Tottori University, Japan, and all patients provided their

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Abbreviations: ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; GS, Gleason score; MRI, magnetic resonance imaging; PBx, prostate biopsy; PCa, prostate cancer; PSA, prostate-specific antigen; PSAD, PSA density; TRUS, transrectal ultrasound

written, informed consent. A total of 333 patients with elevated prostate-specific antigen (PSA) who underwent first-time PBx at the Department of Urology, Tottori University Hospital, between November 2010 and February 2013, were retrospectively investigated. Patients whose PSA level was less than 4 ng/mL or more than 30 ng/mL and who underwent 1 or more previous PBx procedures were excluded. Thus, 238 patients were included in the final analysis. All patients were examined with prostate MRI before undergoing PBx. All PBx procedures were performed within 4 weeks after MRI.

MRI protocol

In our hospital, we used a 1.5-T (Achieva, Philips Healthcare, Best, Netherlands) or a 3.0-T (MAGNETOM skyra, Siemens, Munich, Germany) magnetic resonance imaging (MRI) system. All patients underwent diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) mapping and dynamic imaging, in addition to the imaging sequences as part of a routine prostate MRI protocol. T2-weighted images (T2WI) were acquired in 3 orthogonal planes (axial, sagittal and coronal). All images were reviewed by radiologists blind to the PSA data. Lesions were defined as suspected cancer lesions on MRI if 2 or more of the following 4 findings were present: i) low-intensity on T2WI; ii) high-intensity on DWI; iii) low-intensity on the ADC map and iv) enhancement in the early phase but washed out on dynamic imaging.

Transrectal PBx protocol

All biopsies were obtained under TRUS guidance using a medical ultrasonography scanner (Nemio XG, Toshiba, Tokyo, Japan). PBx was performed by 2 physicians, Physician X, a urologist in his 6th year, and Physician Y, a urologist in his 5th year, using the same methodology and instruments, under caudal anesthesia with an 18-G biopsy needle (BARD Max-Core Disposable Core Biopsy Instrument, Tempe, AZ). Lesions were defined as suspected cancer lesions on TRUS if low-echoic lesions were identified by the operators. The judgment of a suspected cancer lesion on TRUS was left to each operator's discretion. Fourteen systematic biopsies (8, peripheral zone; 4, transitional zone; 2, apex) were obtained in all patients. The systematic biopsy was performed independently of the location of the suspected lesion on MRI and/or TRUS. When a suspected lesion was present on MRI and/or TRUS, that lesion was made a target PBx in addition to the systematic biopsy. If the suspected lesion on MRI could not be identified on TRUS, the target PBx was performed using only anatomical landmarks (shape of the prostate, position of the verumontanum, distance from the apex or the prostate base, presence of a benign cyst or calcification nearby, etc.). In target PBx, on principle, 1 core was taken from 1 suspected lesion (Fig. 1).

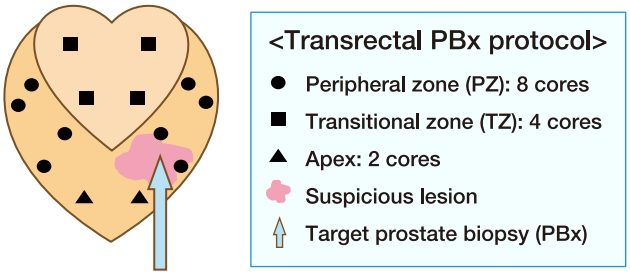

Fig. 1. Transrectal prostate biopsy was performed as follows. Fourteen systematic biopsies (8, peripheral zone; 4, transitional zone; 2, apex) were obtained in all patients. When a suspected lesion was present on MRI and/or TRUS, it was targeted for biopsy, in addition to the systematic biopsy. MRI, magnetic resonance image; TRUS, transrectal ultrasound.

Statistical analyses

All statistical analyses were performed using PASW statistics 18 (SPSS, Chicago, IL). Statistical analysis was performed with the chi-square test for continuous variables. Fisher's exact test was used to compare categorical variables. P-values of less than 0.05 were considered significant.

RESULTS

Patients' characteristics

The characteristics of the patients in each physician's

Table 1. Patients' characteristics

Patients characteristics	Overall	Comparison between 2 physicians		
		Physician X	Physician Y	*P* value
Number of patients	238	137	101	
Age, mean [range], year	69.2 [39–93]	69.6 [42–86]	68.5 [39–93]	0.40
PSA, mean [range], ng/mL	9.60 [3.27–29.63]	9.03 [3.27–24.63]	10.57 [3.48–29.63]	0.12
Prostate volume, mean [range], mL	45.8 [14–231]	45.6 [14–231]	46.3 [14–158]	0.84
PSAD, mean [range], ng/mL/mL	0.25 [0.04–1.34]	0.23 [0.04–0.83]	0.28 [0.07–1.34]	0.26
Number of patients with target PBx (%)	188 (79%)	104 (76%)	84 (83%)	0.29

PBx, prostate biopsy; PSA, prostate-specific antigen; PSAD, PSA density.

Table 2. The overall PBx outcome including both patients with and without target PBx

PCa detection ratio	Overall	Comparison between 2 physicians		
		Physician X	Physician Y	*P* value
Number of patients	238	137	101	–
PCa (%)	106/ 238 (45%)	55/137 (40%)	51/101 (50%)	0.11
Low GS (%)	21/106 (20%)	10/ 55 (19%)	11/ 51 (22%)	0.62
Moderate GS (%)	36/ 106 (37%)	21/ 55 (38%)	17/ 51 (34%)	0.65
High GS (%)	47/ 106 (43%)	24/ 55 (43%)	23/ 51 (44%)	0.88
PCa with MRI suspicion (%)	89/ 155 (58%)	43/ 76 (57%)	46/ 79 (58%)	0.91
PCa with TRUS suspicion (%)	66/ 138 (48%)	39/ 95 (41%)	27/ 43 (62%)	0.02*

GS, Gleason score; MRI, magnetic resonance imaging; PBx, prostate biopsy; PCa, prostate cancer; TRUS, transrectal ultrasonography.

Table 3. The cancer detection rate of target PBx by imaging modality

Image modality in target PBx	Overall	Comparison between 2 physicians		
		Physician X	Physician Y	*P* value
Number of patients (%)	188/238 (79%)	104/137 (76%)	84/101 (83%)	–
Total (%)	61/188 (32%)	27/104 (26%)	34/ 84 (40%)	0.04*
Only on MRI (%)	23/ 73 (32%)	4/ 17 (24%)	19/ 56 (34%)	0.42
Only on TRUS (%)	6/ 76 (8%)	3/ 50 (6%)	3/ 26 (11%)	0.39
On both MRI and TRUS (%)	38/ 73 (52%)	22/ 51 (43%)	16/ 22 (73%)	0.001**

MRI, magnetic resonance imaging; PBx, prostate biopsy; TRUS, transrectal ultrasonography.

group are summarized in Table 1. Physician X's group had 137 patients, and Physician Y's group had 101 patients. The baseline characteristics of the patients in each group showed no significant differences in age, PSA levels, prostate volume, PSA density (PSAD) and the rate of patients with target PBx.

The overall PBx outcome

The overall outcomes of PBx are presented in Table 2. The overall detection rate of PCa including both patients with and without target PBx was 45% (106/238), and 43% (47/106) of PCa patients was diagnosed as having a high Gleason score (GS) (4 + 4 = 8 or more). There were no significant differences between the 2 physician groups. The overall detection rate in patients with suspected lesions on MRI was 58% (89/155), while that on TRUS was 48% (66/138). (This was not related to whether PCa was identified with the target PBx.) In all groups, the cancer detection rate was higher in patients with suspected lesions on imaging modalities. Especially in patients with suspected lesions on MRI, the increase in the cancer detection rate was the highest in all groups, approximately 60%. However, the cancer detection rate of patients with a suspected lesion on TRUS was lower and showed a significant difference between the 2 physician groups ($P = 0.02$).

Target PBx outcome

The outcomes of target PBx are presented in Table 3. Of a total of 238 patients, 188 (79%) underwent target PBx. The overall detection rate of PCa with target PBx was 32% (61/188). If the overall detection rate for each imaging modalities was compared, that of patients with a suspected lesion only on MRI was 32% (23/73), that of patients with a suspected lesion only on TRUS was 8% (6/76) and that of patients with a suspected lesion seen on both MRI and TRUS was 52% (38/73). However, if more than 1 suspected lesion were found in a prostate, they were counted respectively. The detection rate was highest if the suspected lesion appeared on both MRI and TRUS, while that of a lesion seen only on TRUS was the lowest. As for the outcome in each physician's group, the same overall tendency was seen. However, the total detection rate of target PBx ($P = 0.04$) and the detection rate with a suspected lesion seen on both MRI and TRUS ($P = 0.001$) were significantly different between the physician groups.

Table 4. The rate of GS upgrading by the addition of target PBx to systematic PBx

	Overall	Comparison between 2 physicians		
		Physician X	Physician Y	*P* value
GS upgraded in target PBx (%)	8 / 61 (13%)	2 / 27 (7%)	6 / 34 (17%)	0.22
Low → Moderate GS	3	1	2	–
Moderate → High GS	0	0	0	–
0 → Moderate GS	2	1	1	–
0 → High GS	3	0	3	–

GS, Gleason score; PBx, prostate biopsy.

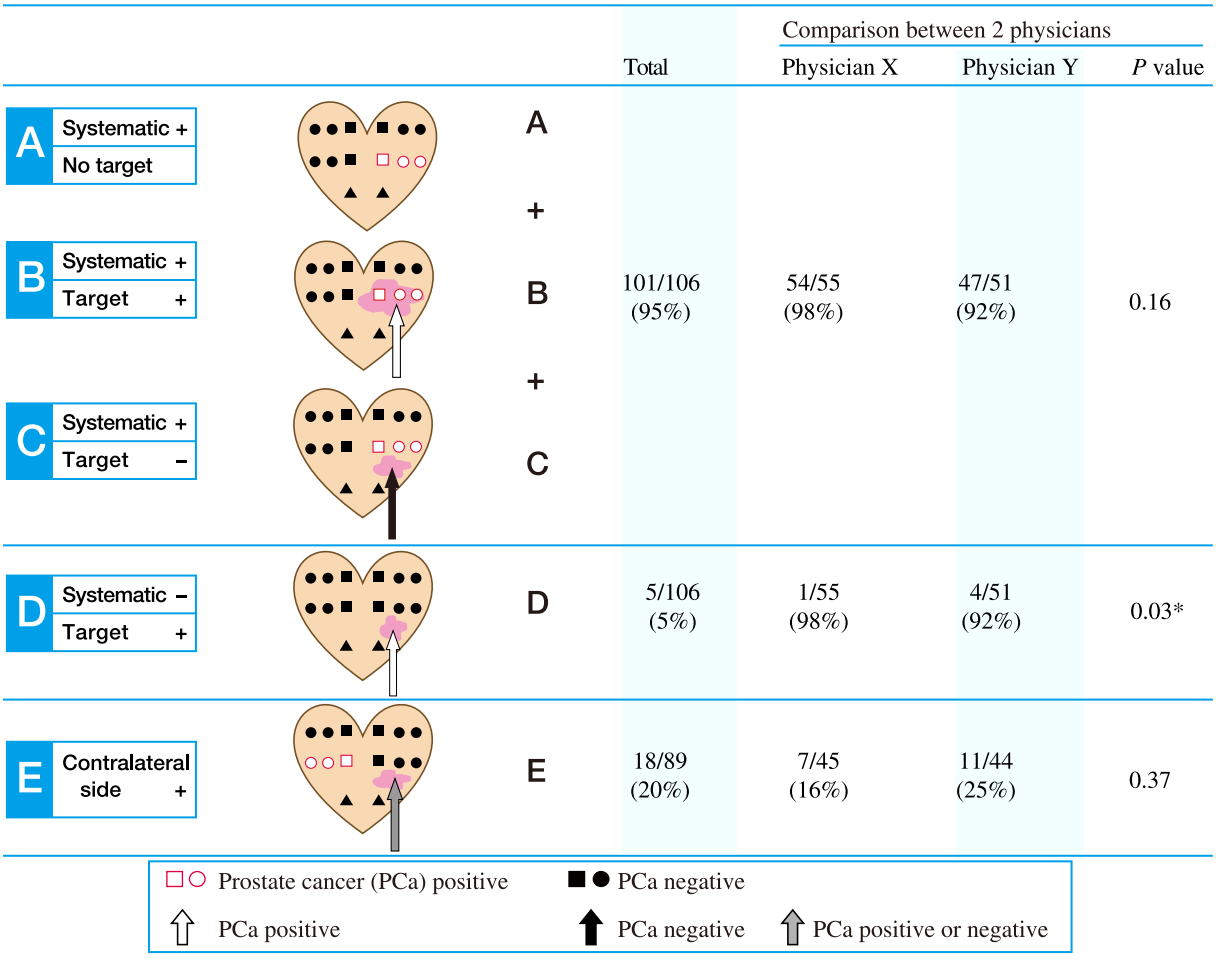

Fig. 2. The detection rate was investigated according to the site from which PCa was detected. The overall rate of PCa detected only by systematic PBx, which therefore did not need target PBx, was 95%. Furthermore, PCa was also detected from one lobe contralateral to the other with a suspected cancer lesion on MRI or TRUS in approximately 20% of patients (18/89). PBx, prostate biopsy; PCa, prostate cancer; MRI, magnetic resonance imaging; TRUS, transrectal ultrasonography.

Comparison of systematic PBx and target PBx

In the cases in which PCa was detected by both systematic PBx and target PBx, the overall rate of GS upgrading with target PBx as compared with systematic PBx was 13%. There was no significant difference between the 2 physicians' groups. Interestingly, in some cases PCa was detected only by target PBx but not by systematic PBx, including PCa with a high GS (4 + 4 = 8 or more) (Table 4).

Furthermore, the detection rate was investigated according to the site at which PCa was detected (Fig. 2). The rate of PCa detection with only systematic PBx, which did not need target PBx to detect PCa, was 95% on the whole, 98% in physician X's group and 92% in physician Y's group (Fig. 2; A + B + C). There was no significant difference between the 2 physicians' groups. However, the detection rate of PCa which was detectable only by a target PBx was significantly different between the physicians' groups.

Interestingly enough, in the 89 PCa patients with target PBx (Fig. 2; B + C + D), PCa was detected also in one lobe contralateral to the other lobe that had a suspected cancer lesion on MRI or TRUS in approximately 20% (18/89). Of the 18 patients, 5 (28%) were diagnosed with high GS (4 + 4 = 8 or more), and in 3 of the 5 patients, target PBx did not detect PCa.

DISCUSSION

Urologists have been continuing to explore the optimal methodologies to improve the detection rate of PCa with PBx. The addition of anterior directed biopsy cores,[11] saturation biopsy templates[12, 13] and transperineal template-guided biopsy[14] has been attempted. Although all of these methodologies added some diagnostic usefulness, some reports denied the usefulness of these methodologies. The reason the PCa detection rate does not

improve dramatically is probably related to the fact that these methodologies ultimately remain dependent on random sampling.

On the other hand, the MRI/US fusion PBx system has appeared as a more advanced method of PBx. Pint et al. reported that PCa was detected in 12 of 43 (27.9%), 26 of 39 (66.7%) and 17 of 19 (89.5%) patients with low, moderate and high suspicion on MRI, respectively. They suggested that their methodology might be useful in focal therapy for PCa.[9] Moreover, they reported in their current study that the diagnostic yield of MRI/US fusion PBx was not affected by the increased number of prior negative PBx procedures, especially for the detection of high-grade PCa.[10] Certainly, their outcome of fusion PBx exceeded that of the past methodology. However, this system is not likely to immediately spread worldwide because the system is very expensive, and focal therapy is not standard therapy worldwide. Therefore, the methodology adopted in the present study was the most common and economical, since it uses the most widely available imaging modalities, TRUS and MRI.

In the present study, the overall detection rate of PCa, including both patients with and without target PBx, was almost equivalent to past studies. In patients with a suspected lesion on the imaging modalities, especially MRI, there was a tendency for the rate of cancer detection to be higher. However, the detection rate of patients with a suspected lesion on TRUS was significantly different between the 2 physician groups. This was thought to be due to variation in judging the imaging findings on TRUS between the 2 physicians. Evaluated exclusively on the outcome of target PBx, the overall rate of cancer detection (32%) was not as high as we had expected; the cancer detection rate of target PBx of a suspected lesion seen only on TRUS was very low (8%). This suggests that the evaluation of imaging findings on TRUS was poorly reproducible. Interestingly, the cancer detection rate of target PBx of a suspected lesion on both MRI and TRUS was increased in all groups, and that of Physician Y's group was higher (73%). However, there was a significant difference between the 2 physician groups, likely due to the difference in the hit probability to the suspected lesion in target PBx between the 2 physicians and the small number of patients in this study. Comparing the outcomes of systematic PBx and target PBx, the GS was upgraded in 13% of cancer patients; thus, more accurate risk classification was obtained in approximately 1 in 10 patients by performing a target PBx. It was found that minute cancer with a high GS, which was detectable only by a target PBx, was not uncommon. Furthermore, in the evaluation according to the site from which PCa was detected, since 95% of the overall patients in whom PCa was detected did not need target PBx, it must be said that target PBx was not useful in terms of improvement of cancer detection. Shigemura et al.[7] reported that, by using the PBx methodology as in the present study, only 1 of the 96 patients (1.04%) with additional cores based on MRI findings had a cancer-positive core that would have been missed by the standard 12-core PBx, suggesting that additional PBx could be omitted. Singh et al.[8] also stated that 3-T MRI-targeted PBx showed similar PCa detection compared to systematic PBx. The present outcome supports these conclusions. Moreover, it was also confirmed that the overall cancer detection rate was not affected by the difference in physicians. However, the hit probability of target PBx was significantly different between the two physicians, although the cancer detection rate of target PBx was not so high as to suggest the usefulness of target PBx. PCa was also detected in approximately 20% from one lobe without a suspected cancer lesion contralateral to the other lobe with a suspected cancer lesion on MRI or TRUS; although the probability was low, patients with a high GS PCa were included. Summarizing the above data, although the probability of PCa in a suspected lesion identified on imaging, especially MRI, is high, owing to the lack of reproducibility and the difference in hit probability of the suspected lesion between physicians in target PBx without using an MRI/US fusion system, there is a limit to the improvement of the cancer detection rate.

Then the question becomes, "Is the target PBx without using MRI/US fusion system completely meaningless?" as Shigemura said.[7] Certainly, target PBx without using an MRI/US fusion system might not be useful from the perspective of improving the cancer detection rate. However, it can be immediately implemented in many institutions and may facilitate more accurate staging with detection of minute cancer with a high GS. Therefore, target PBx of a suspected cancer lesion seen on both MRI and TRUS should be carried out, since the probability of the existence of cancer is expected to be high.

Furthermore, an ink mark was placed on the rectal, prostatic fascia side of the biopsy cores to estimate the distance of the cancer lesion from the prostatic fascia. This information was used to determine the nerve-sparing policy more oncologically in robotic-assisted laparoscopic radical prostatectomy, sparing as much nerve as possible while maintaining the radical cure of the cancer. Such small efforts do not improve the cancer detection rate, but may improve treatment outcomes.

This study has several limitations. Without the evaluation of whole mount prostatectomy specimens, the

difference in accuracy between target PBx and systematic PBx cannot be determined. The MRI system, 1.5-T or 3.0-T, was not unified because some of the patients who visited our hospital from distant places underwent MRI at another hospital. The cancer detection rate of target PBx might be better if more cores were obtained from the suspected lesion. However, because the complication rate may increase with the core number, the principle of taking only one core from a suspected lesion was adopted. There were no serious complications that resulted in the need to extend the duration of scheduled hospitalization (data not shown).

In conclusion, the addition of target PBx of suspected cancer lesions detected by MRI and/or TRUS to a systematic 14-core initial PBx might not be useful from the perspective of improving the cancer detection rate regardless of operator differences. However, it can be immediately implemented in many institutions and may make it possible to achieve more accurate risk classification with detection of minute cancer with a high GS. Moreover, by adding a little ingenuity as ink application, it may be useful for determination of treatment policy.

The authors declare no conflict of interest.

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