



# Comparison of prostate cancer detection rates between magnetic resonance imaging-targeted biopsy and transrectal ultrasound-guided biopsy according to Prostate Imaging Reporting and Data System in patients with PSA $\geq 4$ ng/mL: a systematic review and meta-analysis

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**Background:** Previous studies have investigated magnetic resonance imaging-targeted biopsy (MRI-TBx) on the detection for prostate cancer (PCa). Prostate Imaging Reporting and Data System (PI-RADS), as a standardized MRI reporting system, has widely been used in the management of PCa. However, basing the PI-RADS score, the comparability between MRI-TBx and transrectal ultrasound-guided biopsy (TRUS-Bx) in diagnosing PCa remained inconsistent or even controversial. Thus, this systematic meta-analysis aimed to assess the value of PI-RADS in sifting better prostate biopsy method.

**Methods:** A meta-analysis including 10 articles was performed. In these included studies, biopsy-naive subjects with concerning PSA levels and/or an abnormal digital rectal examination (DRE) were consecutively enrolled by referral from urologists. All subjects underwent multiparameter MRI (mpMRI) prostate and the results were scored independently by PI-RADS. Subjects with equivocal (PI-RADS 3) and intermediate/high-risk (PI-RADS 4/5) lesions underwent MRI-TBx and followed by TRUS-Bx performed by a urologist. The online databases PubMed, Embase and Web of Science were searched to find all correlated articles until October 1<sup>st</sup>, 2019. Data were pooled by odds ratios (ORs) with 95% confidence intervals (CIs) to assess the strength of the associations. Subgroup analyses were conducted based on Gleason score.

**Results:** Overall, 10 studies were included in this meta-analysis from January, 2015 to June, 2019. In the comparison of the detection of MRI-TBx and TRUS-Bx in PCa patients, TRUS-Bx had a significant advantage in overall PCa detection compared with MRI-TBx (OR =0.78, 95% CI: 0.62–0.98) in PI-RADS 3. Basing subgroup analysis of Gleason score (csPCa: Gleason score  $\geq 7$ ; non-csPCa: Gleason score  $< 7$ ), a summary analysis of the detection rate of csPCa showed that no significant difference was found (OR =0.82, 95% CI: 0.58–1.16); Meanwhile, no significant difference in non-csPCa patients was also detected (OR =0.83, 95% CI: 0.53–1.28). In PI-RADS 4 or 5, no significant results were detected between MRI-TBx and TRUS-Bx (OR =0.96, 95% CI: 0.87–1.06) for overall PCa detection. The stratification analyses by Gleason score found that TRUS-Bx had an advantage over MRI-TBx in non-csPCa patients (OR =0.76, 95% CI: 0.60–0.98); However, there was no significant difference in the detection rate of csPCa (OR =1.05, 95% CI: 0.93–1.20).

**Conclusions:** This meta-analysis indicated that using TRUS-Bx was better than MRI-TBx for the diagnosis of PCa in PI-RADS 3; Besides, TRUS-Bx have an advantage over MRI-TBx in the detection for non-csPCa in PI-RADS 4 or 5. Therefore, PI-RADS could be used as a MRI evaluation system in the selection of prostate biopsy.

**Keywords:** Prostate cancer (PCa); Prostate Imaging Reporting and Data System (PI-RADS); transrectal ultrasound-guided biopsy (TRUS-Bx); magnetic resonance imaging-targeted biopsy (MRI-TBx); meta-analysis

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## Introduction

Prostate cancer (PCa) is the second most common malignancy among men worldwide (1). Therefore, screening is very important for integrated management of PCa. The discovery of PSA not only increased the detection rate of PCa, but also decreased the mortality rate of PCa. However, PSA might increase the risk of overdiagnosis and overtreatment, which leads to the necessity of random and systematic sampling of the whole prostate under ultrasound guidance (2). Currently, the standard technique for PCa diagnosis is transrectal ultrasound-guided biopsy (TRUS-Bx) (3). Nevertheless, the limitation of TRUS-Bx random sampling for PCa is that gray-scale ultrasound cannot distinguish PCa tissue from benign prostatic tissue (4,5). Therefore, TRUS-Bx is less sensitive and specific to PCa.

According to the European Society of Urogenital Radiology (ESUR), multiparameter magnetic resonance imaging (mpMRI) has improved the imaging sensitivity of PCa, because of its increasing availability, advances in anatomical and functional data, as well as more and more studies have confirmed it (6,7). Therefore, the clinical guidelines recommend that although the results of initial TRUS biopsy are negative, the suspicions of PCa remain and mpMRI should be performed (8). Several radiologists used different mpMRI scores to indicate their suspicion of PCa, which contributed to great interference for clinicians (9). Due to the lack of a standardized diagnostic criteria for reporting results, it hinders the widespread acceptance of prostate MRI.

To improve the readers reliability and meaningful communication with clinicians, ESUR issued a consensus-based guide in 2012 called the Prostate Imaging Reporting and Data System (PI-RADS), and it was updated to version 2.0 in 2015 (7,10). It evaluates three imaging modalities of intraprostatic lesions with mpMRI using a five-point

scale to predict the possibility of clinically significant prostate cancer (csPCa). Since the application of PI-RADS, numerous studies based on PI-RADS and mpMRI have been published (11-13). However, no one has conducted a systematic review and meta-analysis to assess the value of the selection of prostate biopsy methods by PI-RADS. Therefore, this study aimed to evaluate whether PI-RADS could be used as a MRI reporting system to compare the PCa detection rates between magnetic resonance imaging-targeted biopsy (MRI-TBx) and TRUS-Bx by collecting the data from all correlated articles.

## Methods

We primarily aimed to systematically evaluate the diagnostic ability of PI-RADS to compare between MRI-TBx and TRUS-Bx in the detection of PCa, including csPCa and non-csPCa.

### Search strategy

The online databases PubMed, Embase and Web of Science were searched from inception to find all relevant articles until October 1<sup>st</sup>, 2019. Systematic literature retrieval was carried out with the help of information experts in medical libraries. For each database, the search terms used were (“PI-RADS”) AND (“prostate cancer OR prostatic Cancer OR prostate Neoplasm OR prostate Neoplasms OR Prostatic Neoplasm OR Prostatic Neoplasms”) AND (“biopsy OR prostate biopsy”) AND (“nuclear magnetic resonance imaging” OR “nuclear magnetic resonance” OR “MRI”).

### Inclusion and exclusion criteria

Inclusive studies focused on suspected PCa patients, who

elevated PSA ( $\geq 4$  ng/mL) and/or positive rectal digital examination (RDE). In addition, among these patients who underwent positive MRI (defined as finding suspicious PCa lesions in prostate MRI scans), the mpMRI results were scored independently by PI-RADS, and the patients with equivocal (PI-RADS 3) and intermediate/high-risk (PI-RADS 4/5) lesions were only selected, and of all, these patients were biopsy naïve. Meanwhile, the included studies examined the same person underwent MRI-TBx and followed by TRUS-Bx performed by a urologist, and compared the detection rate of PCa between these two methods in the most objective measure (14). Accordingly, we only included the articles comparing MRI-TBx with TRUS-Bx on the basis of PI-RADS in biopsy naïve patient.

Some studies were excluded according to the following criteria: (I) unable to extract the required information of PCa and determine the quality of research; (II) some articles such as non-case-control studies, case reports, letters, reviewed editorial articles; (III) when repeated or identical patients were used in multiple publications, only the most recent or complete studies were selected in this meta-analysis.

#### Data extraction

Data collection was independently carried out by two reviewers (Z.K and Q.ZQ). According to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (15), a flow chart to show the number of studies identified and included or excluded at each literature screening stage was established. If there were inconsistencies, we reviewed and discussed it with the third reviewers (X.JX). In the process of searching studies, we first browsed the titles or abstracts related to our chosen topic. If it was not clear, we would move on to the full text. The references cited in the included studies were also considered as potential related studies. The collection of data included the publication information (author and year); the method of recruitment; the publication information (race, mean age, mean PSA and mean volume of prostate); the collection and evaluation of MRI performance; PI-RADS scores; the number of cores collected by systems biopsy; the definition of csPCa; the detection rate of overall PCa, csPCa and non-csPCa based on different PI-RADS score.

#### Statistical analysis

The odds ratios (ORs) of 95% confidence intervals (95%

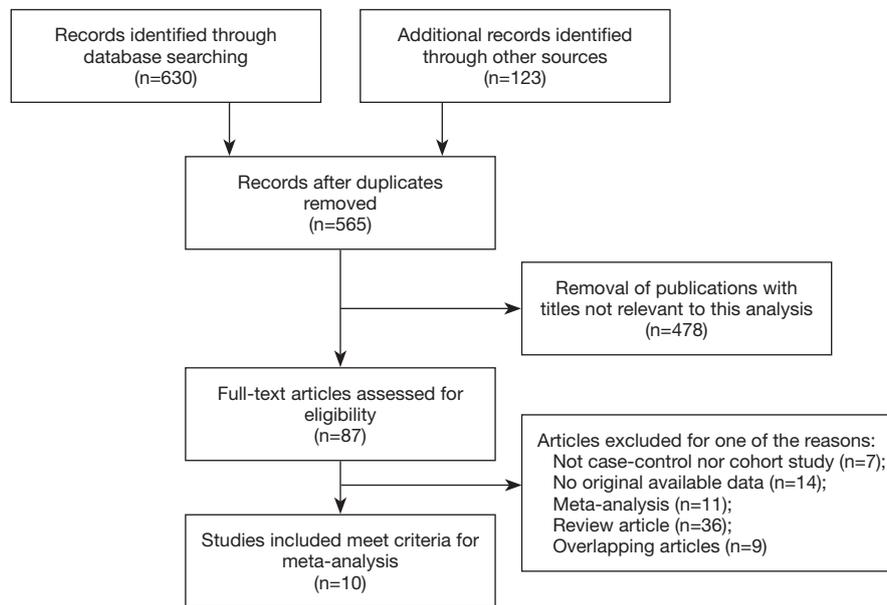
CI) were used to evaluate the correlations between MRI-TBx and TRUS-Bx in the diagnosis of PCa. The goodness-of-fit chi-square test to assess the sources of heterogeneity about such association was adopted, and  $P < 0.05$  regarded as significant imbalance (16). According to the P value of heterogeneity, the fixed effect model (Mantel-Haenszel method) or random effect model (DerSimonian-Laird method) were used to calculate the pooled ORs (17). Then, subgroup analysis was performed by Gleason score based on the results of prostate biopsy to explore its impact on heterogeneity. Sensitivity analysis was performed by excluding one single study and recalculating their ORs to test the stability and reliability of the overall meta-analysis. In addition, Begg's funnel plot and Egger's linear regression test were used to find the publication bias. When the P value was less than 0.05, it was regarded as significant selection bias. We utilized STATA software (version 12.0; StataCorp LP, College Station, TX) to deal with all above statistical analyses.

## Results

### Studies characteristics

As shown in *Figure 1*, a total of 753 records were obtained by a systematic literature search from the above databases. According to the inclusion and exclusion criteria, 188 duplicates were removed. Subsequently, 478 records were excluded by screening titles and abstracts and 87 full-text articles were eligible. Besides, 77 articles were eliminated due to insufficient data after carefully reading the full texts. Finally, 10 articles were included in this meta-analysis (18-27); and all included articles were to assess the diagnostic value of MRI-TBx and TRUS-Bx for the detection of PCa. Among these, seven studies were about the influence of Gleason score for PCa diagnosis.

The patient characteristics about number of cases, race, age, prostate volume, and PSA levels of the selected studies were shown in *Table 1*. The race of most population was German, the rest also included Asian, British, Australian, Hispanic and so on. In addition, the methodology assessment of these studies included was also collected in this meta-analysis (*Table 2*). The different parameters, consisted of T2 or T1-weighted imaging, diffusion weighted imaging, and dynamic contrast enhancement (DCE) imaging on based on 3.0T MRI, were considered by radiologists to divide the suspicious lesions into different PI-RADS. The suspicion of PCa in all included studies on



**Figure 1** Flowchart of literature search and selection process.

**Table 1** The patient characteristics of individual studies included in the meta-analysis

Identifier			Patient population			
Author	Year	Number of cases	Race	Mean age [range], year	Mean PSA [range], ng/mL	Mean prostate volume [range], mL
Preisser <i>et al.</i> (18)	2019	141	German	67 [60–73]	6.8 [5.0–9.9]	40 [30.0–57.0]
van der Leest <i>et al.</i> (19)	2019	317	Netherlander	65 [59–68]	6.4 [4.6–8.2]	55 [41–77]
Maxeiner <i>et al.</i> (20)	2018	318	German	68 [60–72]	7.14 [5.13–10.3]	47 [36–65]
Tan <i>et al.</i> (21)	2017	115	Southeast Asian Men	69 [65–74]	8.7 [6.2–13.9]	56 [40–82]
Gunzel <i>et al.</i> (22)	2017	162	German	67 [61–72]	8.10 [6.05–14.00]	48 [35–60]
Truong <i>et al.</i> (23)	2018	240	White/Black/Hispanic/Asian	67 [61–72]	8.4 [5.9–12.6]	51.4 [35.6–76.6]
Hansen <i>et al.</i> (24)	2018	807	British/German/Australian	65 [59–70]	6.5 [4.9–8.8]	42 [30–58]
Gunzel <i>et al.</i> (25)	2017	251	German	68 [61–72]	6.5 [4.9–8.9]	49 [36–64]
Kesch <i>et al.</i> (26)	2016	287	German	66 [60–72]	9.7 [7.0–13.9]	52.0 [35.9–75.2]
Pokorny <i>et al.</i> (27)	2014	142	Australian/Netherlander	63 [57–68]	5.3 [4.1–6.6]	41 [30–59]

the basis of PI-RADS was reported on a scale of 3–5. In addition, the suspicious lesions of PI-RADS <3 were not included; because it was impossibly considered PCa. The detection rate of PCa, csPCa and non-csPCa was detected to compare the value of MRI-TBx and TRUS-Bx based on PI-RADS (Table 3).

### Quantitative synthesis results

In the comparison of the diagnostic value of MRI-TBx and TRUS-Bx in PCa patients, there was a significant difference advantage of comparing MRI-TBx with TRUS-Bx for overall PCa detection (OR =0.78, 95% CI: 0.62–0.98) (MRI-TBx: sensitivity =0.31, 95% CI: 0.25–0.36; TRUS-

**Table 2** The methodology assessment of individual studies included in this meta-analysis

Identifier	Methodology				MRI		Biopsy	
	Year	Recruitment	Scoring system	Field strength, T (vendor)	Sequence for defining target	Navigation system	TRUS-Bx comparator (cores)	Definition of csPCa
Preisser <i>et al.</i> (18)	2019	PI-RADS $\geq 3$	PI-RADS v2	3-Tesla	T2/T1/DWI/DCEI	Hitachi Medical Systems, Wiesbaden, Germany	12	Gleason score $\geq 3 + 4$
van der Leest <i>et al.</i> (19)	2019	PI-RADS 3–5 lesion(s)	PI-RADS v2	3-Tesla	T2/DCEI/DWI	MR biopsy device (Invivo, Gainesville, FL, USA)	12	Gleason score $\geq 3 + 4$
Maxeiner <i>et al.</i> (20)	2018	Suspicious mpMRI (PI-RADS score $\geq 3$ )	PI-RADS v2	3-Tesla	T2/DCEI/DWI	MRI/US fusion guided platform	10	Gleason Score $\geq 4+3=7$ or maximal cancer core length $\geq 6$ mm
Tan <i>et al.</i> (21)	2017	At least one PI-RADS $\geq 3$	PI-RADS v2	3 Tesla	T2/DCEI	UroNav MRI/TRUS fusion system	12	Gleason Score $\geq 7$
Gunzel <i>et al.</i> (22)	2017	At least one suspicious lesion on mpMRI (PI-RADS $\geq 3$ )	NA	3-Tesla	T2/T1/DWI/DCEI	Sensor-based MRI/US fusion platform	10	Gleason score $\geq 7$
Truong <i>et al.</i> (23)	2018	PI-RADS score 3–5	PI-RADS v2	3-Tesla	NA	A software-based fusion biopsy platform UroNav	12	NA
Hansen <i>et al.</i> (24)	2018	PI-RADS $\geq 3$	PI-RADS v1/v2	3-Tesla	T2/T1/DWI/DCEI	MRI/TRUS-fusion biopsy system	18–24	Gleason score $\geq 4 + 3$ or a maximum cancer core length 6 mm or longer
Gunzel <i>et al.</i> (25)	2017	PI-RADS $\geq 3$	PI-RADS v1	3-Tesla	T2/T1/DWI	A sensor-based, real-time MRI/US target biopsy	10	Gleason Score $\geq 4 + 3$
Kesch <i>et al.</i> (26)	2016	PI-RADS $\geq 2$	PI-RADS v1	3-Tesla	T2/DCEI/DWI	MRI-TRUS fusion biopsy	24	Gleason Score =3 +3 and PSA $\geq 10$ ng/ml or GS $\geq 3 + 4$
Pokorny <i>et al.</i> (27)	2014	PI-RADS score 1–5	PI-RADS v1	3-Tesla	T2/DCEI/DWI	MRI/TRUS-fusion biopsy system	12	Gleason score $>7$

mpMRI, multiparameter magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; DCE, dynamic contrast enhanced imaging; DWI, diffusion weighted imaging; TRUS, transrectal ultrasound; US, ultrasound; PCa, prostate cancer; csPCa, clinical significance prostate cancer; NA, not available.

Table 3 The extracted data analysis of each study in the meta-analysis

Identifier	Sensitivity of PI-RADS3, n/N (%)						Sensitivity of PI-RADS4+5, n/N (%)											
	Overall PCa			csPCa			Non-csPCa			Overall PCa			csPCa			Non-csPCa		
	MRI-TBx	TRUS-Bx	Year	MRI-TBx	TRUS-Bx	Year	MRI-TBx	TRUS-Bx	Year	MRI-TBx	TRUS-Bx	Year	MRI-TBx	TRUS-Bx	Year	MRI-TBx	TRUS-Bx	Year
Preisser et al. (18)	9/29	8/29	2019	5/29	5/29	2019	3/29	3/29	2019	83/112	87/112	2019	68/112	71/112	2019	15/112	15/112	2019
van der Leest et al. (19)	14/40	17/40	2019	7/40	6/40	2019	11/40	11/40	2019	233/277	211/277	2019	152/277	130/277	2019	81/277	81/277	2019
Maxeiner et al. (20)	14/55	17/55	2018	5/55	11/55	2018	6/55	6/55	2018	199/263	205/263	2018	157/263	134/263	2018	42/263	42/263	2018
Tan et al. (21)	15/70	18/70	2017	11/70	9/70	2017	4/70	9/70	2017	26/45	26/45	2017	24/45	15/45	2017	2/45	2/45	2017
Gunzel et al. (22)	13/31	15/31	2017	NA	NA	2017	NA	NA	2017	76/131	93/131	2017	NA	NA	2017	NA	NA	2017
Truong et al. (23)	12/65	25/65	2018	NA	NA	2018	NA	NA	2018	109/175	107/175	2018	NA	NA	2018	NA	NA	2018
Hansen et al. (24)	52/137	72/137	2018	29/137	37/137	2018	23/137	35/137	2018	270/370	295/370	2018	220/370	227/370	2018	50/370	50/370	2018
Gunzel et al. (25)	15/39	18/39	2017	NA	NA	2017	NA	NA	2017	142/212	158/212	2017	NA	NA	2017	NA	NA	2017
Kesch et al. (26)	19/76	33/76	2016	11/76	19/76	2016	8/76	14/76	2016	79/120	83/120	2016	73/120	73/120	2016	6/120	6/120	2016
Pokorny et al. (27)	15/33	5/33	2014	5/33	2/33	2014	10/33	3/33	2014	86/109	94/109	2014	74/109	82/109	2014	12/109	12/109	2014

csPCa, clinical significance prostate cancer; MRI-TBx, magnetic resonance imaging-targeted biopsy; TRUS-Bx, transrectal ultrasound-guided biopsy; PCa, prostate cancer; NA, not available.

Bx: sensitivity =0.37, 95% CI: 0.29–0.45) in PI-RADS 3 (Figure 2A). Basing subgroup analysis of Gleason score (csPCa: Gleason score  $\geq 7$ ; non-csPCa: Gleason score  $< 7$ ), a summary analysis of the detection rate of csPCa showed that no significant difference was found (OR =0.82, 95% CI: 0.58–1.16) (MRI-TBx: sensitivity =0.16, 95% CI: 0.12–0.19, TRUS-Bx: sensitivity =0.18, 95% CI: 0.11–0.24) (Figure 2B); meanwhile, no significant differences was also detected in non-csPCa patients (OR =0.83, 95% CI: 0.53–1.28) (MRI-TBx: sensitivity =0.14, 95% CI: 0.09–0.19, TRUS-Bx: sensitivity =0.16, 95% CI: 0.11–0.22) (Figure 2C).

In PI-RADS 4 or 5, no significant results were detected between MRI-TBx and TRUS-Bx (OR =0.96, 95% CI: 0.87–1.06) (MRI-TBx: sensitivity =0.70, 95% CI: 0.65–0.76, TRUS-Bx: sensitivity =0.74, 95% CI: 0.70–0.79) for overall PCa detection (Figure 3A). The stratification analyses by Gleason score found that there was no significant difference in the detection rate of csPCa (OR =1.05, 95% CI: 0.93–1.20) (MRI-TBx: sensitivity =0.59, 95% CI: 0.57–0.62, TRUS-Bx: sensitivity =0.57, 95% CI: 0.48–0.65) (Figure 3B); However, TRUS-Bx had an advantage over MRI-TBx in non-csPCa patients (OR =0.76, 95% CI: 0.60–0.98) (MRI-TBx: sensitivity =0.13, 95% CI: 0.07–0.19, TRUS-Bx: sensitivity =0.19, 95% CI: 0.12–0.25) (Figure 3C).

### Test of heterogeneity

Subgroup analyses could decrease the heterogeneity, and Gleason score might contribute to one aspect of substantial heterogeneity. Figure 4 showed the results of a Galbraith radial plot, suggesting no obvious heterogeneity between these studies.

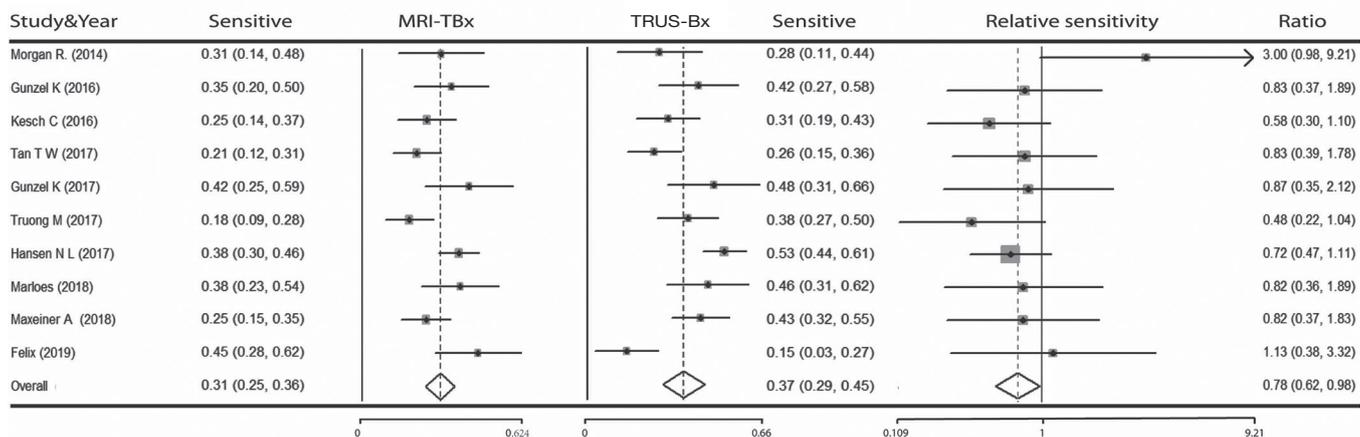
### Sensitivity analysis

Sensitivity analysis was carried out by omitting one single study to check the influence of each individual study on the recalculated ORs by repeating the meta-analysis. The results demonstrated that the pooled ORs were not significantly influenced, thus to suggest that the results were robust and stability in this meta-analysis (Figure 5).

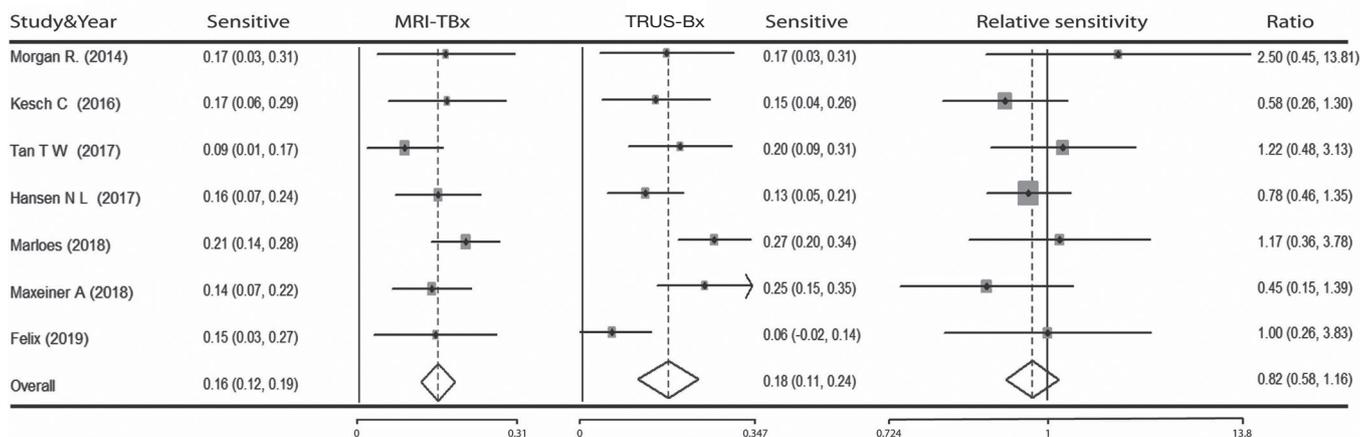
### Publication bias

The Begg's funnel plot and Egger's test were applied to assess the publication bias for all data. The shapes of the

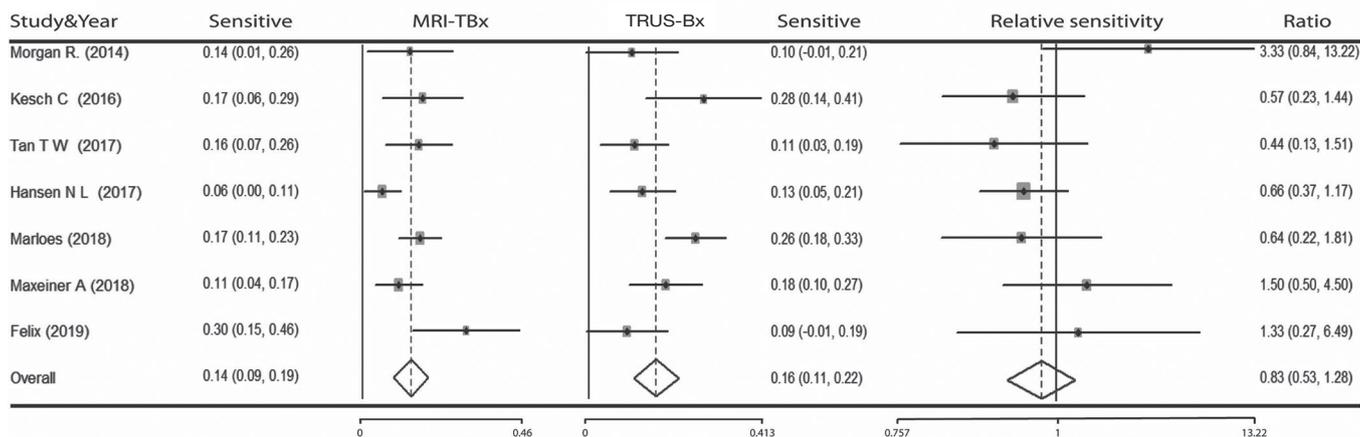
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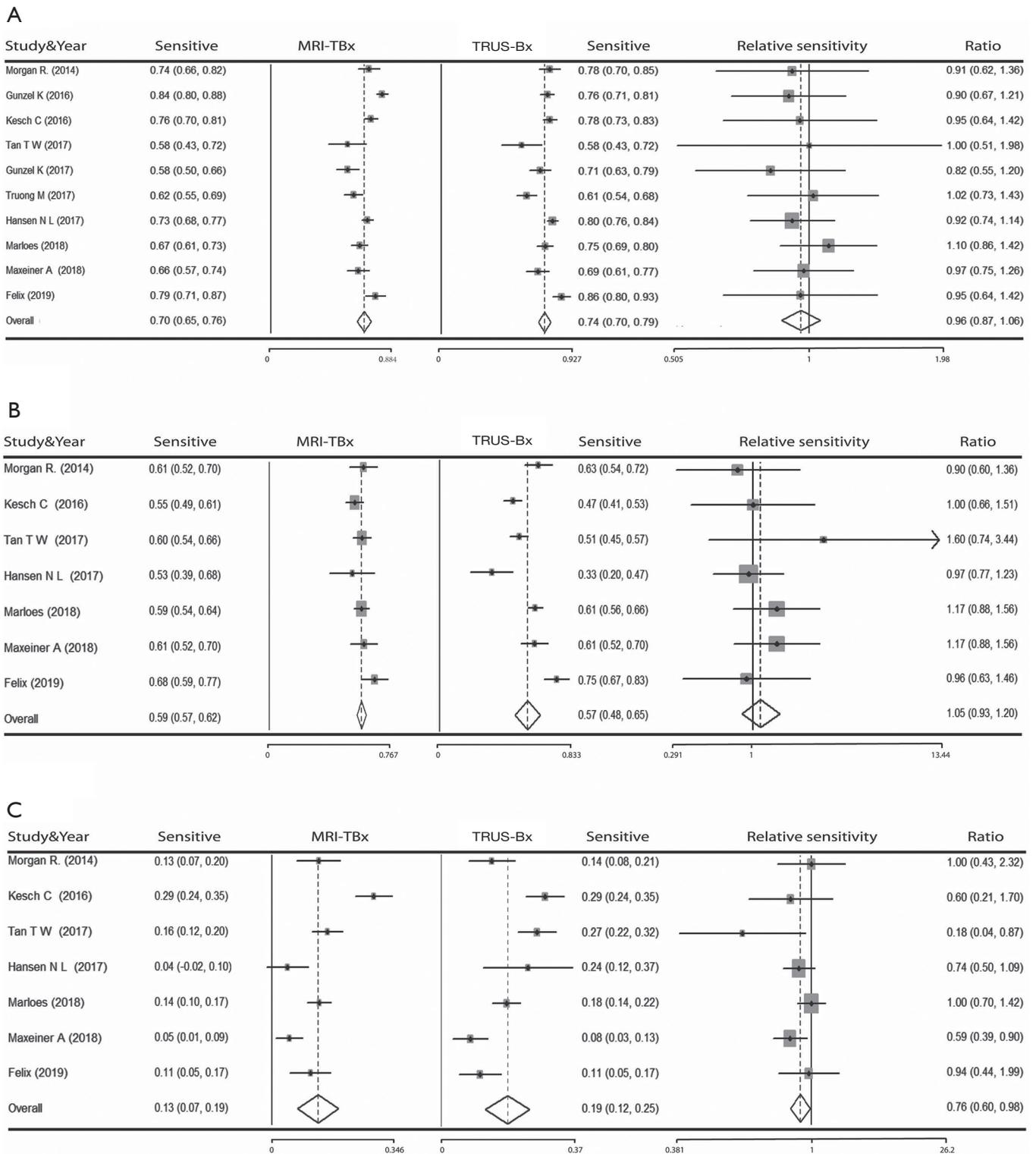
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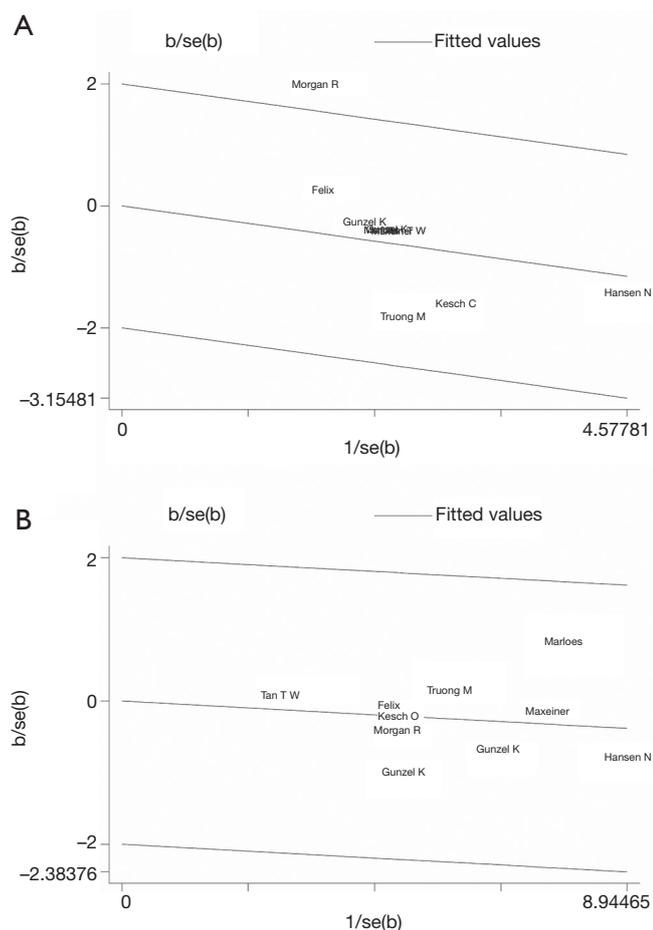
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**Figure 2** Forest plots of the comparison between MRI-TBx and TRUS-Bx in detection of PCa with PI-RADS 3. (A) All PCa-suspected patients; (B) Gleason score  $\geq 7$ ; (C) Gleason score  $< 7$ . MRI-TBx, magnetic resonance imaging-targeted biopsy; TRUS-Bx, transrectal ultrasound-guided biopsy; PCa, prostate cancer; PI-RADS, Prostate Imaging Reporting and Data System.



**Figure 3** Forest plots of the comparison between MRI-TBx and TRUS-Bx in detection of PCa with PI-RADS 4 or 5. (A) All PCa-suspected patients; (B) Gleason score  $\geq 7$ ; (C) Gleason score  $< 7$ . MRI-TBx, magnetic resonance imaging-targeted biopsy; TRUS-Bx, transrectal ultrasound-guided biopsy; PCa, prostate cancer; PI-RADS, Prostate Imaging Reporting and Data System.

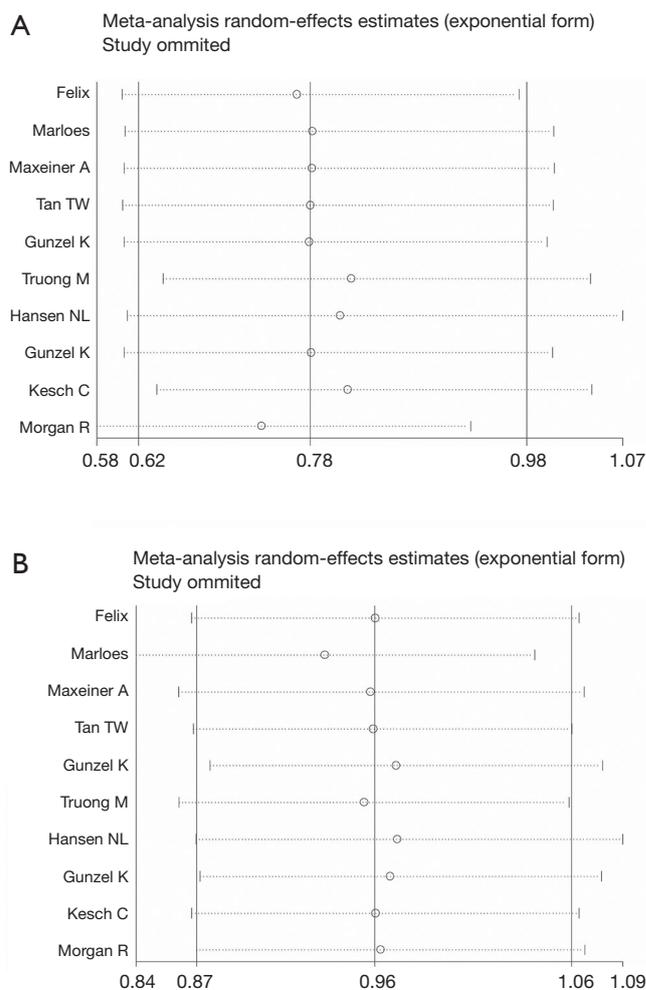


**Figure 4** Galbraith plot of the comparison between MRI-TBx and TRUS-Bx in detection of PCa. (A) PI-RADS 3; (B) PI-RADS 4 or 5. MRI-TBx, magnetic resonance imaging-targeted biopsy; TRUS-Bx, transrectal ultrasound-guided biopsy; PCa, prostate cancer; PI-RADS, Prostate Imaging Reporting and Data System.

funnel plots seemed symmetrically distributed in the funnel plots (*Figure 6*), indicating little evidence of significant publication bias across studies, which were confirmed by Egger’s test (PI-RADS 3:  $P=0.104$ ; PI-RADS 4 or 5:  $P=0.651$ ).

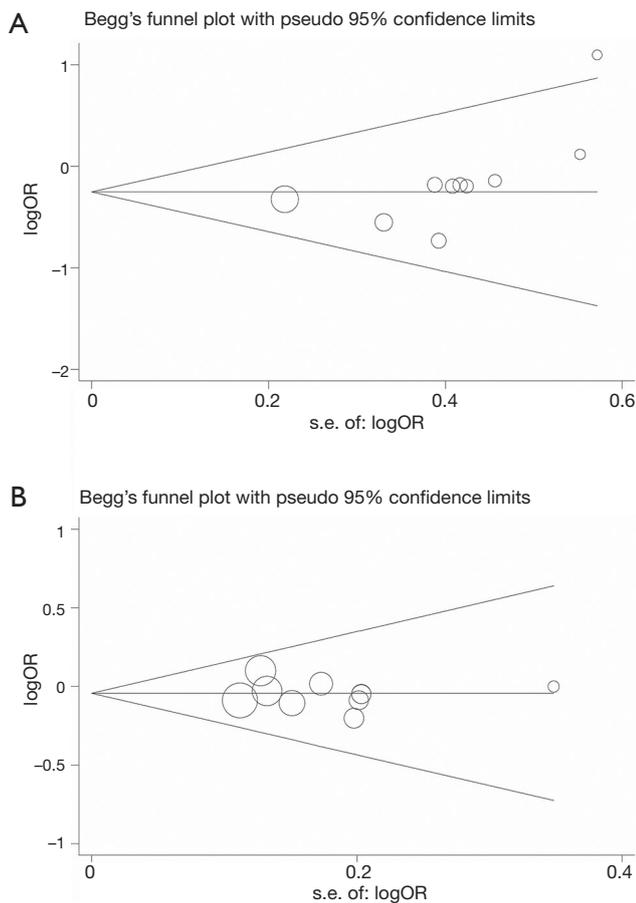
**Discussion**

Among a series of diagnostic criteria for PCa, the most important one is the result of biopsy, which is considered as the gold diagnostic criterion for PCa nowadays (28). Therefore, the sensitivity and specificity of prostate biopsy has become the focus of more and more researchers. At present, MRI-TBx and TRUS-Bx are coexisting in



**Figure 5** Sensitivity analysis of the comparison between MRI-TBx and TRUS-Bx in detection of PCa. (A) PI-RADS 3; (B) PI-RADS 4 or 5. MRI-TBx, magnetic resonance imaging-targeted biopsy; TRUS-Bx, transrectal ultrasound-guided biopsy; PCa, prostate cancer; PI-RADS, Prostate Imaging Reporting and Data System.

clinic; However, the selection of two puncture methods is still controversial (29,30). Schoots *et al.* suggested that the selection of puncture method was associated with pathological grading of PCa (29). Besdies, Schouten *et al.* reported that the missing detection of biopsy was related to the location of PCa (30). Thus, all these characteristics of PCa are included in PI-RADS (7). Following the publication of PI-RADS, standardized MRI reports have been used by more and more radiologists (31,32). The definitions of the PI-RADS can be expressed in terms of volume (measured on T2 or contrast-enhanced images) or radiological characteristics, so we used some prominent



**Figure 6** Begg's funnel plot of publication bias test. (A) PI-RADS 3; (B) PI-RADS 4 or 5. PI-RADS, Prostate Imaging Reporting and Data System.

features of MRI changes, such as the difference between the lesion and its surrounding background prostate, the visibility of ADC values or any parameters used (10). Therefore, the PI-RADS of targeted biopsy samples and standard biopsy samples was extracted from each literature, to judge whether the use of PI-RADS reporting criteria could be helpful to distinguish the practicability between systematic biopsy and MRI-targeted biopsy.

Choosing MRI examination before prostate biopsy not only has advantages of the highly sensitivity for detecting PCa, but may also show the location of the lesion (33,34). However, as a new monitoring tool, it might require PCa-suspected patients to bear more financial burdens. Meanwhile, the result of MRI might influence the selection of the way of prostate biopsy, and help clinicians to determine the patients with PSA  $\geq 4$  ng/mL to choose the

most appropriate biopsy. In this meta-analysis, the results indicated that in the patients with biopsy naïve in PI-RADS 3, the detection rate of TRUS-Bx was better than that of MRI-TBx, while in PI-RADS 4 or 5, no significant difference in detection rate of PCa was found. Then, it is important to recognize that clinically significant disease's detection might differ between MRI-TBx and TRUS-Bx. Gleason score as the subgroup were further investigated, and these patients were divided into two groups (csPCa: Gleason score  $\geq 7$ ; non-csPCa: Gleason score  $< 7$ ). The results showed that the patients with PI-RADS 4 or 5 in Gleason score  $< 7$ , TRUS-Bx was better than with MRI-TBx in the detection rate of non-csPCa; Yet no significant difference between MRI-TBx and TRUS-Bx was found in Gleason score  $\geq 7$ .

The main reason for a negative MRI-TBx when patients with PI-RADS 3 or Gleason score  $< 7$  was the possibility of invisible PCa on MRI, and numerous studies about the relationship between MRI findings and pathological specimens of prostatectomy showed that 30–48% of PCa patients were underestimated on MRI (35,36). In addition, the failure of MRI-TBx might also be caused by varying agreement of inter-reader on MRI imaging, patient movement, prostate movement/deformation, incorrect match of image planes, especially at the base of the prostate (37). Furthermore, the slightly lower detection rate of PCa by MRI-TBx in our cohort might also be related to differences in the biopsy learning curve (18). In the screened literature, both TRUS-Bx and MRI-TBx are performed on the same patient, and targeted biopsy was first performed. If MRI-TBx is first performed, needle tracks after biopsy may make TRUS-Bx more likely to puncture sample tissues of the same position as MRI-TBx, even if they are blinding. Meanwhile, some researchers suggested that finding suspicious lesions on MRI might have a positive impact on TRUS-Bx results (29,38). This deviation results in the thinking whether targeted biopsy prior to systematic biopsy affect the results of this meta-analysis. Although these patients are interested in MRI in active monitoring, it is not only an early re-classification strategy, but also a monitoring tool. The results of MRI-TBx depend on the identification of suspicious MRI lesions, which may lead to potential bias.

Ultimately, several limitations still existed in our meta-analysis as follows: (I) the included studies were mainly conducted on Germans, only five studies had other population. Thus, more researches should pay attention to the influence of ethnicity factors to avoid selection bias in

the subsequent years; (II) the threshold effect and obvious heterogeneity existed in this study, which might be due to large differences in reagent resources, lifestyle, ethnicity, gender, age, cores of biopsy, type of determination, and critical values; (III) the present meta-analysis included only 10 studies, which might undermine the reliability of our results; (IV) evaluating negative results is necessary, but we could not get the original data of included studies. Therefore, more well-designed studies should be conducted on large sample sizes to verify the guidance value of selecting the better prostate biopsy for PCa-suspected patients.

## Conclusions

In summary, this meta-analysis revealed that using TRUS-Bx was better than MRI-TBx for the diagnosis of PCa in PI-RADS 3; Besides, TRUS-Bx had an advantage over MRI-TBx in the detection for non-csPCa in PI-RADS 4 or 5. Therefore, PI-RADS could be used as an MRI evaluation system in the selection of prostate biopsy. More large-scale multicenter prospective randomized controlled trials are warranted to verify the effectiveness of PI-RADS in the guidance of PCa patients.

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## Footnote

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

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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