*research article*

# Effects of dynamic contrast enhancement on transition zone prostate cancer in Prostate Imaging Reporting and Data System Version 2.1

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**Background.** The aim of the study was to analyse the effects of dynamic contrast enhanced (DCE)-MRI on transitional-zone prostate cancer (tzPCa) and clinically significant transitional-zone prostate cancer (cs-tzPCa) in Prostate Imaging Reporting and Data System (PI-RADS) Version 2.1.

**Patients and methods.** The diagnostic efficiencies of T2-weighted imaging (T2WI) + diffusion-weighted imaging (DWI), T2WI + dynamic contrast-enhancement (DCE), and T2WI + DWI + DCE in tzPCa and cs-tzPCa were compared using the score of ≥ 4 as the positive threshold and prostate biopsy as the reference standard.

**Results.** A total of 425 prostate cases were included in the study: 203 cases in the tzPCa group, and 146 in the cs-tzPCa group. The three sequence combinations had the similar areas under the curves in diagnosing tzPCa and cs-tzPCa (all $P > 0.05$). The sensitivity of T2WI + DCE and T2WI + DWI + DCE (84.7% and 85.7% for tzPCa; 88.4% and 89.7% for cs-tzPCa, respectively) in diagnosing tzPCa and cs-tzPCa was significantly greater than that of T2WI + DWI (79.3% for tzPCa; 82.9% for cs-tzPCa). The specificity of T2WI + DWI (86.5% for tzPCa; 74.9% for cs-tzPCa) were significantly greater than those of T2WI + DCE and T2WI + DWI + DCE (68.0% and 68.5% for tzPCa; 59.1% and 59.5% for cs-tzPCa, respectively) (all $P < 0.05$). The diagnostic efficacies of T2WI + DCE and T2WI + DWI + DCE had no significant differences (all $P > 0.05$).

**Conclusions.** DCE can improve the sensitivity of diagnosis for tzPCa and cs-tzPCa, and it is useful for small PCa lesion diagnosis.

Key words: prostate cancer; transitional zone; magnetic resonance imaging; dynamic contrast enhancement

## Introduction

Prostate cancer (PCa) is a common malignant tumour and has the second highest incidence of all cancers worldwide in males[1]; it is the second deadliest among male cancer patients in the United States.[2] Prostate-specific antigen (PSA) assays and magnetic resonance imaging (MRI) are widespread in the diagnosis and follow-up examination of PCa, and thus the PCa detection rate continues to increase yearly worldwide.[3] MRI is a non-invasive examination and can clearly show the anatomy of the prostate. It is one of the most valuable imaging methods for the diagnosis of PCa.[4,5] PCa is primarily located in the peripheral zone, but approximately 25% of PCa cases are lo-

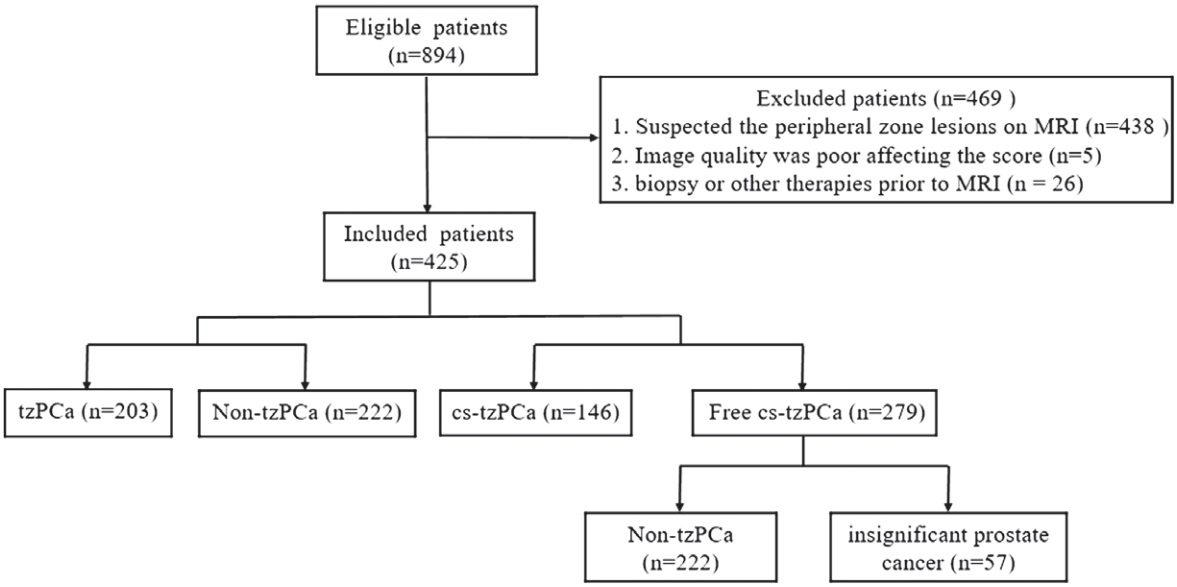


**FIGURE 1.** Flowchart showing the patient recruitment process.

cated in the transitional zone. The MRI features of PCa in the transitional zone are similar to central glandular benign prostatic hyperplasia (BPH) in signal intensity and morphological characteristics, thus making it difficult to differentiate between BPH and PCa.[6] The early diagnosis and timely intervention of PCa is key to improve the prognosis of PCa patients.[7] Thus, it is of great significance to improve the diagnostic accuracy of transitional-zone prostate cancer (tzPCa).

The Prostate Imaging Reporting and Data System (PI-RADS) is currently recognized as an important guideline for prostate examination and diagnosis via MRI. The first and second editions of PI-RADS guidelines (v1, v2) were proposed in 2012 and 2015, respectively.[8,9] In 2019, PI-RADS Version 2.1 (v2.1) reformulated the research specifications for MRI acquisition technology in prostate scanning and analysed the diagnostic values of multiparametric MRI (mpMRI), which includes T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE)-MRI sequencing.[10] A prostate transitional-zone lesion score criterion of PI-RADS v2.1 only includes T2WI and DWI sequences; DCE-MRI has no effect on the transitional-zone lesion score. The benefits and drawbacks of the DCE-MRI sequence for PCa diagnosis are increasingly being recognized. The advantages of omitting the DCE sequence are that it shortens the scan time and reduces examination costs. However, the DCE sequence with a higher spatial resolution could be less prone to motion artefacts, susceptibility artefacts from metallic implants, or rectal gas. It can be used informally as a "safety-net" or "back-up" sequence to detect lesions that might otherwise be missed on T2WI or DWI, *e.g.*, when the readers have less experience or when there is insufficient image quality.[10-12] Therefore, the value of DCE-MRI as a routine sequence has been debated.[10,13-17]

Prompt intervention is needed for clinically significant prostate cancer (Gleason score ≥ 3 + 4), which usually has poor differentiation, a damaged gland structure, a high degree of malignancy, and strong invasiveness.[9] This study used three sequence combinations (T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE) to analyse the diagnostic value of DCE-MRI for detecting tzPCa and clinically significant transitional-zone prostate cancer (cs-tzPCa) in PI-RADS Version 2.1, using transperineal ultrasound-guided prostate biopsy as the reference standard.

## Patients and methods

### Patients

The Institutional Review Board (IRB) of our hospital approved this retrospective study (IRB number JS-2114), and the requirement for informed consent was waived. The clinical and MRI data of 894 patients with prostate diseases admitted to our hospital from January 2015 to December 2019 were continuously collected. The inclusion criteria were

**TABLE 1.** Sequence parameters for prostate MRI

| Parameters | T2WI | DWI | DCE |
|---|---|---|---|
| Sequence | FRFSE | SE-EPI | 3D-GRE |
| TR/TE (ms) | 4137/86 | 4200/90 | 4.3/1.3 |
| Flip angle | 110° | 90° | 12° |
| Echo train length | 32 | 1 | N/A |
| FOV (mm × mm) | 270 × 270 | 360 × 360 | 400 × 400 |
| Matrix size | 288 × 192 | 128 × 96 | 320 × 192 |
| Slice thickness (mm) | 3.0 | 3.0 | 3.0 |
| Other | | b values = 0, 50, 100, 150, 200, 500, 800, 1000, 1500, 2000 sec/mm$^2$ | Temporal resolution < 10s, total scan time of 5 min |

DCE = dynamic contrast-enhancement; DWI = diffusion-weighted imaging; FOV = field of view; FRFSE = fast relaxation fast spin echo; SE-EPI = spin echo echo planar imaging; T2WI = T2-weighted imaging; TE = time echo; TR = repetition time; 3D-GRE = 3D-gradient echo

as follows: (1) a complete MRI examination including T1WI, T2WI, and DWI with the corresponding apparent diffusion coefficient (ADC) map and DCE sequences; (2) diagnosis confirmed by trans-perineal ultrasound-guided prostate biopsy after MRI; and (3) no biopsy, radiation therapy, chemotherapy, hormonal therapy, or other therapies prior to MRI examination. The exclusion criteria were as follows: (1) after MRI examination, the lesion was suspected to be located in the peripheral zone (n = 438); (2) poor MRI image quality affected scoring (n = 5); and (3) biopsy or other therapies prior to MRI (n = 26). Figure 1 shows the flowchart of the patient recruitment process. In total, 425 cases were included. Non-tzPCa indicates transitional-zone lesions other than cancer, such as BPH or normal prostate. Free cs-tzPCa indicates transitional-zone lesions other than clinically significant prostate cancer, including insignificant prostate cancer and non-tzPCa.

## MRI protocol

This work used a 3.0-T, eight-channel, surface-phased array coil abdominal MRI scanning system (GE750; GE Health care, Milwaukee, WI, USA). The centre of the coil was placed at the pubic symphysis during positioning and fixed with a band to reduce artefacts from breathing movements. The scan sequence included axial T1WI and T2WI, coronal and sagittal T2WI, DWI, and DCE. When the b-value was 100 and 1000 sec/mm$^2$, we used the corresponding ADC graph for evaluation. Gadolinium diethylene-triamine penta-acetic acid (Gd-DTPA) offered enhanced contrast at a dose of 0.1 mmol/kg and a flow rate of 3 ml/s. The MRI image-acquisition parameters are shown in Table 1.

## Pathological diagnosis

The Gleason grading system for histopathological grading of PCa was adopted.[18] Here, cs-tzPCa was confirmed if the tumour's Gleason score was ≥ 3 + 4 with or without ≥ 0.5-cm$^3$ tumour volume and/or extraprostatic extension.[9,19] According to the 2014 International Society of Urological Pathology (ISUP) criteria, cs-tzPCa was defined as ISUP grade≥2.[20] Patients biopsied all underwent a 12-core systematic trans-perineal ultrasound-guided prostate biopsy by one urinary specialist. The prostate gland was divided into 11 regions on ultrasound scans. At least one additional targeted biopsy was performed; the cognitive targeted biopsy using cognitive registration was based on zonal anatomy or imaging landmarks such as remarkable nodules. The details of the cognitive targeted biopsy are as follows: first, the urologist reviewed the MRI results; and second, the urologist used the MRI information to perform the targeted biopsy for the most remarkable nodules guided by ultrasound images. A pathologist reported the pathological score of prostate biopsy specimens. The radiologist matched the lesions with the highest PI-RADS v2.1 scores on the MRI images with the pathology report.

## Image analysis

Two radiologists with 10 and 5 years of experience in prostate imaging/diagnosis independently

analysed the images under double-blinded conditions. The radiologists scored the images of index lesions in each sequence using PI-RADS v2.1 and then calculated scores for T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE. When multiple lesions were present, the lesion with the highest PI-RADS score was used for statistical analysis. In the case of disagreement between the two radiologists, the final score was discussed with a third radiologist to reach a consensus. On PI-RADS v2.1, both T2WI and DWI scored 1–5 points whereas the DCE score was binary [negative (–) or positive (+)]. The final total score of T2WI + DCE and T2WI + DWI + DCE was increased by one point when the image showed early and focal enhancement (positive) of DCE; the final total score of T2WI + DCE and T2WI + DWI + DCE remained unchanged when the image was negative regarding DCE. The final score was 5 when the image scored 5 on T2WI regardless of the DWI and DCE scores. Detailed scoring criteria are shown in Table 2. Figure 2 shows a case of cs-tzPCa located in the right lobe of the prostate.

## Statistical analysis

SPSS version 22.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 15.0 (MedCalc Software, Ostend, Belgium) were used for statistical analysis. Agreement of readings between the two radiologists was evaluated by a kappa (κ) coefficient with $\kappa < 0.20$ indicating no agreement, $\kappa = 0.21–0.40$ indicating fair agreement, $\kappa = 0.41–0.60$ indicating moderate agreement, $\kappa = 0.61–0.80$ indicating good agreement, and $\kappa = 0.81–1.00$ indicating excellent agreement. Using PI-RADS ≥ 4 as the positive threshold and prostate biopsy as the reference standard, receiver operating characteristic (ROC) curves for T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE in the diagnosis of tzPCa and cs-tzPCa were separately drawn to calculate areas under the curve (AUCs), sensitivities, specificities, positive predictive values (PPVs), negative predictive values (PNVs), and accuracies to evaluate the corresponding diagnostic efficacies. We also compared differences among the detection rates of tzPCa and cs-tzPCa via three sequence combinations. The DeLong test was used to evaluate differences among AUCs, and McNemar's test was used to compare the sensitivities, specificities, and accuracies of different sequence combinations. The chi-square test was used to compare differences among the detection rates. $P < 0.05$ was considered statistically significant for all statistical tests.

**TABLE 2.** Scoring criteria of transition zone prostate for three sequence combinations

| Scoring Criteria | | | | | |
|---|---|---|---|---|---|
| T2WI | DWI | DCE | T2WI + DWI | T2WI + DCE | T2WI + DWI + DCE |
| 1 | 1~5 | – | 1 | 1 | 1 |
| 1 | 1~5 | + | 1 | 2 | 2 |
| 2 | 1~3 | – | 2 | 2 | 2 |
| 2 | 1~3 | + | 2 | 3 | 3 |
| 2 | 4~5 | – | 3 | 2 | 3 |
| 2 | 4~5 | + | 3 | 3 | 4 |
| 3 | 1~4 | – | 3 | 3 | 3 |
| 3 | 1~4 | + | 3 | 4 | 4 |
| 3 | 5 | – | 4 | 3 | 4 |
| 3 | 5 | + | 4 | 4 | 5 |
| 4 | 1~5 | – | 4 | 4 | 4 |
| 4 | 1~5 | + | 4 | 5 | 5 |
| 5 | 1~5 | – | 5 | 5 | 5 |
| 5 | 1~5 | + | 5 | 5 | 5 |

DCE = dynamic contrast-enhancement; DWI = diffusion-weighted imaging; T2WI = T2-weighted imaging

**TABLE 3.** Clinicopathological data of patients included in this study

| Clinicopathological data | Patients |
|---|---|
| Age (year), Mean ± SD | 66 ± 9.0 |
| T-PSA (ng/ml), Median (Upper and lower quartiles) | 9.4 (6.3 + 15.4) |
| tzPCa, n (%) | 203 (48%) |
| Non-tzPCa, n (%) | 222 (52%) |
| cs-tzPCa, n (%) | 146 (34%) |
| Free cs-tzPCa, n (%) | 279 (66%) |
| Tumor size (mm), Median (Upper and lower quartiles) | 12.7 (9.1 + 22.5) |
| **GS, n (%)** | |
| 3 + 3 | 57 (28%) |
| 3 + 4 | 56 (28%) |
| 4 + 3 | 24 (12%) |
| 3 + 5 | 3 (1.5%) |
| 4 + 4 | 18 (8.9%) |
| 4 + 5 | 28 (13.8%) |
| 5 + 3 | 1 (0.5%) |
| 5 + 4 | 13 (6.4%) |
| 5 + 5 | 3 (1.5%) |

cs-tzPCa = clinically significant transitional-zone prostate cancer; PSA = prostate-specific antigen; SD = standard deviation; tzPCa = transitional-zone prostate cancer

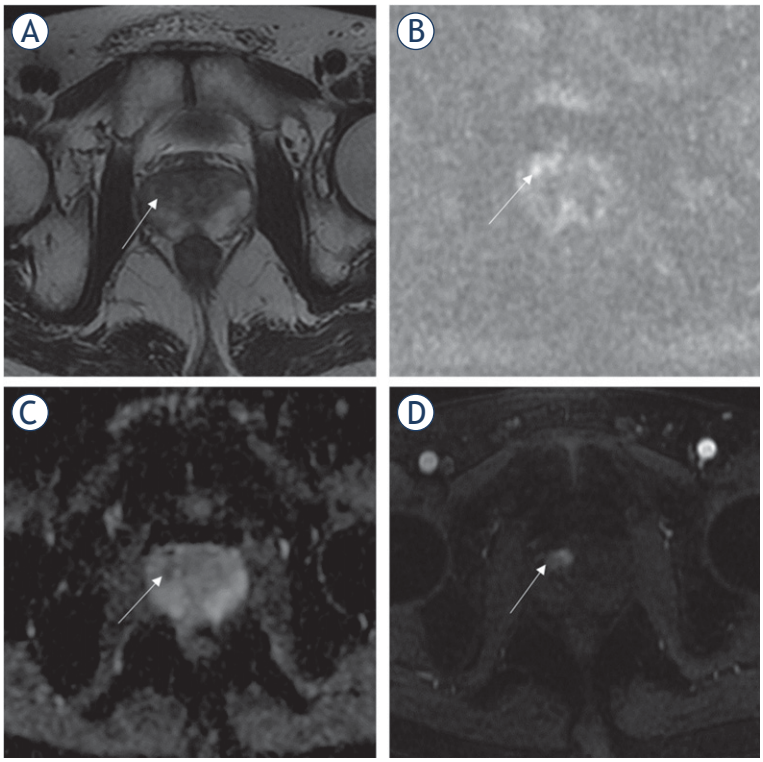


**FIGURE 2.** Images from a 62-year-old male patient with a total prostate-specific antigen (PSA) of 7.66 ng/mL. **(A)** Axial T2-weighted imaging (T2WI) showed focal hypointensity on the right lobe of the prostate in the transitional zone with a blurred margin and a T2WI score of 3. **(B)** Diffusion-weighted imaging (DWI) showed a slight increase in lesion signal. **(C)** Reduced corresponding apparent diffusion coefficient (ADC) value with a score of 3. **(D)** dynamic contrast-enhancement (DCE) showed obvious enhancement in the early stage of the lesion, thus indicating that the DCE score was positive. Scores were 3, 4, and 4 based on T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE, respectively. The lesion was confirmed to be clinically significant transitional-zone prostate cancer (cs-tzPCa) based on biopsy (Gleason score of 5 + 4).

# Results

## Clinicopathological data

This study included 425 prostate cases per the aforementioned inclusion criteria. There were 203 cases in the tzPCa group (48%) and 222 in the non-tzPCa group (52%). There were 146 cases in the cs-tzPCa group (34%) and 279 in the free cs-tzPCa group (66%). The patient age range was 34–86 years (mean age, 66 years), and the median PSA value was 9.4 ng/mL. The main clinical manifestations were elevated PSA, dysuria, frequent urination, and urinary urgency. Abnormalities may be found in the patients during digital rectal examination, including a stiff prostate or palpation of nodules. Table 3 shows the patients' clinicopathological information.

## Agreement between the two radiologists

The PI-RADS v2.1 scores provided by the two radiologists were analysed for agreement. The reading agreement between PI-RADS v2.1 scores for T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE was $\kappa$ = 0.869, 0.855, and 0.868, respectively.

## Comparative analysis of the diagnostic efficacies of three sequence combinations in tzPCa and cs-tzPCa

The diagnostic efficacies of three sequence combinations in tzPCa and cs-tzPCa were shown in Tables 4 and 5. The AUCs were 0.863, 0.868, and 0.863 for tzPCa and 0.840, 0.833, and 0.824 for cs-tzPCa in T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE, respectively. The AUCs of three sequence combinations in diagnosing tzPCa and cs-tzPCa had no significant differences (all $P > 0.05$). The sensitivity of T2WI + DCE and T2WI + DWI + DCE in diagnosing tzPCa and cs-tzPCa was significantly greater than that of T2WI + DWI (all $P < 0.05$). The specificity and accuracy of T2WI + DWI in diagnosing tzPCa and cs-tzPCa were significantly greater than those of T2WI + DCE and T2WI + DWI + DCE (all $P < 0.05$). The sensitivity, specificity, and accuracy of T2WI + DCE and T2WI + DWI + DCE in diagnosing tzPCa and cs-tzPCa had no significant differences (all $P > 0.05$).

## Comparative analysis of the cancer detection rates of three sequence combinations in tzPCa and cs-tzPCa

Figures 3 and 4 show the cancer detection rates of three sequence combinations in tzPCa and cs-tzPCa. When the PI-RADS score was 4, T2WI + DWI had the highest cancer detection rate. The cancer detection rates of T2WI + DWI were significantly greater than those of T2WI + DCE and T2WI + DWI + DCE in tzPCa (69.4%, 29.8%, and 33.7%, respectively, all $P < 0.05$) and cs-tzPCa (43.9%, 19.2%, and 25.0%, respectively, all $P < 0.05$). The cancer detection rates of the three sequence combinations had no significant differences in tzPCa or cs-tzPCa when the PI-RADS score was 1, 2, 3, and 5 (all $P > 0.05$).

# Discussion

Some studies questioned whether DCE is a necessary sequence for routine MRI dynamic scanning

**TABLE 4.** Comparison of diagnostic efficacy of three sequence combinations in tzPCa

| | | tzPCa (n =203) | Non-tzPCa (n=222) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV(%) | Accuracy (%) | AUC (95% CI) |
|---|---|---|---|---|---|---|---|---|---|
| T2WI + DWI | ≥ 4 (n=191) | 161 | 30 | 79.3 | 86.5 | 84.3 | 82.1 | 83.1 | 0.863 (0.827–0.894) |
| | < 4 (n=234) | 42 | 192 | | | | | | |
| T2WI + DCE | ≥ 4 (n=243) | 172 | 71 | 84.7 | 68.0 | 70.8 | 83.0 | 76.0 | 0.868 (0.832 + 0.899) |
| | < 4 (n=182) | 31 | 151 | | | | | | |
| T2WI + DWI + DCE | ≥ 4 (n=244) | 174 | 70 | 85.7 | 68.5 | 71.3 | 84.0 | 76.7 | 0.863 (0.827 + 0.895) |
| | < 4 (n=181) | 29 | 152 | | | | | | |
| [a]*P* | | | | 0.001 | < 0.001 | NA | NA | 0.002 | 0.424 |
| [b]*P* | | | | < 0.001 | < 0.001 | NA | NA | < 0.001 | 0.968 |
| [c]*P* | | | | 0.500 | 1.000 | NA | NA | 0.250 | 0.369 |

AUC = area under curve; CI = confidence interval; DCE = dynamic contrast-enhancement; DWI = diffusion-weighted imaging; NPV = negative predictive value; PPV = positive predictive value; tzPCa = transitional-zone prostate cancer; T2WI = T2-weighted imaging

[a]*P* value between T2WI + DWI and T2WI + DCE; [b]*P* value between T2WI + DWI and T2WI + DWI + DCE; [c]*P* value between T2WI + DCE and T2WI + DWI + DCE

**TABLE 5.** Comparison of diagnostic efficacy of three sequence combinations in cs-tzPCa

| | | cs-tzPCa (n=146) | Free cs-tzPCa (n=279) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) | AUC (95%CI) |
|---|---|---|---|---|---|---|---|---|---|
| T2WI + DWI | ≥ 4 (n=191) | 121 | 70 | 82.9 | 74.9 | 63.4 | 89.3 | 77.6 | 0.840 (0.802–0.874) |
| | < 4 (n=234) | 25 | 209 | | | | | | |
| T2WI + DCE | ≥ 4 (n=243) | 129 | 114 | 88.4 | 59.1 | 53.1 | 90.7 | 69.2 | 0.833 (0.795–0.868) |
| | < 4 (n=182) | 17 | 165 | | | | | | |
| T2WI + DWI + DCE | ≥ 4 (n=244) | 131 | 113 | 89.7 | 59.5 | 53.7 | 91.7 | 69.9 | 0.824 (0.785–0.869) |
| | < 4 (n=181) | 15 | 166 | | | | | | |
| [a]*P* | | | | 0.008 | < 0.001 | NA | NA | < 0.001 | 0.430 |
| [b]*P* | | | | 0.002 | < 0.001 | NA | NA | < 0.001 | 0.101 |
| [c]*P* | | | | 0.500 | 1.000 | NA | NA | 0.250 | 0.193 |

AUC = area under curve; CI = confidence interval; DCE = dynamic contrast-enhancement; DWI = diffusion-weighted imaging; NPV = negative predictive value; PPV = positive predictive value; tzPCa = transitional-zone prostate cancer; T2WI = T2-weighted imaging

[a]*P* value between T2WI + DWI and T2WI + DCE; [b]*P* value between T2WI + DWI and T2WI + DWI + DCE; [c]*P* value between T2WI + DCE and T2WI + DWI + DCE

of the prostate.[13-17] To the best of our knowledge, no prior studies have yet analysed the value of DCE-MRI in diagnosing tzPCa and cs-tzPCa. To investigate whether DCE-MRI can improve the diagnostic accuracy of tzPCa, this study innovatively compared and analysed the diagnostic efficiencies of T2WI + DWI, T2WI + DCE, and T2WI + DWI + DCE for detecting tzPCa and cs-tzPCa. This study had a large sample size and included 425 prostate cases—the results were reliable. The results of this study showed T2WI + DWI had higher specificity and accuracy, and DCE-MRI had higher sensitivity in diagnosing tzPCa and cs-tzPCa. DCE-MRI could have a potential impact on the detection of tzPCa and cs-tzPCa.

The AUCs of three sequence combinations in diagnosing tzPCa and cs-tzPCa had no significant differences. However, AUC values only reflect the global performance of the test; sensitivity and specificity trade-offs must also be compared between the three sequence combinations. The specificity and accuracy of T2WI + DWI was significantly greater than those of T2WI + DCE and T2WI + DWI + DCE in diagnosing tzPCa and cs-tzPCa. The prostate patients with an elevated PSA value and a positive digital rectal examination were more con-

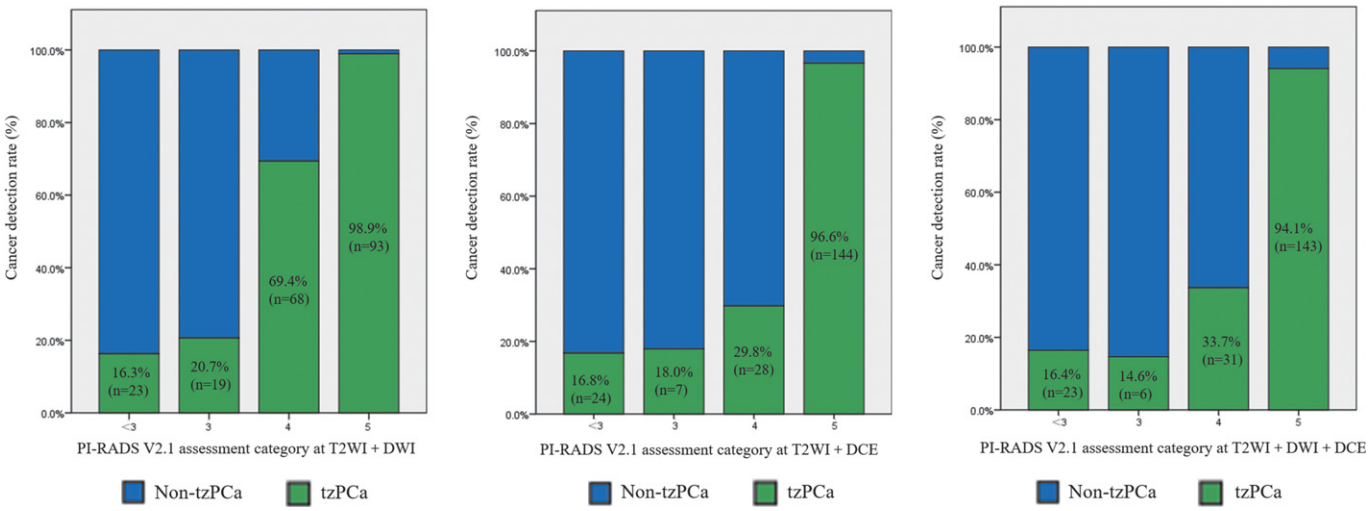


**FIGURE 3.** Histograms showing cancer detection rates of tzPCa based on the T2-weighted imaging (T2WI) + diffusion-weighted imaging (DWI), T2WI + dynamic contrast-enhancement (DCE), and T2WI + DWI + DCE.

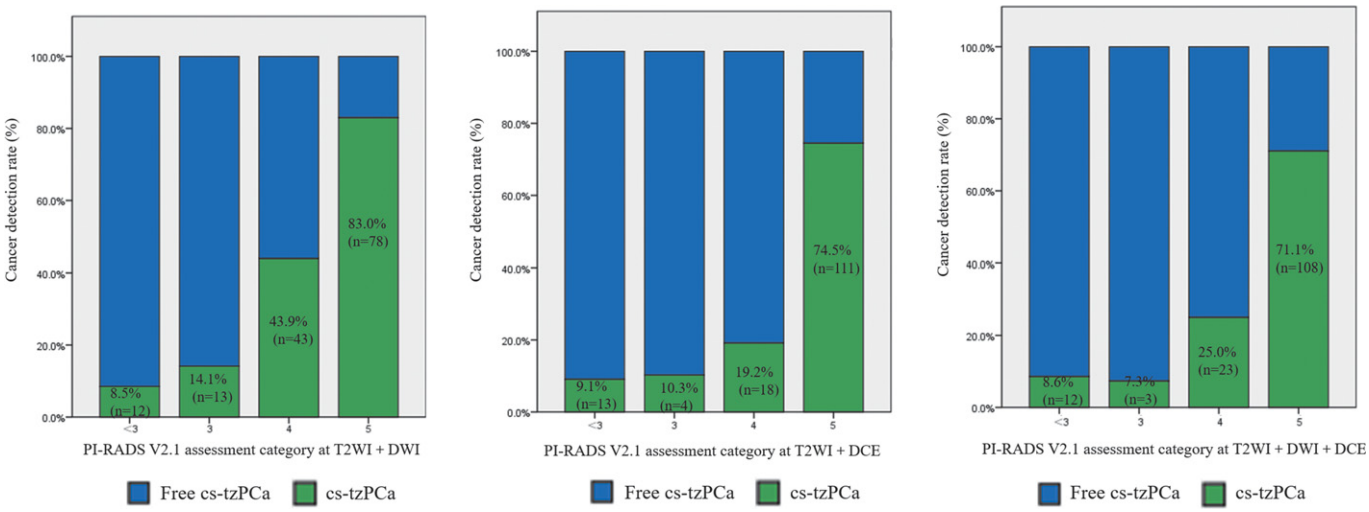


**FIGURE 4.** Histograms showing cancer detection rates of cs-tzPCa based on the T2-weighted imaging (T2WI) + diffusion-weighted imaging (DWI), T2WI + dynamic contrast-enhancement (DCE), and T2WI + DWI + DCE.

fident in the diagnosis of cancer when DWI results were positive. T2WI + DCE and T2WI + DWI + DCE showed significantly higher sensitivity in both tzPCa and cs-tzPCa. Tamada *et al.*[21] compared and analysed the diagnostic efficiencies of PI-RADS v2.1 scoring between T2WI + DWI + DCE and T2WI + DWI in clinically significant prostate cancer of 165 cases. Their results were similar to ours, but their study did not distinguish between peripheral zone cancers and transitional zone cancers.

Eleven tzPCa cases that were not diagnosed by T2WI + DWI were diagnosed by T2WI + DCE and T2WI + DWI + DCE. The reason is that DCE can clearly show small PCa lesions and improve the sensitivity of diagnosis[22], while the T2WI and DWI sequences are more likely to miss small lesions. A previous study demonstrated that DCE also improves the differential diagnosis of lesions located on the front edge of the peripheral zone with an unclear transition zone from the normal transition zone.[19] T2WI + DCE and T2WI + DWI + DCE had higher diagnostic sensitivity, which could potentially help reduce repeat biopsies when the results were negative. However, active surveillance is still necessary. PCa is characterized by more angiogenic factors and numerous tumour blood vessels

that exhibit increased permeability versus healthy blood vessels. PCa lesions typically enhance earlier and more obviously on DCE than adjacent prostate tissues.[23,24] Vascular permeability also increases in benign diseases such as BPH.[25] These factors might explain the low specificity and high false-positive rate of T2WI + DCE and T2WI + DWI + DCE in the diagnosis of tzPCa and cs-tzPCa.

When the PI-RADS score was 4, the cancer detection rates of T2WI + DWI were significantly greater than those of T2WI + DCE and T2WI + DWI + DCE in tzPCa and cs-tzPCa, which showed T2WI + DWI had lower false-positive rate than T2WI + DCE and T2WI + DWI + DCE. This may be because when BPH lesions strengthened earlier and were more obvious on DCE than adjacent prostate tissues, and when the score of T2WI or T2WI + DWI was 3, the scores of T2WI + DCE and T2WI + DWI + DCE would be increased by one point, thus becoming 4.

This study does have some limitations: (1) This was a single-centre clinical retrospective analysis, which may have selection bias. In future work, we will use a multi-centre, prospective clinical study. (2) This work used prostate biopsy as the reference standard. Prostate biopsy specimens sometimes did not reflect the final pathological findings, which might have yielded false-negative results. (3) In addition to providing qualitative parameters, DCE-MRI can also provide quantitative and semi-quantitative parameters[26], which were not discussed further in this work. It remains unclear whether these parameters are useful in the early diagnosis of tzPCa and cs-tzPCa.

In conclusion, DCE-MRI can improve the sensitivity of diagnosis and has a potential impact on the detection and active surveillance of tzPCa and cs-tzPCa. Meanwhile, DCE-MRI can clearly show small cancers and is useful for small PCa lesion diagnosis.

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## References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; **71:** 209-49. doi: 10.3322/caac.21660
2. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin* 2021; **71:** 7-33. doi: 10.3322/caac.21654
3. Teoh J, Hirai H W, Ho J, Chan F, Tsoi K, Ng C. Global incidence of prostate cancer in developing and developed countries with changing age structures. *PLoS One* 2019; **14:** e221775. doi: 10.1371/journal.pone.0221775
4. Turkbey B, Brown AM, Sankineni S, Wood BJ, Pinto PA, Choyke PL. Multiparametric prostate magnetic resonance imaging in the evaluation of prostate cancer. *CA Cancer J Clin* 2016; **66:** 326-36. doi: 10.3322/caac.21333
5. Ueno Y, Tamada T, Bist V, Reinhold C, Miyake H, Tanaka U, et al. Multiparametric magnetic resonance imaging: current role in prostate cancer management. *Int J Urol* 2016; **23:** 550-7. doi: 10.1111/iju.13119
6. Litjens G, Elliott R, Shih N, Feldman M, Kobus T, Kaa C, et al. Computer-extracted features can distinguish noncancerous confounding disease from prostatic adenocarcinoma at multiparametric MR imaging. *Radiology* 2016; **278:** 135-45. doi: 10.1148/radiol.201514285
7. Remmers S, Roobol M J. Personalized strategies in population screening for prostate cancer. *Int J Cancer* 2020; **147:** 2977-87. doi: 10.1002/ijc.33045
8. Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, et al. ESUR prostate MR guidelines 2012. *Eur Radiol* 2012; **22:** 746-57. doi: 10.1007/s00330-011-2377-y. 9
9. Gupta RT, Mehta KA, Turkbey B, Verma S. PI-RADS: past, present, and future. *J Magn Reson Imaging* 2020; **52:** 33-53. doi: 10.1002/jmri.26896
10. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, et al. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. *Eur Urol* 2019; **76:** 340-51. doi: 10.1016/j.eururo.2019.02.033
11. Gatti M, Faletti R, Calleris G, Giglio J, Berzovini C, Gentile F, et al. Prostate cancer detection with biparametric magnetic resonance imaging (bpMRI) by readers with different experience: performance and comparison with multiparametric (mpMRI). *Abdom Radiol* 2019; **44:** 1883-93. doi: 10.1007/s00261-019-01934-3
12. Wassberg C, Akin O, Vargas HA, Dave AS, Zhang Jb, Hricak H. The incremental value of contrast-enhanced MRI in the detection of biopsy-proven local recurrence of prostate cancer after radical prostatectomy: effect of reader experience. *AJR Am J Roentgenol* 2012; **199:** 360-6. doi: 10.2214/AJR.11.6923
13. Tamada T, Sone T, Jo Y, Hiratsuka J, Higaki A, Higashi H, et al. Locally recurrent prostate cancer after high- dose-rate brachytherapy: the value of diffusion-weighted imaging, dynamic contrast-enhanced MRI, and T2- weighted imaging in localizing tumors. *AJR Am J Roentgenol* 2011; **197:** 408-14. doi: 10.2214/AJR.10.5772
14. Kuhl CK, Bruhn R, Krämer N, Nebelung S, Heidenreich A, Schrading S. Abbreviated biparametric prostate MR imaging in men with elevated prostate-specific antigen. *Radiology* 2017; **285:** 493-505. doi: 10.1148/radiol.2017170129
15. Junker D, Steinkohl F, Fritz V, Bektic J, Tokas T, Aigner F, et al. Comparison of multiparametric and biparametric MRI of the prostate: are gadolinium-based contrast agents needed for routine examinations? *World J Urol* 2019; **37:** 691-9. doi: 10.1007/s00345-018-2428-y
16. Di Campli E, Delli P A, Seccia B, Cianci R, d'Annibale M, Colasante A, et al. Diagnostic accuracy of biparametric vs multiparametric MRI in clinically significant prostate cancer: comparison between readers with different experience. *Eur J Radiol* 2018; **101:** 17-23. doi: 10.1016/j.ejrad.2018.01.028
17. Huebner NA, Korn S, Resch I, Grubmüller B, Gross T, Gale R, et al. Visibility of significant prostate cancer on multiparametric magnetic resonance imaging (MRI)-do we still need contrast media? *Eur Radiol* 2021; **31:** 3754-64. doi: 10.1007/s00330-020-07494-1
18. Epstein JI, Amin MB, Reuter VE, Humphrey PA. Contemporary Gleason grading of prostatic carcinoma: an update with discussion on practical issues to implement the 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol* 2017; **41:** e1-7. doi: 10.1097/PAS.0000000000000820

19. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. *Eur Urol* 2016; **69:** 16-40. doi: 10.1016/j.eururo.2015.08.05

20. Oishi M, Shin T, Ohe C, Nassiri N, Palmer SL, Aron M, et al. Which patients with negative magnetic resonance imaging can safely avoid biopsy for prostate cancer? *J Urol* 2019; **201:** 268-76. doi: 10.1016/j.juro.2018.08.046

21. Tamada T, Kido A, Yamamoto A, Takeuchi M, Miyaji Y, Moriya T, et al. Comparison of biparametric and multiparametric MRI for clinically significant prostate cancer detection with PI-RADS version 2.1. *J Magn Reson Imaging* 2021; **53:** 283-91. doi: 10.1002/jmri.27283

22. Taghipour M, Ziaei A, Alessandrino F, Hassanzadeh E, Harisinghani M, Vangel M, et al. Investigating the role of DCE-MRI, over T2 and DWI, in accurate PI-RADS v2 assessment of clinically significant peripheral zone prostate lesions as defined at radical prostatectomy. *Abdom Radiol* 2019; **44:** 1520-7. doi: 10.1007/s00261-018-1807-6

23. Engelbrecht MR, Huisman HJ, Laheij RJ, Jager GJ, van Leenders GJ, Hulsbergen-Van De Kaa CA, et al. Discrimination of prostate cancer from normal peripheral zone and central gland tissue by using dynamic contrast-enhanced MR imaging. *Radiology* 2003; **229:** 248-54. doi: 10.1148/radiol.2291020200

24. Nicholson B, Theodorescu D. Angiogenesis and prostate cancer tumor growth. *J Cell Biochem* 2004; **91:** 125- 50. doi: 10.1002/jcb.10772

25. Verma S, Turkbey B, Muradyan N, Rajesh A, Cornud F, Haider MA, et al. Overview of dynamic contrast- enhanced MRI in prostate cancer diagnosis and management. *AJR Am J Roentgenol* 2012; **198:** 1277-88. doi: 10.2214/AJR.12.8510

26. Sanz-Requena R, Martí-Bonmatí L, Pérez-Martínez R, García-Martí G. Dynamic contrast-enhanced case- control analysis in 3T MRI of prostate cancer can help to characterize tumor aggressiveness. *Eur J Radiol* 2016; **85:** 2119-26. doi: 10.1016/j.ejrad.2016.09.022