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Prostate Magnetic Resonance Imaging Using the Prostate Imaging for Recurrence Reporting (PI-RR) Scoring System to Detect Recurrent Prostate Cancer: A Systematic Review and Meta-analysis

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Abstract
Background and objective: Prostate Imaging for Recurrence Reporting (PI-RR) was introduced in 2021 to standardize the interpretation and reporting of multiparametric magnetic resonance imaging (MRI) for prostate cancer following whole-gland treatment. The system scores image on a scale from 1 to 5 and has shown promising results in single- center studies. The aim of our systematic review and meta-analysis was to assess the diagnostic performance of the PI-RR system in predicting the likelihood of local recur- rence after whole-gland treatment.
Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for diagnostic test accuracy were followed. Relevant databases were searched up to December 2023. Primary studies met the eligibility criteria if they reported MRI diagnostic performance in prostate cancer recurrence using PI-RR. Diagnostic performance for MRI was assessed using two different cutoff points (3 or 4

for positivity according to the PI-RR system). A meta-analysis with a random- effects model was used to estimate pooled sensitivity and specificity values.
Key findings and limitations: Sixteen articles were identified for full-text reading, of which six were considered eligible, involving a total of 467 patients. Using a cutoff of PI-RR 3 (4 studies) for recurrent disease, the sensitivity was 77.8% (95% confidence interval [CI] 69.9–84.1%) and the specificity was 80.2% (95% CI 58.2–92.2%). Using a cut- off of PI-RR 4 (4 studies), the sensitivity was 61.9% (95% CI 35.6–82.7%) and the speci- ficity was 86.6% (95% CI 75.1–93.3%). Overall, the inter-rater agreement varied from fair to excellent.
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Conclusions and clinical implications: PI-RR is accurate in detecting local recurrence after whole-gland treatment for prostate cancer and shows fair-to-good to excellent inter-reader agreement. Overall, a PI-RR cutoff of 3 showed high sensitivity and specificity.
Patient summary: We reviewed studies that reported on how good MRI scans using a scoring system called PI-RR were in detecting recurrence of prostate cancer. We found that this system shows good performance, with fair to excellent agreement between dif- ferent radiologists.

1. Introduction

Prostate cancer is a public health problem as it is one of the most frequently diagnosed malignancies and a leading cause of mortality worldwide [1]. The main therapeutic options for localized disease include primary radiotherapy (RT) and radical prostatectomy (RP). However, approxi- mately 20–50% of these patients experience biochemical recurrence (BCR) by 10 years [2–4]. In these cases, accurate diagnosis and localization of disease recurrence is para- mount for effective patient management and guiding appropriate salvage treatment.
The imaging modalities available offer complementary roles. According to current guidelines, prostate-specific membrane antigen (PSMA) positron emission tomography/- computed tomography (PET/CT) is the most suitable imag- ing modality for detection of distant metastasis [5]. Conversely, for detection of local recurrences that could be amenable to curative-intent treatments, it has been demon- strated that

multiparametric magnetic resonance imaging (mpMRI) of the prostate is accurate in both post-RT and post-RP settings [6]. The European Association of Urology guidelines recommend the use of mpMRI and PET/CT for cases of BCR after RT. In addition, guidelines from the Amer- ican Society for Radiation Oncology, American Urological Association, and the National Comprehensive Cancer Net- work recommend mpMRI in patients experiencing BCR after RP to assess for local recurrence [7–9].

The Prostate Imaging for Recurrence Reporting (PI-RR) scoring system was introduced in 2021 to standardize mpMRI interpretation and reporting in prostate cancer cases following whole-gland treatment (RT or RP) [10]. Indi- vidual studies that evaluated the performance of mpMRI using PI-RR have shown encouraging results [11–16]. The PI-RR system uses a 5-point scale to classify and document local recurrence in patients with prostate cancer patient [10]. A lesion with a score of 1 or 2 points is defined as a very low or low likelihood of recurrence; a score of 3 points is defined as uncertain; and a score of 4 or 5 points is defined as a high or very high likelihood of recurrence.

To the best of our knowledge, there have been no meta- analyses on the performance of the PI-RR system in identi- fying prostate cancer recurrence. The aim of our systematic review and meta-analysis was to assess the diagnostic per- formance of the PI-RR system in detecting the presence of local recurrence of prostate cancer after whole-gland treatment.

2. Methods

2.1. Search strategy

Our study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines on diagnostic test accuracy [17]. The literature was searched up to December 2023 in the PubMed/MEDLINE, EMBASE, and Cochrane databases. The search strategy for each database is provided in Supplemen- tary Table 1. The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42024506028).

2.2. Inclusion and exclusion criteria

We included studies that evaluated the diagnostic perfor- mance of the PI-RR system for detection of prostate cancer recurrence after whole-gland therapy. We excluded case reports, case series, letters to the editor, and review articles. There were no language restrictions. The population, index test, and target condition approach was used to define study eligibility according to the Cochrane handbook on systematic reviews of diagnostic test accuracy [18]. The terms used in the database searches are included in Supplementary Table 1.

2.3. Assessment of study quality

The quality of all eligible studies was assessed by two reviewers independently using the Quality Assessment of Diagnostic Studies (QUADAS)-2 tool [19]. In cases of any discrepancy between the two reviewers, a third reviewer was involved to resolve the issue via consensus.

2.4. Data extraction

Two reviewers conducted the study selection indepen- dently and extracted relevant data from the selected studies into a standardized form, including study characteristics, demographics, and diagnostic performance of MRI (includ- ing true positive, false positive, true negative, and false neg- ative rates). Any disagreement

between the two reviewers was resolved via consensus with the assistance of a third reviewer.

2.5. Statistical analysis

Diagnostic performance for MRI was assessed using two dif- ferent cutoff points (PI-RR 3 or 4) to define imaging-

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predicted disease recurrence. In studies with multiple read- ers, the consensus result was used for meta-analysis. If con- sensus values were not reported, the average results among the readers were calculated for true positive, false positive, true negative, and false negative rates for use in the meta- analysis. When available, the diagnostic performance per MRI sequence (T2-weighted imaging [T2WI], dynamic con- trast enhancement [DCE], and diffusion-weighted imaging [DWI]) was also included. Pooled sensitivity and specificity values with 95% confi- dence intervals (CIs) were calculated (random-effect analy- sis). Analysis was performed to investigate potential reasons for heterogeneity. Inter-rater agreement was recorded and Cohen's j was interpreted according to previ- ous reports [20]. All analyses were performed using Rstudio 2023.09.1 with R v4.3.2 and the mada and meta packages.

3. Results

3.1. Study selection

The initial search yielded 632 articles (Fig. 1). After screen- ing, the full text of 16 articles was assessed, of which six studies involving a total of 467 patients were considered eligible [11–16]. The characteristics of these studies are listed in Table 1 and Table 2. One study only reported

Fig. 1 – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for study selection. * Park et al [16] was only included in the qualitative analysis.

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Table 1 – Main characteristics of the studies included in the review

Study and location	Design	TSA Pts (d)	Patient age (yr)
Bergaglio 2023 [11] Italy			72.4 a
Franco 2023 [13] Spain, Italy, and Portugal			
Kim 2022 [15] South Korea			

73.4 (76.1–69.1) b
72 (62–82) b
66.2 ± 6.9 c
Time since iTx
5.1 (8.51.5) b
2.5 (0.2–17.2) d
1042.7 ± 820.5 c
Reference standard
Correlative imaging, PSA after Tx/FU, new lesions on subsequent imaging
Lesion Bx, PSA after Tx/FU, lesion size at FUI
PSA levels after Tx/FU, lesion size at FUI
Prostate-specific antigen (ng/ml)
SCR 35
23 SCR 271
179
SCR 46 176
76
RT: 8 RP: 68
120
RT: 12 RP: 108
468 All RPg
Before iTx (ng/ml)
NA
7.34 (4.3–41.2) b
26.3 ± 108.2 c
MRI or BCR
1.01 a,e
0.27 (0.21–0.76) b,e
0.32 (0.18–5.38) d
1.3 ± 4.6 c
Ciccarese 2022 [12] SCR Italy
19 69.2 ± 6.6 c NA Lesion Bx NA 0.79 (0.0–5.85) f All RP
Pecoraro 2022 [14] SCR Italy, USA, Belgium,
and Netherlands
100 RT: 76 (70–82) b RT: 37 mo (12–78) b Lesion Bx, PSA after RT: 7.34 (0.02–46) d RT:
1.9 (0.015–10.77) d RT: 48 RP: 70 (66–74) b RP: 43 mo (20–82) b Tx/FU, lesion size at FUI
RP: 7.32 (1.1–28.8) d RP: 0.28 (0.01–1.82) d RP: 52
Park 2022 [16] SCR South Korea
272 66.6 ± 7.4 c 138 (102–365) d HPx for surgical margin NA 0.06 a All RP a
BCR = biochemical recurrence; Bx = biopsy; FU = follow-up; FUI =
MRI = magnetic resonance imaging; NA = not available; PSA = prostate-specific antigen;
RT = radiation therapy; RP = radical prostatectomy; SCR = single-center retrospective
study; TSA = time from submission to acceptance; Tx = treatment.
Only the dynamic contrast enhancement sequence was analyzed.
a Mean.
b Median (interquartile range).
c Mean ± standard deviation.

d Median (range).
e Results reported as ng/ml.
f Mean (range)
g Only 153 patients were analyzed according to the PI RR system.
Table 2 – Characteristics of the MRI protocol and reader experience in the studies
follow-up imaging; HPx = histopathology; IQR
= interquartile range; iTx = initial treatment;
Study
3 (3, 6, and 2023 10 yr)
[11]
Number of readers (PMRI experience)
Inter-reader agreement
Gwet's j = 0.74 for individual scores (good agreement).
Type of analysis
RDP reported separately
MRI field strength (scanner)
1.5T (Magnetom AERA, Siemens)
MRI acquisition protocol
T2WI: axial, coronal, and sagittal; DWI and DCE obtained with the same ST and plane to obtain a match DWI: SSEP sequence with a high b-value (1400 s/mm2) and another sequence with 0, 750, 1000 s/mm2); the latter was used to obtain the ADC map
DCE: Gd contrast agent (0.2 ml/kg) at 3 ml/s followed by 15 ml of saline solution; temporal resolution 9 s
T2WI: sagittal, axial, coronal planes; TR/TE 2636–3542/ 90–100 ms; FOV 200 ——— 200 mm; ST 3 mm (0.3 mm gap) DWI: TR/TE 5991/90 ms; FOV 180 ——— 323 mm; ST 3 mm (no gap); b-values: 0, 100, 1000, 1500 s/mm2
DCE: TR/TE 4.5/2.3 ms; FOV 250 ——— 300 mm; ST 4 mm (——— 2 mm gap)
T2WI: RP: axial, sagittal, and coronal; RT: axial and coronal; TR/TE 5000/100 ms; ST 3 mm (no gap); FOV 120 ——— 200 mm
DWI: TR/TE 3000/90 ms; ST 3 mm (no gap); FOV 160 ——— 220 mm; b-values 100, 800–1000, 2000 s/mm2; ADC map calculated at 2000 s/mm2
DCE: TR/TE <100/<5 ms; ST 3 mm (no gap); temporal resolution 5 s
PI-RR adherence
T2W: Yes DWI: Yes DCE: Yes
Bergaglio
Ciccarese 2022
[12]
2 (5 and 10 Reporting score
Consensus 1.5T (SignaHDxt; GE
T2WI: FRFSE sequences in the sagittal, axial and T2W: Yes coronal planes, covering the prostate lodge DWI: Yes DWI: SSEP sequence with a high b-value (2000 s/mm2) DCE: Yes and another with 50 and 1000 s/mm2; ADC map
calculated at 1000 s/mm2
DCE: 3D T1-weighted ToFSGR axial sequence during i.v. injection of a Gd contrast agent at 3 ml/s followed by 15 ml of saline solution; temporal resolution 10 s; acquisitions before contrast injection were analyzed to detect foci of hemorrhage

yr)
agreement j = 0.884 (almost perfect agreement)
between readers
Healthcare)
5(3,4,5,9, 2023 and 20 yr)
[13]
Cohen’s j 0.52–0.77 (moderate to substantial agreement)
Cohen’s j 0.33–0.62 (fair to moderate agreement)
ICC (95% CI):
RT: 0.87 (0.81– 0.93) RP: 0.87 (0.80–0.92)
Franco
RDP reported separately
RDP reported separately
3.0 T
(Ingenia, Philips)
3.0 T
(Discovery MR750, GE Healthcare)
1.5 T
(Achieva, Philips)
T2W: Yes DWI: Yes DCE: Yes a
T2W: Yes DWI: Yes DCE: Yes
1.5 T
(Achieva, Philips)
T2WI: sagittal, axial, and coronal; TR/TE 3505–3853/ 90–105 ms; FOV 240 ——————— 240 mm; ST 3 mm (0.3 mm gap) DWI: TR/TE 5991/90 ms; FOV 180 ——————— 323 mm; ST 3 mm (0.3 mm gap); b-value: 0, 100, 1000, 1500 s/mm2 DCE: TR/TE 5/2 ms; FOV 270 ——————————— 270 mm; ST 4 mm (——————————— 2 mm gap)
4 (10, 11, 2022 14, and 20
Pecoraro
[14] yr)
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Table 2 (continued)
Study Number of readers
(PMRI experience)
Park 2022 1 (5 yr)
[16]
Inter-reader agreement
–
Type of analysis
NA

MRI field strength (scanner)
3.0 T (Ingenia, Philips Healthcare; Architect, GE Healthcare; Skyra, Siemens Healthcare)
MRI acquisition protocol
T2WI: axial, sagittal, and coronal; TR/TE 2400–2700/ 100 ms; ST 3 mm; FOV 180 ——— 180 mm; matrix 512 ——————————— 512
DWI: SSEP; TR/TE 3800–4000/82 ms; ST 3 mm; FOV 180 ——————————— 180 mm; matrix 176 ——————————— 176 mm; b-values 0, 50, 500, 1000 s/mm2 and a calculated image set reconstructed for 1500 s/mm2
DCE: TR/TE 5.8–6.2/1.5 ms; FOV 230 ——————————— 230 mm; acquisition time, 0, 30, 60, 90, and 120 s after contrast injection
PI-RR adherence
T2W: Yes DWI: Yes DCE: Yes c
Kim 2022 2 (3 and 20 j = 0.80, p < 0.05 [15] yr) (substantial agreement)
Consensus 3.0 T (Achieva or Ingenia, between Philips) or 1.5 T (Amira, readers Siemens)
T2WI: axial, sagittal and coronal; TR/TE 2500–3000/ T2W: Yes 70–90 ms; ST 3 mm (gap 1 mm); FOV 160 ——————————— 160 mm; DWI: Yes matrix 320 ——————— 320; number of excitations 1 DCE: DWI: b-values 0, 100, 1000, 1500 s/mm2 Partially b
DCE: axial 3D sequence in 137/468 patients, single
phase in 331/468 patients for 180–210 s
3D = three-dimensional; MRI = magnetic resonance imaging; PMRI = prostate MRI; T2WI = T2-weighted imaging; DWI = diffusion-weighted imaging; DCE = dynamic contrast enhancement; TR/TE = repetition time/time to echo; RT = radiation therapy; RP = radical prostatectomy; ICC = intraclass correlation coefficient; RDP = reader diagnostic performance; NA = not available; PI-RR = Prostate Imaging for Recurrence Reporting; ADC = apparent diffusion coefficient; ToFSGR = time-of-flight spoiled gradient-recalled; FOV = field of view; SSEP = single-shot echo planar; FRFSE = fast relaxation fast spin echo; ST = slice thickness i.v. = intravenous.
a DCE reporting adhered to PI-RR, but the temporal resolution was not specified.
b DCE was obtained in 137/468 patients. Single-phase contrast enhancement was used in 331/468 patients.
c DCE reporting adhered to PI-RR, but the temporal resolution was limited.
results for the DCE sequence [16] and was thus included in the systematic review but not the quantitative analysis.
3.2. QUADAS-2 assessment
QUADAS-2 results are presented in Figure 2. For all studies, patient selection and the index test were considered at low risk of bias. However, the reference standard was regarded as having some concerns of bias in two studies [11,15] as they did not include biopsy results. Overall, two studies
had some concerns of bias [11,15] and three had a low risk of bias [12–14].
3.3. Diagnostic accuracy of PI-RR
The studies described analyses on a per-patient basis. Three studies reported the diagnostic performance of PI-RR for both cutoff values [12–14]. Only one study reported the accuracy for PI-RR 3 [11], while another study only reported results for PI-RR 4 [15].
Fig. 2 – Quality Assessment of Diagnostic Studies (QUADAS)-2 results. Green = low risk of bias; yellow = some concerns.

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Table 3 – Overall diagnostic performance

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	DOR (95% CI)
All studies	70.2 (55.5–81.6)	84.2 (75.1–90.4)	12.1 (6.3–23.5)
PI-RR cutoff 3	77.8 (69.9–84.1)	80.2 (58.2–92.2)	16.9 (8.6–33.1)
PI-RR cutoff 4 All studies	61.9 (35.6–82.7)	86.6 (75.1–93.3)	9.6 (3.2–28.8)
Excluding Kim [15]	74.5 (64.7–82.4)	84.0 (62.7–94.3)	17.3 (7.4–40.6)

CI = confidence interval; DOR = diagnostic odds ratio; PI-RR = Prostate Imaging for Recurrence Reporting.

Using a cutoff of PI-RR 3 (4 studies), the pooled sensi- tivity was 70.2% (95% CI 55.5–81.6%) and the pooled speci- ficity was 84.2% (95% CI 75.1–90.4%). For a cutoff of PI-RR 4 (4 studies), the pooled sensitivity was 61.9% (95% CI 35.6–82.7%) and the pooled specificity was 86.6% (95% CI 75.1–93.3%; Table 3).

3.4. Performance of PI-RR by sequence

Only Pecoraro et al [14] reported the diagnostic perfor- mance per MRI sequence. Overall, DCE sequences per- formed better than T2WI and DWI for detection of recurrence after both RT and RP. Park et al [16] reported high diagnostic performance for DCE alone, with sensitivity of 84.2% and specificity of 82.3% using a cutoff of DCE 3.

3.5. Heterogeneity analysis

In the pooled analysis for PI-RR 3, there was no significant heterogeneity for sensitivity and there was moderate heterogeneity for specificity (Fig. 3). The latter finding seemed to be driven by one of the studies [12] and could be partly related to its small sample size (19 patients).

For the analysis using PI-RR 4, there was high hetero- geneity for sensitivity but not for specificity (Fig. 3). The heterogeneity for sensitivity was driven by one study [15] that reported substantially lower sensitivity than the other studies, which is likely to be related to population selection, as most patients (53.6%) had a prostate-specific antigen (PSA) level lower than 0.4 ng/ml. However, the other studies only reported PSA as the median and corresponding range or interquartile range, so it was not possible to further assess the contribution of this or other factors to the hetero- geneity observed. In addition, imaging for most of the patients included in the study by Kim et al [15] did not meet
the PI-RR standard for the DCE sequence (Table 2), which might also have contributed to heterogeneity.

Additional subgroup analysis was not feasible given the limited number of studies.

3.6. Inter-rater agreement

All studies with more than one reader reported on inter- rater agreement [11–15], which ranged from fair-to-good to excellent (Table 2). Four studies [12–15] reported Cohen's j coefficients, which ranged from 0.33 [14] to 0.88 [12] (fair to excellent). One study reported a Gwet's j value of 0.74 for three readers (good agreement) [11].

4. Discussion

Our systematic review and meta-analysis comprising six studies and 467 patients demonstrated that the PI-RR scor- ing system has high sensitivity and specificity for detection of local recurrence after RT or RP for prostate cancer. Our findings indicate that PI-RR retains the accuracy of MRI in detecting local tumor recurrence while providing a struc- tured assessment score. Notably, a cutoff point of 3 (on a 5-point scale) yields high sensitivity and specificity for diag- nosing recurrent disease.

A potential challenge with the scheme arises from classi- fication of PI-RR 3 lesions as uncertain, leading to diagnostic dilemmas and impacting clinical decision-making. We assessed the diagnostic performance using two different cutoffs (PI-RR 3 and 4). We noted greater sensitivity at the threshold of PI-RR 3, with comparable specificity. This implies that classifying lesions as positive at PI-RR 3 may be the most efficient strategy.

PI-RR recommends similar patient preparation, MRI equipment, and imaging protocols to those described in

Fig. 3 – Forest plots of (A) sensitivity and (B) specificity of the Prostate Imaging for Recurrence Reporting (PI-RR) scoring system. CP = cutoff point.

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Prostate Imaging-Reporting and Data System v2.1 [21]. Analysis of T2WI, DCE, and DWI sequences is necessary to assess the likelihood of local recurrence. However, only one study reported the diagnostic accuracy per MRI sequence [14] and showed that DCE performed better in both RT and RP patients. These findings were expected, as it has been reported that DCE is highly sensitive in evaluat- ing local recurrence after RP, identifying small lesions in the prostate bed even at low PSA levels [22,23]. In line with this, Park et al [16] reported excellent DCE performance in rela- tion to the presence and location of positive surgical mar- gins. Furthermore, the authors also observed an association between focal nodular enhancement on DCE sequences at postoperative MRI among patients without BCR at the time, and demonstrated that this finding was correlated with a shorter time to subsequent BCR.

A standardized MRI protocol and reporting system can enhance the quality of imaging examinations, improve the consistency of clinical management, and facilitate multicen- ter research [24]. A standardized protocol can also improve MRI reports and satisfaction among referring providers [25]. Systematization can lead to better concordance among dif- ferent readers, which is crucial for utility in everyday prac- tice [26]. The studies included in our meta-analysis showed a high range of interobserver agreement, varying from fair to excellent (Table 2). It is important to emphasize that these studies predominantly involved experienced geni- tourinary radiologists, so the reproducibility of results in centers with less expertise is still unknown.

Previous systematic reviews have shown that MRI is a valuable tool for detecting local recurrence after RP or RT, with high diagnostic accuracy and the potential to differenti-

ate tissue types (such as scar/fibrotic tissue and tumor recur- rence), even at low PSA levels [6,27–30]. However, these reviews also highlight significant differences regarding the MRI sequences used among studies. For instance, the system- atic review by Barchetti and Panebianco [29] revealed that most studies did not include all three sequences (T2WI, DCE, and DWI) endorsed by the PI-RR system. Consequently, studies conducted before the PI-RR system exhibit consider- able heterogeneity in imaging acquisition, which complicates extrapolation of diagnostic study findings to contemporary clinical practice. Our systematic review reaffirms the high diagnostic performance of mpMRI for detection of recurrent prostate cancer when adhering to the PI-RR system.

It is noteworthy that the emergence of PSMA tracers such as 68Ga-PSMA-11 and 18F-piflufolastat (18F-DCFPyL) marks a transformative shift in the imaging landscape for BCR of prostate cancer. While PSMA PET/CT is valuable for detection of extrapelvic nodal and distant metastatic dis- ease [31,32], its limitations for detection of local recurrence, particularly when not combined with mpMRI, need careful consideration. Urinary excretion of PSMA may obscure local recurrence in the prostate or prostate bed, impacting detec- tion rates [33–35]. Freitag et al [36] reported that only half of the local recurrences seen on MRI after RP were detect- able on PSMA PET. They also observed that the proximity of the recurrent lesion to the bladder was significantly asso- ciated with false-negative PSMA PET results, while the size of the recurrent lesion was not associated with false-

negative PSMA PET results. This challenge is addressed by incorporating fusion PET/MRI, either through a hybrid sys- tem or retrospective fusion of separate mpMRI and PET/CT examinations. In 2022, Panebianco and Turkbey [37] pro- posed a risk-adapted pathway with integrated imaging for detection and localization of recurrence. According to the risk of disease progression, patients at low risk start with MRI, while those at intermediate or high risk should undergo PSMA PET/CT as a priority for effective manage- ment of recurrent prostate cancer. Our results support the use of mpMRI as a crucial tool for assessing recurrence after whole-gland treatment. Nonetheless, a comprehensive head-to-head comparison between MRI and PSMA PET is essential to determine the optimal imaging tool across diverse clinical scenarios.

Our study has some limitations. First, only six studies fulfilled the eligibility criteria, a limitation that could be attributed to the recent introduction of PI-RR [10]. Despite active research and publications on the use of MRI after whole-gland treatment, a structured assessment and reporting system was only established and made available in 2021. Second, according to PI-RR, DWI and DCE sequences are recognized as higher-yield modalities follow- ing RT, while DCE is considered the best sequence after RP. These distinctions may result in varying diagnostic accuracy of the PI-RR system between patients who have undergone RP and RT. Unfortunately, due to insufficient data, we could not perform subgroup calculations to pool performances based on treatment modality. Third, our primary analysis showed significant heterogeneity, mostly related to dis- parate performance in a single study [15], as demonstrated in the secondary analysis. This heterogeneity could be attributed to two factors: (1) the threshold effect, as this study exhibited one of the highest specificity and lowest sensitivity values; and (2) in most patients, single phase contrast enhancement was used instead of DCE, as recom- mended for PI-RR. More granular analysis of heterogeneity is limited by the number of studies available.

5. Conclusions

In conclusion, we found that PI-RR is accurate in detecting local recurrence after whole-gland treatment for prostate cancer. In particular, a cutoff point of 3 (on a 5-point scale) demonstrated high sensitivity and specificity for diagnosing recurrent disease. The inter-rater agreement among readers ranged from fair to excellent. Our meta-analysis results sup- port the use of this standardized method for assessment and reporting of mpMRI in the post-RT or post-RP prostate cancer setting and highlight a need for additional research with larger sample sizes, a multicenter approach, a prospec- tive design, and extended follow-up.

Author contributions: Felipe A. Mourato had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Dias, Torri. Acquisition of data: Mourato, Schmitt, Mariussi.

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Analysis and interpretation of data: Mourato, Altmayer, Torri, Dias. Drafting of the manuscript: Mourato, Dias.

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Appendix A. Supplementary data

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References

[1] Rawla P. Epidemiology of prostate cancer. World J Oncol 2019;10:63–89.

[2] Shore ND, Moul JW, Pienta KJ, Czernin J, King MT, Freedland SJ. Biochemical recurrence in patients with prostate cancer after primary definitive therapy: treatment based on risk stratification. Prostate Cancer Prostatc Dis. In press. https://doi.org/10.1038/ s41391-023-00712-z.

[3] Chalieopanyarwong V, Attawettayanon W, Kanchanawanichkul W, Pripatnanont C. The prognostic factors of biochemical recurrence- free survival following radical prostatectomy. Asian Pacific J Cancer Prev 2017;18:2555–9.

[4] Kotb AF, Elabbady AA. Prognostic factors for the development of biochemical recurrence after radical prostatectomy. Prostate Cancer 2011;2011:485189.

[5] Gillessen S, Armstrong A, Attard G, et al. Management of patients with advanced prostate cancer: report from the Advanced Prostate Cancer Consensus Conference 2021. Eur Urol 2022;82:115–41.
[6] De Visschere PJL, Standaert C, Fütterer JJ, et al. A systematic review on the role of imaging in early recurrent prostate cancer. Eur Urol Oncol 2019;2:47–76.
[7] Mottet N, Cornford P, van den Bergh RCN, et al. EAU-EANM-ESTRO- ESUR-ISUP-SIOG guidelines on prostate cancer. Arnhem, The Netherlands: European Association of Urology; 2023.
[8] Pisansky TM, Thompson IM, Valicenti RK, D'Amico AV, Selvarajah S. Adjuvant and salvage radiotherapy after prostatectomy: ASTRO/ AUA guideline amendment 2018–2019. J Urol 2019;202:533–8. https://doi.org/10.1097/JU.0000000000000295.
[9] Schaeffer EM, Srinivas S, Adra N, et al. NCCN guidelinesÒ insights: prostate cancer, version 1.2023. J Natl Compr Cancer Netw 2022;20:1288–98.
[10] Panebianco V, Villeirs G, Weinreb JC, et al. Prostate Magnetic Resonance Imaging for Local Recurrence Reporting (PI-RR): international consensus-based guidelines on multiparametric magnetic resonance imaging for prostate cancer recurrence after radiation therapy and radical prostatectomy. Eur Urol Oncol 2021;4:868–76. https://doi.org/10.1016/j.euo.2021.01.003.
[11] Bergaglio C, Giasotto V, Marcenaro M, et al. The role of mpMRI in the assessment of prostate cancer recurrence using the PI-RR system: diagnostic accuracy and interobserver agreement in readers with different expertise. Diagnostics 2023;13:387.
[12] Ciccarese F, Corcioni B, Bianchi L, et al. Clinical application of the new Prostate Imaging for Recurrence Reporting (PI-RR) score proposed to evaluate the local recurrence of prostate cancer after radical prostatectomy. Cancers 2022;14:4725.
[13] Franco PN, Frade-Santos S, García-Baizán A, et al. An MRI assessment of prostate cancer local recurrence using the PI-RR system: diagnostic accuracy, inter-observer reliability among readers with variable experience, and correlation with PSA values. Eur Radiol 2024;34:1790–803. https://doi.org/10.1007/s00330- 023-09949-7.
[14] Pecoraro M, Turkbey B, Purysko AS, et al. Diagnostic accuracy and observer agreement of the MRI Prostate Imaging for Recurrence Reporting assessment score. Radiology 2022;304:342–50.
[15] Kim M, Il HS, Ahn H, et al. Diagnostic yield of multiparametric MRI for local recurrence at biochemical recurrence after radical prostatectomy. Prostate Int 2022;10:135–41. https://doi.org/ 10.1016/j.prnil.2022.05.001.
[16] Park MY, Park KJ, Kim MH, Kim JK. Focal nodular enhancement on DCE MRI of the prostatectomy bed: radiologic-pathologic correlations and prognostic value. Eur Radiol 2023;33:2985–94.
[17] McInnes MDF, Moher D, Thombs BD, et al. Preferred Reporting Items for a Systematic Review and Meta-Analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. JAMA 2018;319:388.
[18] Deeks JJ, Bossuyt PM, Leeflang MM, Takwoingi Y, editors. Cochrane handbook for systematic reviews of diagnostic test accuracy. Chichester, UK: Wiley; 2023.
[19] Whiting PF. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529. https:// doi.org/10.7326/0003-4819-155-8-201110180-00009.
[20] Altman DG. Practical statistics for medical research. London, UK: Chapman Hall/CRC Press; 1999.

[21] Purysko AS, Rosenkrantz AB, Turkbey IB, Macura KJ. RadioGraphics update: PI-RADS version 2.1—a pictorial update. RadioGraphics 2020;40:E33–7. https://doi.org/10.1148/rg.2020190207.
[22] Liauw SL, Pitroda SP, Eggener SE, et al. Evaluation of the prostate bed for local recurrence after radical prostatectomy using endorectal magnetic resonance imaging. Int J Radiat Oncol Biol Phys 2013;85:378–84. https://doi.org/10.1016/j.ijrobp.2012.05.015.
[23] Couñago F, Recio M, del Cerro E, et al. Role of 3.0 T multiparametric MRI in local staging in prostate cancer and clinical implications for radiation oncology. Clin Transl Oncol 2014;16:993–9.
[24] Huang C, Simeone DM, Luk L, et al. Standardization of MRI screening and reporting in individuals with elevated risk of pancreatic ductal adenocarcinoma: consensus statement of the PRECEDE Consortium. Am J Roentgenol 2022;219:903–14.
[25] Gupta NA, Mahajan S, Sumankumar A, Saklani A, Engineer R, Baheti AD. Impact of a standardized reporting format on the quality of MRI reports for rectal cancer staging. Indian J Radiol Imaging 2020;30:7–12. https://doi.org/10.4103/ijri.IJRI_308_19.
[26] Benchoufi M, Matzner-Lober E, Molinari N, Jannot AS, Soyer P. Interobserver agreement issues in radiology. Diagn Interv Imaging 2020;101:639–41. https://doi.org/10.1016/j.diii.2020.09.001.
[27] Maurer T, Eiber M, Fanti S, Budäus L, Panebianco V. Imaging for prostate cancer recurrence. Eur Urol Focus 2016;2:139–50.
[28] Panebianco V, Barchetti F, Musio D, et al. Advanced imaging for the early diagnosis of local recurrence prostate cancer after radical prostatectomy. Biomed Res Int 2014;2014:827265.
[29] Barchetti F, Panebianco V. Multiparametric MRI for recurrent prostate cancer post radical prostatectomy and postradiation therapy. Biomed Res Int 2014;2014:316272.
[30] Sandgren K, Westerlinck P, Jonsson JH, et al. Imaging for the detection of locoregional recurrences in biochemical progression after radical prostatectomy—a systematic review. Eur Urol Focus 2019;5:550–60.
[31] Metser U, Zukotynski K, Mak V, et al. Effect of 18F-DCFPyL PET/CT on the management of patients with recurrent prostate cancer: results of a prospective multicenter registry trial. Radiology 2022;303:414–22.
[32] Basso Dias A, Finelli A, Bauman G, et al. Impact of 18F-DCFPyL PET on staging and treatment of unfavorable intermediate or high-risk prostate cancer. Radiology 2022;304:600–8. https://doi.org/ 10.1148/radiol.211836.
[33] Radzina M, Tirane M, Roznere L, et al. Accuracy of 68Ga-PSMA-11 PET/CT and multiparametric MRI for the detection of local tumor and lymph node metastases in early biochemical recurrence of prostate cancer. Am J Nucl Med Mol Imaging 2020;10:106–18.
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[34] Pecoraro M, Panebianco V. Multiparametric prostate MRI for biochemical failure in the era of targeted PET radiotracers: counterpoint—MRI remains a specific and

accessible test for targeted management. Am J Roentgenol 2023;220:188–9. https://doi.org/10.2214/AJR.22.28042.
[35] Abreu-Gomez J, Dias AB, Ghai S. PI-RR: the Prostate Imaging for Recurrence Reporting system for MRI assessment of local prostate cancer recurrence after radiation therapy or radical prostatectomy—a review. Am J Roentgenol 2023;220:852–61. https://doi.org/10.2214/ AJR.22.28665.
[36] Freitag MT, Radtke JP, Afshar-Oromieh A, et al. Local recurrence of prostate cancer after radical prostatectomy is at risk to be missed in 68Ga-PSMA-11-PET and PET.MRI: comparison with mpMRI integrated in simultaneous PET/MRI. Eur J Med Mol Imaging 2017;44:776–87.
[37] Panebianco V, Turkbey B. Magnetic resonance imaging for prostate cancer recurrence: it's time for precision diagnostic with Prostate Imaging for Recurrence Reporting (PI-RR) score. Eur Radiol 2022;33:748–51.

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