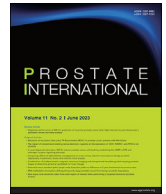




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Research Article

Combination of multiparametric magnetic resonance imaging and transperineal template-guided mapping prostate biopsy to determine potential candidates for focal therapy

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ABSTRACT

Background: We assessed the ability of the combination of multiparametric magnetic resonance imaging (mpMRI) and transperineal template-guided mapping biopsy (TTMB) to determine the eligibility for focal therapy (FT) (hemiablation) in men and compared it with that of histology from radical prostatectomy (RP) specimens.

Materials and methods: In this study, 120 men who underwent mpMRI, TTMB, and RP in a single tertiary center from May 2017 to June 2021 were analyzed. The criteria of hemiablation eligibility were unilateral low-to intermediate-risk prostate cancer (limited to a maximum of International Society of Urological Pathology (ISUP) grade group 3 and prostate-specific antigen (PSA) <20 ng/mL) and clinical stage $\leq$ T2. Evidence of non-organ-confined disease or contralateral Prostate Imaging Reporting and Data System (PI-RADS) v2 score $\geq$ 4 on mpMRI was classified as ineligible for hemiablation. Clinically significant cancer at RP was defined as any of the following: (1) ISUP grade group 1 with tumor volume $\geq$ 1.3 mL; (2) ISUP grade group $\geq$ 2; or (3) the presence of advanced stage ($\geq$ pT3).

Results: Of the 120 men, data of 52 men who met the selection criteria for hemiablation were compared with final RP findings. Of these 52 men, 42 (80.7%) could be considered suitable for hemiablation on RP. The sensitivity, specificity, and accuracy of mpMRI and TTMB in predicting FT eligibility were 80.7%, 85.1%, and 82.5%, respectively. The rate of undetected contralateral significant cancer was 10 (19.2%) on mpMRI and TTMB. Six had bilateral significant cancer and four had small volumes of ISUP grade group $\geq$ 2.

Conclusions: The combination of mpMRI and TTMB substantially improves the prediction of potential candidates for hemiablation based on consensus recommendations. Improved selection criteria and further investigative tools are required to improve patient selection for hemiablation.

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1. Introduction

Active surveillance (AS) or whole-gland treatment (i.e., radical prostatectomy (RP) and radiotherapy) are considered the standard treatment options for localized prostate cancer.^{1,2} While both treatments are effective, AS is associated with higher disease progression, and radical treatments can be associated with a deterioration in urinary, sexual, and bowel function, decreasing the quality of life.^{3–5} To reduce adverse effects and maintain beneficial oncologic outcomes, alternative treatments have been developed as an intermediate option between AS and whole-gland

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treatments; focal therapy (FT) seems to be such a promising alternative in highly selected patients.

One key challenge is to accurately identify the population of men who are potentially suitable for FT. According to several consensus recommendations, FT should be sought in patients with a D'Amico low-to intermediate-risk prostate cancer, including International Society of Urological Pathology (ISUP) grade group 3, and those with life expectancies of at least 10 years.^{6–9} Additionally, for the success of FT, physicians must accurately identify and localize the index and clinically significant satellite tumors within the prostate to ensure an appropriate treatment region and patient selection.

Multiparametric magnetic resonance imaging (mpMRI) is a useful tool to detect clinically significant cancer and to distinguish which areas of the prostate do not require ablation.^{10,11} However, the combination of mpMRI and transrectal ultrasound (TRUS)-guided prostate biopsy cannot determine the exact tumor location and help select suitable patients for FT.¹² Regardless of the biopsy modality, mpMRI-targeted biopsy based on Prostate Imaging Reporting and Data System (PI-RADS) v2 should be performed in addition to systematic biopsy.^{8,9,13} Systematic biopsy remains necessary to assess mpMRI-negative areas.

A retrospective study reported that MRI/ultrasound fusion biopsy has 75% accuracy to determine eligibility for FT compared to the whole-mount histology.¹⁴ However, detailed information based on the combination of mpMRI and transperineal template-guided mapping biopsy (TTMB) for determining FT eligibility is missing. Therefore, this study was designed to evaluate the ability of the combination of mpMRI and TTMB to determine the eligibility for FT in men and compared it with that of whole-mount histology after RP, according to the consensus criteria for FT.

2. Materials and methods

2.1. Study population

The Institutional Review Board (IRB) of Samsung Medical Center approved this retrospective study and waived the requirement for informed consent (IRB no. 2022-08-100-001). From May 2017 to June 2021, 692 patients underwent the combination of mpMRI and TTMB at a single tertiary center. Of the 348 patients with confirmed prostate cancer, 120 men who subsequently underwent robot-assisted laparoscopic RP were retrospectively included in this study. Patients who received hormone therapy before surgery or had missing data from biopsy or mpMRI were excluded from this study.

2.2. Data collection

The clinical, laboratory, and pathological data of the patients, including age, prostate-specific antigen (PSA) level, the number of biopsies and positive cores, ISUP grade group on biopsies, PI-RADS scores on mpMRI, and clinical tumor stage, were reviewed from the electronic medical records.

Histopathologic biopsy and RP specimen analyses were examined by one dedicated uropathologist with over 15 years of experience. We recorded the ISUP grade group, location, and volume of each tumor focus and the pathological stage. Tumor laterality was referenced on the urethra as the midline in the sagittal plane. Bilateral unifocal means the presence of a single tumor crossing the midline, and bilateral multifocal means the presence of at least one tumor in each bilateral lobe. Based on the RP specimen analyses, the lobes were stratified into lobes with insignificant cancer, significant cancer, and those without cancer. Moreover, we compared these data with the results of the combination mpMRI and TTMB.

Clinically significant cancer at RP was defined as any of the following: (1) ISUP grade group 1 with tumor volume ≥ 1.3 mL; (2) ISUP grade group ≥ 2 ; or (3) presence of extracapsular extension (ECE) or seminal vesicle invasion (SVI). If index tumors extended into the contralateral lobe, both lobes were defined as lobes with significant cancer.¹⁵

2.3. Imaging and biopsy protocol

All mpMRI procedures were performed using a 3 Tesla system (Intera Achieva TX; Philips Healthcare, Best, The Netherlands) with a six-channel, phase-array body coil. The parameters of mpMRI sequences included T1-weighted, T2-weighted, and diffusion-weighted imaging with b values of 0, 100, and 1,000 s/mm², and dynamic contrast-enhanced imaging after intravenous injection of gadolinium diethylenetriamine pentaacetic acid (Gadovist; Schering, Berlin, Germany). Two expert urologists with >10 years of experience, who were blinded to the clinical and pathologic information of the patients, independently reviewed the different MR images. Suspicious lesions were assessed using the validated PI-RADS v2. PI-RADS v2 assessment categories were scored from 1 (low) to score 5 (high) according to the likelihood of significant prostate cancer being present.¹⁶

All TTMB procedures performed on the inpatients under general anesthesia are a standard technique at our center. Systematic biopsies were performed through the perineum by urologists using a biplanar TRUS 8848 brachytherapy probe (BK Medical, Herlev, Denmark) covered with a water-filled brachytherapy balloon, Classic STEPPER™ device (CIVCP, Kalona, IA, USA), 18G 20 cm long biopsy needle (ACECUT; TSK Laboratory, Tochigi, Japan), and standard brachytherapy grid with 5 mm interval. Then, 24 cores were obtained from each patient depending on the size of the prostate.¹⁷ The patients underwent transperineal cognitive-targeted biopsy of mpMRI-suspicious lesions (2–4 cores per lesion depending on lesion size), followed by conducted systematic biopsy.

2.4. Eligibility criteria for FT (hemiblention)

We applied FT eligibility criteria based on published consensus recommendations⁹ and a prospective multicenter trial on FT.¹⁸ Patients considered suitable for hemiblention FT were retrospectively selected based on the following criteria:

1. Localized prostate cancer with ISUP grade group ≤ 2 (including up to 3)
2. PSA < 15 ng/mL (including up to 20)
3. Biopsy-proven unilateral cancer (ISUP grade group 1 at one core is acceptable in the considered untreated area)

The study exclusion criteria were as follows: evidence of clinical stage $\geq T3a$ and/or potentially significant cancer on the contralateral lobe as defined by PI-RADS score ≥ 4 . Fifty-two patients were available for analysis.

2.5. Statistical analysis

Multivariate logic regression analyses were used to evaluate the association between eight predictor variables and the FT ineligibility. All tests were two-sided and performed within SPSS statistical software v.17.0 (2010; IBM Corp., Armonk, NY, USA), and statistical significance was considered as P value < 0.05.

3. Results

In our cohort, 120 consecutive men underwent mpMRI, TTMB, and RP. Fig. 1 shows the filter steps and excluded patients. Of these patients, 16 were excluded because they had ISUP grade group ≥ 3 or PSA >20 ng/mL. In the second step, 52 were excluded because they had bilateral prostate cancer or evidence of PI-RADS ≥ 3 on the contralateral lobe of the index tumor on mpMRI. As a result, 34.2% ($n = 41$) were considered potential candidates for hemiablation according to the criteria of ISUP grade group ≤ 2 and PSA <15 ng/mL. Additionally, 43.3% ($n = 52$) met the screening criteria according to extended criteria of ISUP grade group 3 or PSA 15–20 ng/mL.

Table 1 shows the baseline characteristics of the 52 FT-eligible patients. In the positive biopsy lobe for consideration of treatment, 32 (61.5%) regions of interest had PI-RADS score of 3–5 and 23 (41.8%) had ISUP grade group ≥ 2 . The median time from biopsy to surgery was 79.50 days (range, 42–179 days).

The descriptive findings of whole-mount histology of RP specimens are shown in Table 2. The laterality was bilateral multifocal in 40.4% of the tumors and unilateral unifocal in 38.5% of the tumors. No man had non-organ-confined disease in this study. The mean overall tumor volume was 1.10 mL (median, 0.57 mL).

Of the 120 patients who underwent mpMRI, prostate biopsy, and RP, 52 would have qualified for FT (hemiblation) based on biopsy and MRI findings (Table 3). Of the 10 patients who were classified as eligible for hemiblation based on MRI and biopsy findings but did not qualify for hemiblation based on RP specimen findings, seven patients were discordant due to a lesion crossing the midline, three were discordant due to a higher ISUP grade group but with a tumor volume <0.5 mL on whole-mount histological findings. This is because anterior or transition zone prostate tumors on mpMRI and TTMB actually crossed the midline on RP. The combination of mpMRI and TTMB had 80.7% sensitivity (42 of

Table 1

Baseline characteristics.

Characteristic	Value
Number of patients	52
Age, years, mean (median)	64.28 (64.00)
PSA, ng/mL, mean (median)	6.58 (5.44)
Prostate volume, mL, mean (median)	36.40 (30.05)
mpMRI findings of the negative biopsy lobe	
PI-RADS score 3, n (%)	7 (12.7)
PI-RADS score 2, n (%)	25 (45.5)
Negative, n (%)	20 (36.4)
TTMB	
Mean (median) number of biopsy cores	29.01 (26.00)
Mean (median) number of positive cores	3.01 (3.00)
ISUP grade group 1, n (%)	29 (52.7)
ISUP grade group 2, n (%)	15 (27.3)
ISUP grade group 3, n (%)	8 (14.5)
Clinical tumor stage, n (%)	
T1c	14 (25.5)
T2a or b	27 (49.1)
T2c	11 (20.0)
Days from biopsy to radical prostatectomy, median (range)	79.50 (42–179)

ISUP, International Society of Urological Pathology; mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; TTMB, transperineal template-guided mapping biopsy.

52), 85.1% specificity (57 of 67), and 82.5% accuracy (99 of 120) in determining the eligibility for hemiblation compared with the whole-mount histology of RP specimens. We investigated the association between clinical variables and FT ineligibility (Table 4). On multivariate logistic regression analysis, we found no statistically significant predictive factor for FT ineligibility.

Fig. 2 shows the proportion of patients suitable for hemiblation. Among the 41 candidates for hemiblation, 19 (43.9%) had unilateral cancer based on the final histopathology of RP

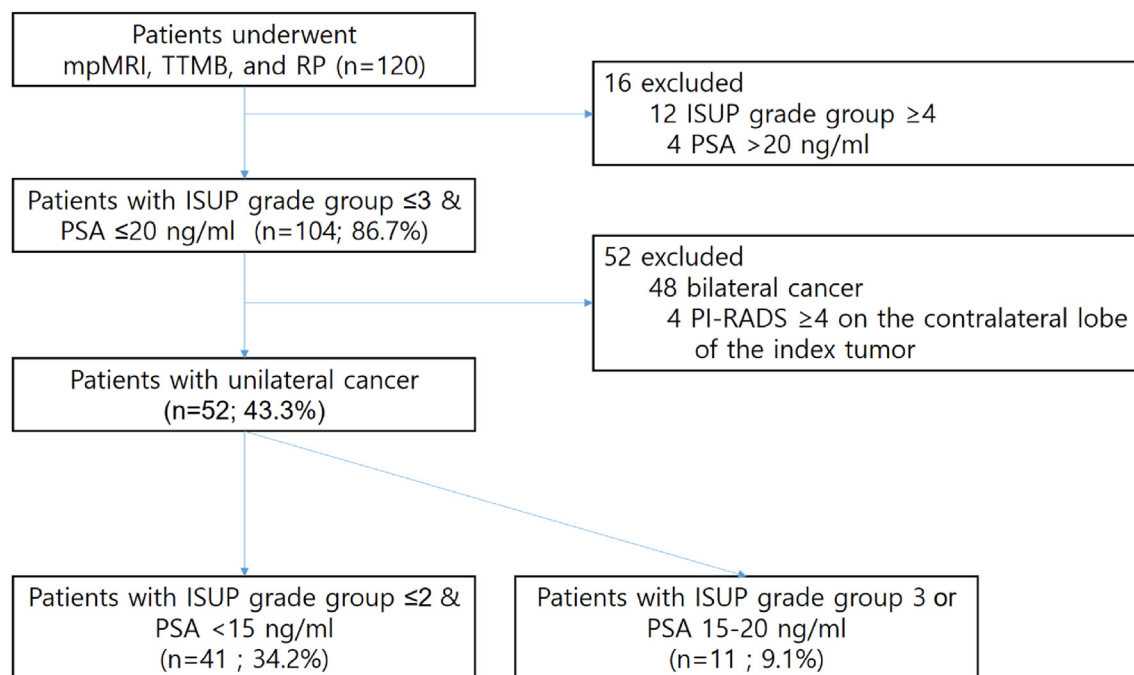


Fig. 1. Flow chart to identify the number of potential candidates for focal therapy. All 120 patients undergoing mpMRI, TTMB, and RP were screened for hemiablation eligibility, of whom 52 had unilateral prostate cancer in the combination of mpMRI and TTMB. Forty-one were considered potential candidates for hemiablation according to the criteria of ISUP grade group ≤ 2 and PSA <15 ng/mL and 11 met the screening criteria according to extended criteria of ISUP grade group 3 or PSA 15–20 ng/mL. ISUP, International Society of Urological Pathology; mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; RP, radical prostatectomy; TTMB, transperineal template-guided mapping biopsy.

Table 2

Tumor characteristics from 52 radical prostatectomy specimens.

Variable	Value
Tumors per patient, mean (median)	1.69 (2.00)
Overall tumor volume, ml, mean (median)	1.10 (0.57)
ISUP grade group	
1, n (%)	19 (36.5)
2, n (%)	27 (51.9)
3, n (%)	6 (11.5)
Total number of lobes	
Lobes with no prostate cancer, n (%)	23 (22.1)
Lobes with insignificant prostate cancer, n (%)	40 (38.5)
Lobes with significant prostate cancer, n (%)	41 (39.4)
Pathologic stage, n (%)	
T2a or b	26 (50.0)
T2c	26 (50.0)
T3a	0
Tumor focality, n (%)	
Unifocal	25 (48.1)
Multifocal	27 (51.9)
Tumor laterality, n (%)	
Unilateral unifocal	20 (38.5)
Unilateral multifocal	6 (11.5)
Bilateral unifocal	5 (9.6)
Bilateral multifocal	21 (40.4)

ISUP, International Society of Urological Pathology.

Table 3

Sensitivity and specificity of mpMRI and TTMB prediction of hemiablation eligibility versus radical prostatectomy specimen findings (n = 120).

mpMRI and TTMB ^a	No. of radical prostatectomy specimens		Total no.
	Eligible	Ineligible	
Eligible	42	10	52
Ineligible	11	57	68
Total	53	67	120

mpMRI, multiparametric magnetic resonance imaging; TTMB, transperineal template-guided mapping biopsy.

^a Sensitivity 80.7% (42/52), specificity 85.1% (57/67), and accuracy 82.5% (99/120).**Table 4**

Multivariate logistic regression analyses to predict the ineligibility for focal therapy.

Variables	OR	(95% CI)	P
Age	1.100	(0.943–1.284)	0.226
PSA	1.004	(0.763–1.321)	0.979
Prostate volume	1.017	(0.942–1.098)	0.660
mpMRI findings of the negative biopsy lobe			
Negative			0.805
PI-RADS score 2	0.493		1.000
PI-RADS score 3	1.240		1.000
Total number of biopsy cores	0.858	(0.662–1.111)	0.245
Number of positive cores	1.759	(0.901–3.435)	0.098
TTMB ISUP grade group, n			
1			0.228
2	4.524	(0.463–44.227)	0.194
3	0.348	(0.015–8.138)	0.512
Clinical tumor stage			
T1c			0.902
T2a or b	1.543	(0.237–10.052)	0.650
T2c	0.000		0.999

CI, confidence interval; ISUP, International Society of Urological Pathology; mpMRI, multiparametric magnetic resonance imaging; OR, odds ratio; PI-RADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; TTMB, transperineal template-guided mapping biopsy.

specimens. Among the 22 patients with bilateral cancers, 14 (36.6%) had a secondary tumor with ISUP grade group 1 and tumor volume <1.3 mL in the contralateral lobe of the index tumor. Therefore, 80.5% (n = 33) of the 41 candidates for hemiablation could be considered suitable for hemiablation. Eleven patients were eligible for hemiablation when FT eligibility criteria included those with maximum ISUP grade group 3 or PSA <20 ng/mL. Of these 11 patients, 9 (81.8%) patients could be considered suitable for hemiablation. In the extended criteria, one had a significant cancer crossing the midline (tumor volume of 1.132 mL) in the ISUP grade group 3 and the other had a small significant lesion (ISUP grade group 2 and tumor volume of 0.0374 mL) in the ISUP grade group ≤2 and PSA 15–20 ng/mL (Fig. 3).

Table 5 presents the results on the agreement between prostate biopsy and RP specimens according to the positive and negative biopsy lobes. Positive biopsy lobe showed a slightly higher ISUP grade group concordance (59.6%) than negative biopsy lobe (53.8%). However, two cases upgraded to ISUP grade group 3 in the positive lobe. No case was upstaged to non-organ-confined disease in both lobes. The false-negative rate of any cancer was 46.2% (24 of 52) on the negative biopsy lobe. Of these, 10 had clinically significant prostate cancers. Six had bilateral significant cancer and four had small volumes of ISUP grade group ≥2.

4. Discussion

The key to a successful FT is to accurately identify suitable patients. This selection requires appropriate investigative tools that can exclude clinically significant prostate cancer outside the area to be ablated while precisely localizing individual tumors that must be selectively destroyed. Several studies have reported that TRUS-guided prostate biopsy alone is insufficient in detecting unilateral prostate cancer.^{19–23} One of these studies showed that the rate of contralateral lobes with significant cancer on RP was 50% in patients with low-risk prostate cancer with unilateral tumors diagnosed using TRUS biopsy.²² The combination of mpMRI and TRUS-guided biopsy was also inadequate for appropriate patient selection in the era of MRI. In our prior study, of 185 patients with unilateral prostate cancer, PSA ≤15 ng/mL, Gleason score ≤3 + 4 diagnosed using TRUS-guided biopsy and mpMRI, approximately 40% were found to harbor bilateral significant prostate cancer on RP specimen analyses.¹² Therefore, an improved diagnostic pathway is required to reliably determine FT eligibility.

TTMB uses a brachytherapy grid placed in the perineum to guide the biopsy while the patient is in the lithotomy position. When considering FT, one advantage of TTMB is that it allows systematic sampling of the entire prostate, providing an accurate three-dimensional representation of the lesion, and has been shown to be superior in detecting anterior lesions.^{24,25} Additionally, TTMB has a higher cancer detection rate than TRUS-guided biopsies and can detect cancers not found in MRI-targeted biopsies.^{26–28}

In this study, we estimated the proportion of men who would be eligible for hemiablation using the combination of mpMRI and TTMB. We implemented eligibility criteria based on consensus statements²⁹ and compared the findings of the combination of mpMRI and TTMB with histology findings on RP specimens. Of the 41 patients deemed eligible for hemiablation, 80.5% (n = 33) were suitable for hemiablation.

Singh et al evaluated the eligibility for FT in 239 men with proven prostate cancer after TTMB.³⁰ MRI was used only for locoregional radiologic staging. The eligibility for FT required the index tumor to be unifocal, unilateral, or bilateral with contralateral

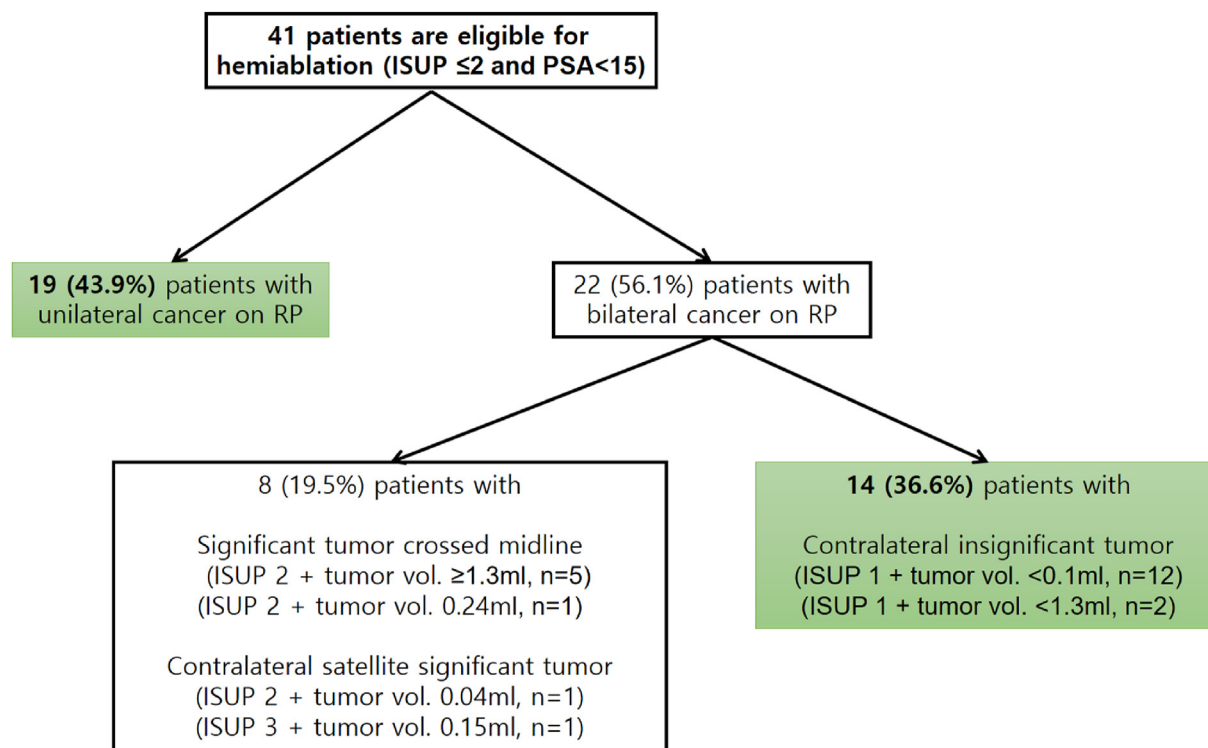


Fig. 2. Flow diagram of patients considered suitable for focal therapy based on mpMRI and TTMB (according to the criteria of ISUP grade group ≤ 2 and PSA < 15 ng/mL). ISUP, International Society of Urological Pathology; PSA, prostate-specific antigen; RP, radical prostatectomy; mpMRI, multiparametric magnetic resonance imaging; TTMB, transperineal template-guided mapping biopsy.

ISUP grade group 1 and size of < 4 mm. Depending on the location of cancer, 22% were identified to be suitable for hemiablation. The rate of eligibility for FT based on the combination of mpMRI and TTMB in this study was higher than that in the study by Singh et al (42.5% vs. 22%).

To the best of our knowledge, one study evaluated the accuracy of the combination of mpMRI and TTMB of the prostate in identifying candidates for hemiablation.³¹ Of the 50 candidates for FT based on consensus statements (PSA ≤ 15 ng/mL, T-stage $\leq$ T2a, Gleason score on biopsy $\leq 3 + 4$, no evidence of ECE or SVI on mpMRI), 21 (42%) had significant unilateral disease on mpMRI and TTMB. Of the 21 candidates, 19 (90%) had unilateral significant disease on the final histology on RP specimens. Regarding the selection of hemiablation candidates, although the combination of mpMRI and TTMB showed a high negative predictive value in detecting lobes with clinically significant prostate cancer, the small sample size is a limitation. TTMB enables a more accurate selection of patients for FT. However, TTMB is more invasive and requires considerable medical resources, and has a higher risk of acute urinary retention.³²

Nassiri et al¹⁴ assessed the correlation of MRI/ultrasound fusion biopsy findings with those of whole-mount histology after RP. FT eligibility was limited to a maximum ISUP grade group 3 within the region of interest with or without other foci (ISUP grade group 1 and size of < 4 mm). Of the 454 patients with a combined targeted and template biopsy-proven prostate cancer, 64 underwent RP. Of them, 25 would have qualified for FT based on fusion biopsy findings, of whom approximately half ($n = 12$) were suitable for FT on the final pathology findings. The authors concluded that improved criteria are required to identify FT eligibility with accuracy. In this study, according to Tran et al, 80.4% (41 of 51) were classified as suitable for FT based on the final RP findings, which was higher than that reported by Nassiri et al (48%).

When considering FT, the most important risk is undertreatment for non-ablated lesion. Therefore, the negative predictive value (NPV) is the most clinically relevant measure of accuracy. Matsouka et al³³ evaluated the accuracy of a combination of MRI and TRUS/transperineal biopsy with 14 cores in identifying unilateral prostate cancer. The NPV of the combination method was 95.7% for lobes with significant disease. Although it showed a high NPV, the definition of insignificant disease included up to ISUP grade group 2. Several lobes with significant disease may have been underestimated because the presence of Gleason pattern 4 was not considered. Tran et al³¹ showed that the combination of mpMRI and TTMB provides a high NPV of 91% in detecting lobes with significant cancer. Another study evaluated the potential for hemiablation in patients with proven unilateral intermediate-risk prostate cancer after MRI fusion prostate biopsy.³⁴ According to the inclusion criteria, the rate of undetected contralateral significant tumors ranged from 41% to 48% on whole-mount pathology specimens as the reference standard. MRI-targeted combined with a systematic biopsy using an MRI/ultrasound fusion system is recommended as a diagnostic tool for evaluating patients for FT. However, to exclude the possibility of significant disease in the contralateral lobe of the treated region, the combination of mpMRI and TTMB appears to have higher accuracy.

This study had several limitations. First, there is a selection bias because this study was retrospectively conducted at a single center. Additionally, because we only analyzed patients who underwent RP as our reference test, they were probably a higher-risk cohort. Many patients who had low-risk prostate cancer underwent alternative treatment options, such as AS, FT, or low-dose-rate brachytherapy. For this reason, a significant portion of the patients considered to be suitable for FT may have been excluded from this study. Second, the sample size of 51 patients who underwent RP was relatively small. The diagnostic pathway in this study is difficult to become the

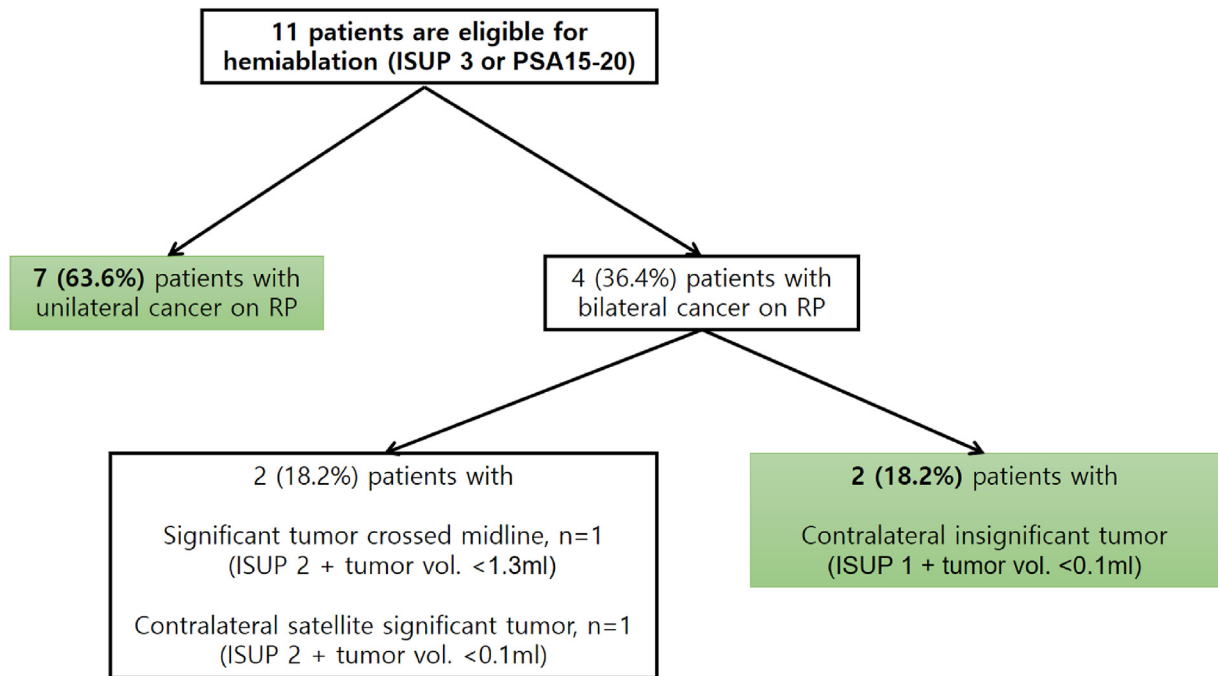


Fig. 3. Flow diagram of patients considered suitable for focal therapy based on mpMRI and TTMB (according to the extended criteria of ISUP grade group 3 or PSA 15–20 ng/mL). ISUP, International Society of Urological Pathology; PSA, prostate-specific antigen; RP, radical prostatectomy; mpMRI, multiparametric magnetic resonance imaging; TTMB, transperineal template-guided mapping biopsy.

Table 5

Pathological concordance and disagreement between prostate biopsies and RP specimens according to positive versus negative biopsy lobes.

	Positive biopsy lobe, n (%)	Negative biopsy lobe, n (%)
	ISUP grade group ≤ 3 Organ-confined disease	No cancer or a core with ISUP grade group 1 PI-RADS ≤ 3 on mpMRI
Concordance	31 (59.6)	28 (53.8)
Disagreement		
Upgrading	13 (25.0)	24 (46.2)
ISUP 1 $\rightarrow$ 2	11	
ISUP 2 $\rightarrow$ 3	2	
Downgrading	8 (15.4)	0
Upstaging (non-organ-confined)	0	0
ISUP grade group		
1	21 (40.4)	19 (36.5)
2	26 (50.0)	9 (17.3)
3	5 (9.6)	1 (1.9)
Tumor volume ≥ 0.7 mL	21 (40.4)	7 (13.5)
Significant prostate cancer	31 (59.6)	10 (19.2)
ISUP 1 and tumor volume ≥ 1.3 mL	1	0
ISUP ≥ 2 and tumor volume ≥ 0.7 mL	19	6
ISUP ≥ 2 and tumor volume < 0.7 mL	11	4

ISUP, International Society of Urological Pathology; mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; RP, radical prostatectomy; TTMB, transperineal template-guided mapping biopsy.

standard diagnostic pathway in the real-world based on the results of this study alone. Nevertheless, the significant concordance between the combination of mpMRI and TTMB and whole-mount histology indicated that the combination of mpMRI and TTMB can help determine FT eligibility. Third, because this study was designed to focus on side-specific analyses to identify candidates for hemiablation, analyses based on whole-mount processing were not performed, which could be a future research objective. A multicenter validation study with a large cohort and more high-quality evidence would also be relevant to confirm the findings of this study. Lastly, all pathologic slides were reviewed by a single genitourinary pathologist, and inter-observer variability for the

ISUP grade group was not assessed. However, the reviewer had been in practice for >20 years.

5. Conclusion

When considering FT, precise investigative tools that accurately localize the index tumor to be ablated while excluding distinct contralateral significant cancer are required for appropriate patient selection. The combination of mpMRI and TTMB substantially improves the prediction of potential candidates for FT based on consensus recommendations. The results of this study should be confirmed in a larger cohort study. Additionally, clinicians must

consider the risk of residual significant disease in the untreated contralateral lobe even after using the combination of mpMRI and TTMB.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Authors' contributions

YH Choi: data analysis, manuscript writing and editing, CU Lee: data collection and analysis, Wan Song: data analysis, HH Sung: data analysis, BC Jeong: data collection and management, SI Seo: data collection and management, SS Jeon: data collection and management, HM Lee: data analysis, HG Jeon, and SJ Lee: project development, data analysis, and supervision.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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