

## ORIGINAL PAPER

# Incremental detection of clinically significant prostate cancer by systematic biopsy outside MRI-targeted lesions during cognitive fusion local anaesthetic transperineal biopsy

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## Summary

*Objective: To evaluate the incremental yield of clinically significant prostate cancer (csPCa) detected by systematic biopsy outside MRI-targeted lesions during cognitive fusion local anaesthetic transperineal prostate biopsy.*

*Patients and methods: This observational cohort study included men undergoing cognitive MRI-targeted prostate biopsy with concurrent systematic sampling. Pre-biopsy MRI findings were recorded using PI-RADS. The primary outcome was csPCa detected exclusively by systematic biopsy outside MRI-targeted lesions despite a negative targeted biopsy. Secondary outcomes included csPCa detection by targeted, systematic, and combined biopsy, PI-RADS subgroup analysis, and multi-variable predictors of csPCa.*

*Results: Overall, 770 men were included, of whom 767 had evaluable paired biopsy data. Most had PI-RADS 4 lesions (636/767, 82.9%). csPCa was detected by targeted biopsy in 320/767 men (41.7%), systematic biopsy outside MRI-targeted lesions in 196/767 (25.6%), and combined biopsy in 384/767 (50.1%). Exclusive outside-target systematic csPCa detection occurred in 64/767 men (8.3%), representing 16.7% of all csPCa detected. This rate was highest in PI-RADS 3 lesions (8/30, 26.7%). On multivariable analysis, overall csPCa detection was associated with age, PSA density, and PI-RADS score, whereas exclusive outside-target detection was inversely associated with PI-RADS score and positively associated with procedures performed by urologists. Spatial analysis showed that most systematic-only csPCa lesions were anatomically distinct from the index MRI-visible lesion.*

*Conclusions: Systematic biopsy outside MRI-targeted lesions detected additional csPCa in 64/767 men (8.3%) and frequently identified anatomically distinct lesions, supporting continued systematic sampling alongside MRI-targeted biopsy in selected patients.*

**KEY WORDS:** Clinically significant prostate cancer; MRI-targeted biopsy; Systematic biopsy.

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## INTRODUCTION

Prostate cancer remains one of the most diagnosed male malignancies worldwide (1). Traditional, systematic transperineal ultrasound-guided biopsy has been criticised for underdetecting clinically significant prostate cancer (csPCa) while simultaneously overdetecting indolent disease (2, 3). Consequently, multiparametric MRI (mpMRI) has become integral to contemporary diagnostic pathways, enabling lesion localisation and PI-RADS-based risk stratification before biopsy (4).

Landmark studies, such as PROMIS (5) and PRECISION (6), showed that MRI-directed pathways improved the detection of csPCa and reduced the identification of clinically insignificant disease (5, 6). However, MRI-targeted biopsy remains imperfect, with concerns regarding inter-reader variability, lesion conspicuity, and the potential omission of significant cancers outside MRI-visible targets.

Despite advances in MRI-targeted biopsy, csPCa may still be missed because some tumours are MRI-occult, multifocal, or located outside the dominant lesion (3, 7, 8). Consequently, many centres continue to combine targeted and systematic biopsy, particularly for men with positive MRI findings or persistent clinical suspicion (8-10). Although combined approaches improve overall detection, the value of systematic biopsy remains debated in the MRI era (11).

Systematic biopsy may identify additional csPCa outside MRI-targeted lesions, potentially altering risk stratification and treatment planning (12). However, the anatomical relationship between these additional cancers and the MRI-visible target lesion remains poorly understood.

The optimal balance between diagnostic accuracy and biopsy burden remains unresolved. Although omission of systematic biopsy may reduce morbidity and overdiagnosis, it may also miss clinically significant tumours outside MRI-visible targets (3, 12).

The aim of this study was to evaluate the detection of clinically significant prostate cancer by systematic biopsy outside MRI-targeted lesions in men undergoing combined MRI-targeted and systematic biopsies. The primary

objective was to determine the proportion of men in whom csPCa was detected exclusively by systematic biopsy outside the MRI-targeted lesion. Secondary objectives were to compare csPCa detection by targeted biopsy, systematic biopsy, and the combined approach; assess detection of any prostate cancer; examine outcomes according to PI-RADS score; and identify predictors of csPCa detection.

## METHODS

### Study design and reporting framework

This observational cohort study evaluated men undergoing prostate biopsy following pre-biopsy multiparametric MRI and was reported according to *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) recommendations. The primary objective was to determine the incremental diagnostic yield of systematic biopsy outside MRI-targeted lesions for detecting clinically significant prostate cancer.

### Study population

Men included in this study underwent prostate MRI followed by local anaesthetic transperineal biopsy comprising targeted and systematic sampling. Of 770 patients, 767 with complete valid paired csPCa outcomes were included in the final paired analysis after excluding patients with missing or invalid biopsy data.

### Setting

This retrospective observational cohort study at Kingston and Richmond Hospital NHS Foundation Trust included consecutive patients undergoing prostate biopsy within an MRI-led diagnostic pathway between November 2023 and March 2026. All patients underwent pre-biopsy MRI for PI-RADS assessment and targeted biopsy guidance. Biopsies were performed by radiologists or urologists. Patients lacking operator-speciality data were excluded from comparative operator analyses.

### Eligibility criteria

Patients were eligible for inclusion if they had undergone both MRI-targeted biopsy and systematic biopsy and if biopsy outcome data were available. Men were included regardless of PI-RADS score, PSA level, prostate volume, previous biopsy status, or operator type.

For the primary outcome analysis, patients were excluded if the targeted csPCa or systematic outside-target csPCa variables were missing or contained invalid coding.

### MRI assessment

Pre-biopsy MRI findings were recorded using the Prostate Imaging Reporting and Data System - PI-RADS score. The PI-RADS score was analysed as both a descriptive subgroup variable and as a predictor in multivariable modelling. For subgroup analyses, patients were stratified according to PI-RADS category.

### Biopsy approach

All patients underwent consultant-led local anaesthetic transperineal prostate biopsy. The biopsy consisted of

MRI-targeted sampling of MRI-visible lesions, performed alongside concurrent systematic sampling. Systematic biopsy outcomes referred specifically to cancers detected outside MRI-targeted lesions.

### Definitions

*Clinically significant prostate cancer* (csPCa) was defined as Gleason Grade Group  $\geq 2$ .

### Outcome measures

#### Primary outcome

The primary outcome was the proportion of men with clinically significant prostate cancer detected exclusively by systematic biopsy outside MRI-targeted lesions.

This was defined as systematic outside-target csPCa-positive and targeted-biopsy csPCa-negative. Therefore, this outcome represented clinically significant cancers that targeted biopsy alone would have missed.

#### Secondary outcomes

csPCa detection rates for targeted biopsy, systematic outside-target biopsy, and the combined approach; detection of any prostate cancer by each method; PI-RADS subgroup analyses; and multivariable logistic regression assessing predictors of csPCa.

### Spatial relationship analysis

A secondary spatial relationship analysis was performed in patients with clinically significant prostate cancer detected exclusively by systematic biopsy outside MRI-targeted lesions. MRI-visible lesions were categorised using predefined prostate sector mapping. In patients with multiple MRI lesions, the highest PI-RADS lesion was designated as the index MRI target lesion. Lesions were classified as same-sector, adjacent-sector, ipsilateral distant, or contralateral relative to the index MRI target lesion.

Patients without an MRI-visible target lesion were excluded from spatial concordance analysis. Sector adjacency was predefined according to anatomical proximity within the transperineal sector map. Twenty-eight patients were excluded from spatial analysis because lesion localisation data were incomplete, non-standardised, or lacked a clearly identifiable MRI-visible index lesion.

### Statistical analysis

Continuous variables were summarised using the median and interquartile ranges, and categorical variables were summarised as frequencies and percentages. Detection rates were calculated with 95% Wilson confidence intervals. Paired biopsy outcomes were cross-tabulated and categorised as no csPCa, targeted only, systematic outside-target only, or both. Subgroup analyses were performed by PI-RADS score. Multivariable logistic regression identified predictors of combined and exclusive systematic outside-target csPCa detection, including age, PSA density, PI-RADS score, previous biopsy status, and operator type.

Results were reported as adjusted odds ratios with 95% confidence intervals. Statistical analyses were performed in Python, with  $p < 0.05$  considered significant.

### Missing data

Three records with incomplete or non-evaluable paired targeted and systematic outside-target csPCa outcome data were excluded from paired analyses.

### Ethical considerations

The study complied with the Declaration of Helsinki and STROBE reporting recommendations. Institutional registration and governance approval were obtained from Kingston and Richmond Hospital for this retrospective evaluation of routinely collected clinical data. Under local policy, individual informed consent and additional formal research ethics committee approval were not required. All patient data were anonymised before analysis and managed according to institutional information governance standards and data protection regulations.

## RESULTS

### Patient cohort

A total of 770 men were included in the dataset. For the primary paired csPCa analysis, 767 men had evaluable paired targeted biopsy and systematic biopsy outcome

data. Three patients were excluded from the paired csPCa analysis because of missing data.

The baseline characteristics of the evaluable cohort are summarised in Table 1. The median age was 68.0 years, and the median PSA was 7.8 ng/mL. Median prostate volume was 44.0 mL, and median PSA density was 0.2 ng/mL/mL. Most patients had PI-RADS 4 lesions, accounting for 636/767 men - 82.9% of the evaluable cohort (Table 1).

### Primary outcome

Cancer detection outcomes are summarised in Table 2. Clinically significant prostate cancer detected exclusively by systematic biopsy outside MRI-targeted lesions was identified in 64/767 men, giving an absolute detection rate of 8.3% (95% CI 6.6-10.5%). Combined biopsy detected csPCa in 50.1% of men, compared with 41.7% using targeted biopsy alone, representing an absolute incremental yield of 8.3%.

### Overlap between targeted and systematic biopsy detection

Among the 767 men with paired csPCa data, 188/767 (24.5%) had csPCa detected by targeted biopsy only, 64/767 (8.3%) had csPCa detected only by systematic biopsy outside the MRI-targeted lesion, and 132/767 (17.2%) had csPCa detected by both approaches. Among men with discordant biopsy results, csPCa was detected by targeted biopsy alone in 188 patients and by systematic biopsy outside the target alone in 64 patients. This difference was statistically significant on paired testing - McNemar exact  $p < 0.001$ .

### Spatial relationship between MRI target lesions and systematic-only csPCa

Spatial relationship analysis was performed in 36 patients with clinically significant prostate cancer detected exclusively on systematic biopsy outside MRI-targeted lesions. No lesions were located within the same sector as the index MRI target lesion. Three lesions (8.3%) were in anatomically adjacent sectors, while 15 (41.7%) were ipsilateral but anatomically distant and 18 (50.0%) were contralateral to the index MRI target lesion.

### Detection according to PI-RADS score

Incremental systematic biopsy yield was highest in PI-RADS 3 lesions and progressively decreased with increas-

**Table 1.**

Baseline characteristics of the evaluable cohort.

| Characteristic         | Overall cohort (n = 767) |
|------------------------|--------------------------|
| Age, years             | 68.0 (62.0-75.0)         |
| PSA, ng/mL             | 7.8 (5.6-12.0)           |
| Prostate volume, mL    | 44.0 (34.0-61.0)         |
| PSA density, ng/mL/mL  | 0.2 (0.1-0.3)            |
| Number of biopsy cores | 12.0 (9.0-14.5)          |
| PI-RADS 2              | 6/767 (0.8%)             |
| PI-RADS 3              | 30/767 (3.9%)            |
| PI-RADS 4              | 636/767 (82.9%)          |
| PI-RADS 5              | 95/767 (12.4%)           |
| Previous biopsy        | 28/766 (3.7%)            |
| Operator: urologist    | 417/767 (54.4%)          |
| Operator: radiologist  | 350/767 (45.6%)          |

Values are presented as median (interquartile range) or n/N (%).  
PI-RADS: Prostate Imaging Reporting and Data System.

| Outcome                                                                        | Patients, n/N % | 95% CI, % |
|--------------------------------------------------------------------------------|-----------------|-----------|
| csPCa detected exclusively by systematic biopsy outside MRI-targeted lesions   | 64/767 (8.3)    | 6.6-10.5  |
| csPCa detected by targeted biopsy                                              | 320/767 (41.7)  | 38.3-45.2 |
| csPCa detected by systematic biopsy outside MRI-targeted lesions               | 196/767 (25.6)  | 22.6-28.8 |
| csPCa detected by either targeted or systematic biopsy                         | 384/767 (50.1)  | 46.5-53.6 |
| Any prostate cancer detected by targeted biopsy                                | 394/769 (51.2)  | 47.7-54.8 |
| Any prostate cancer detected by systematic biopsy outside MRI-targeted lesions | 287/769 (37.3)  | 34.0-40.8 |
| Any prostate cancer detected by either targeted or systematic biopsy           | 485/769 (63.1)  | 59.6-66.4 |

csPCa: clinically significant prostate cancer. CI: confidence interval.

**Table 2.**

Cancer detection outcomes.

| PI-RADS | n   | Targeted csPCa | Systematic Ca outside-target csP | Exclusive systematic outside-target csPCa | Combined csPCa |
|---------|-----|----------------|----------------------------------|-------------------------------------------|----------------|
| 2       | 6   | 0/6 (0.0)      | 0/6 (0.0)                        | 0/6 (0.0)                                 | 0/6 (0.0)      |
| 3       | 30  | 4/30 (13.3)    | 9/30 (30.0)                      | 8/30 (26.7)                               | 12/30 (40.0)   |
| 4       | 636 | 228/636 (35.8) | 140/636 (22.0)                   | 51/636 (8.0)                              | 279/636 (43.9) |
| 5       | 95  | 88/95 (92.6)   | 47/95 (49.5)                     | 5/95 (5.3)                                | 93/95 (97.9)   |

Values are presented as n/N (%). PI-RADS = Prostate Imaging Reporting and Data System.

**Table 3.**  
csPCa detection stratified by PI-RADS score.

ing PI-RADS score. Detailed subgroup detection rates are summarised in Table 3.

### Predictors of csPCa

On multivariable logistic regression, increasing age, higher PSA density, higher PI-RADS score, and operator type were associated with detection of csPCa by either biopsy approach. The strongest predictor was PI-RADS score, with each 1-point increase associated with nearly six-fold higher odds of csPCa detection - adjusted OR 5.99, 95% CI 3.37-10.64,  $p < 0.001$ .

Age was also associated with csPCa detection: adjusted OR 1.82 per 10-year increase, 95% CI 1.50-2.21,  $p < 0.001$ . PSA density was independently associated with csPCa detection: adjusted OR 1.13 per 0.10 increase, 95% CI 1.05-1.23,  $p = 0.002$ . Previous biopsy status was not associated with csPCa detection (Table 4).

**Table 4.**  
Multivariable predictors of csPCa detected by either biopsy approach.

| Predictor                          | Adjusted OR (95% CI) | p value |
|------------------------------------|----------------------|---------|
| Age, per 10 years                  | 1.82 (1.50-2.21)     | < 0.001 |
| PSA density, per 0.10              | 1.13 (1.05-1.23)     | 0.002   |
| PI-RADS, per 1-point increase      | 5.99 (3.37-10.64)    | < 0.001 |
| Previous biopsy, yes vs no         | 1.18 (0.51-2.73)     | 0.699   |
| Operator: urologist vs radiologist | 1.41 (1.03-1.95)     | 0.035   |

Multivariable logistic regression analysis of predictors of clinically significant prostate cancer detected by either biopsy approach.

### Predictors of csPCa detected exclusively by systematic biopsy outside MRI-targeted lesions

For the primary endpoint of csPCa detected exclusively by systematic biopsy outside MRI-targeted lesions, increasing PI-RADS score was inversely associated with exclusive systematic outside-target detection: adjusted OR 0.43 per 1-point increase, 95% CI 0.24-0.76,  $p = 0.004$ .

Operator type was also associated with the primary endpoint. Biopsies performed by urologists had higher odds of exclusive systematic outside-target csPCa detection compared with radiologists: adjusted OR 2.98, 95% CI 1.63-5.43,  $p < 0.001$ .

Age and PSA density were not statistically significant predictors of exclusive systematic outside-target csPCa detection (Table 5). Combined biopsy achieved the highest csPCa detection (50.1%), while systematic outside-

**Table 5.**  
Multivariable predictors of csPCa detected exclusively by systematic biopsy outside MRI-targeted lesions-

| Predictor                          | Adjusted OR (95% CI) | p value |
|------------------------------------|----------------------|---------|
| Age, per 10 years                  | 1.32 (0.96-1.81)     | 0.084   |
| PSA density, per 0.10              | 1.02 (1.00-1.05)     | 0.102   |
| PI-RADS, per 1-point increase      | 0.43 (0.24-0.76)     | 0.004   |
| Previous biopsy, yes vs no         | 0.97 (0.22-4.26)     | 0.970   |
| Operator: urologist vs radiologist | 2.98 (1.63-5.43)     | < 0.001 |

Multivariable logistic regression analysis of predictors of clinically significant prostate cancer detected exclusively by systematic biopsy outside MRI-targeted lesions.

target biopsy alone identified additional csPCa in 8.3%, as shown in Figure 1.

Also, Figure 2 shows that incremental systematic biopsy yield was highest in PI-RADS 3 lesions, with lower additional csPCa detection in PI-RADS 4-5.

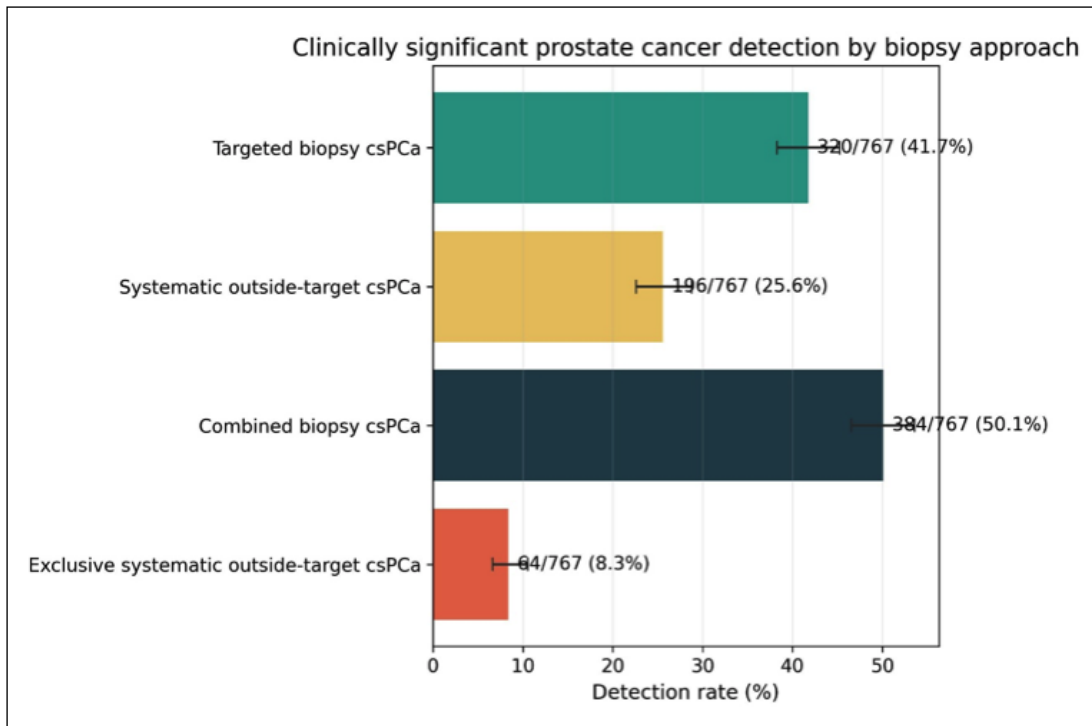
Forest plots of the multivariable models are shown in Figure 4. Adjusted odds ratios were derived from logistic regression models including age, PSA density, PI-RADS score, previous biopsy status, and operator speciality. Continuous predictors were scaled as age per 10-year increase and PSA density per 0.10 ng/mL/mL increase, while PI-RADS was modelled per one-point increase. Radiologist operator status was used as the reference category for operator comparisons. Multivariable models demonstrated moderate discrimination for csPCa prediction, with higher accuracy for combined biopsy detection (AUC 0.75) than exclusive systematic detection (AUC 0.68).

## DISCUSSION

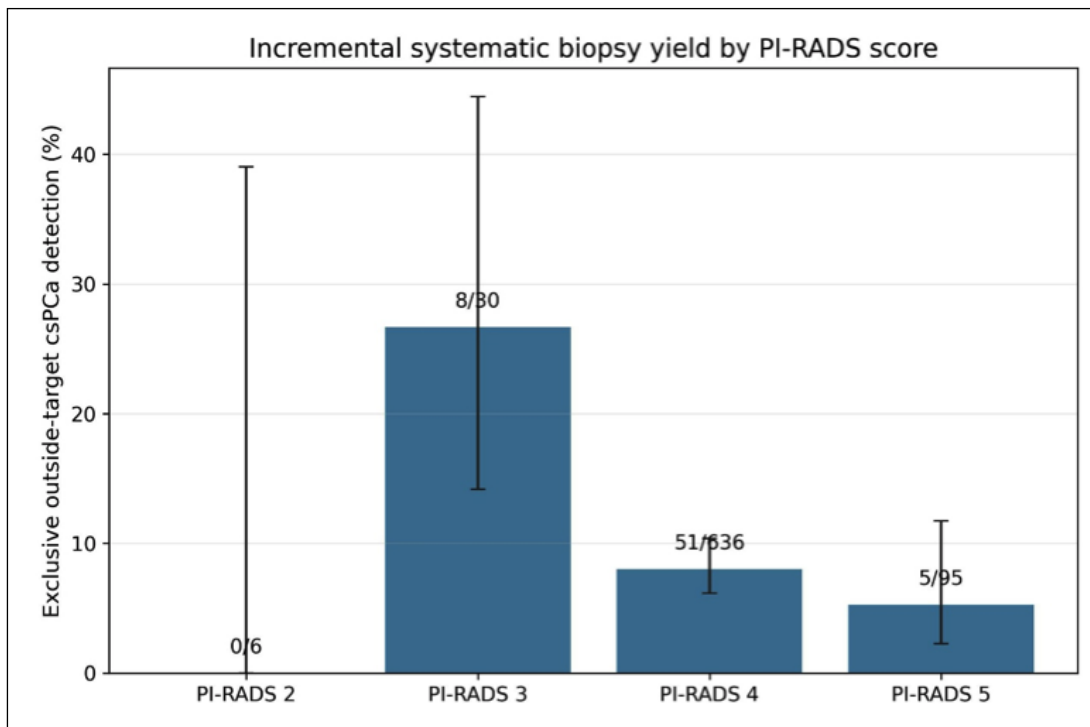
### Principal findings

In this cohort of men undergoing MRI-directed prostate biopsy, systematic sampling outside MRI-targeted lesions provided a clinically meaningful incremental yield for the detection of clinically significant prostate cancer. The primary outcome, csPCa detected exclusively by systematic biopsy outside the MRI-targeted lesion, occurred in 64 of 767 evaluable men, corresponding to an absolute detection rate of 8.3%. Importantly, these cases represented 16.7% of all csPCa detected by either biopsy approach. Combined biopsy improved csPCa detection beyond targeted biopsy alone, supporting the continued value of systematic sampling in selected patients.

A notable finding of the present study was that most clinically significant cancers detected exclusively by system-



**Figure 1.**  
Detection rates  
by biopsy  
approach.



**Figure 2.**  
Incremental  
systematic  
biopsy yield by  
PI-RADS score.

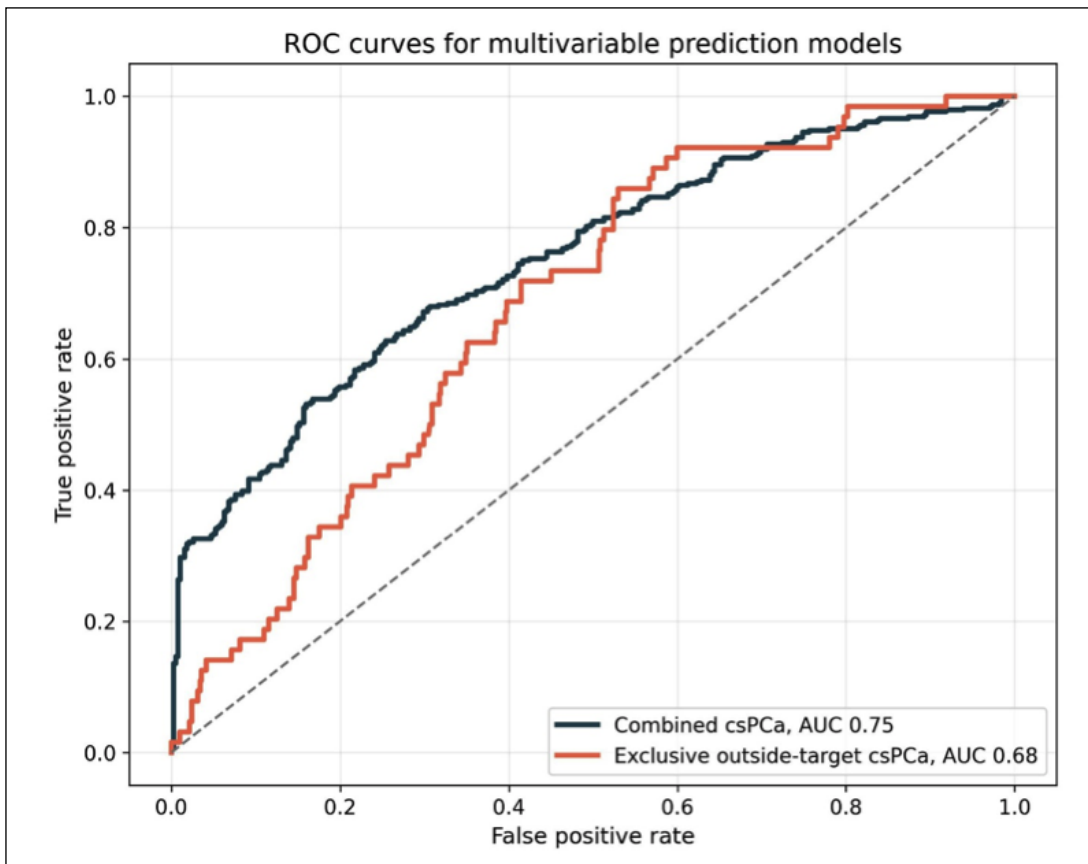
atic biopsy were anatomically distinct from the index MRI-visible lesion. Only a small proportion of systematic-only csPCa lesions were in anatomically adjacent sectors, while most were either ipsilaterally distant or contralateral to the MRI target.

These findings suggest that the additional yield of systematic biopsy is not explained solely by targeting imprecision or undersampling of MRI-visible lesions. Instead, many systematic-only csPCa lesions may represent sepa-

rate clinically significant tumour foci not adequately visualised on MRI.

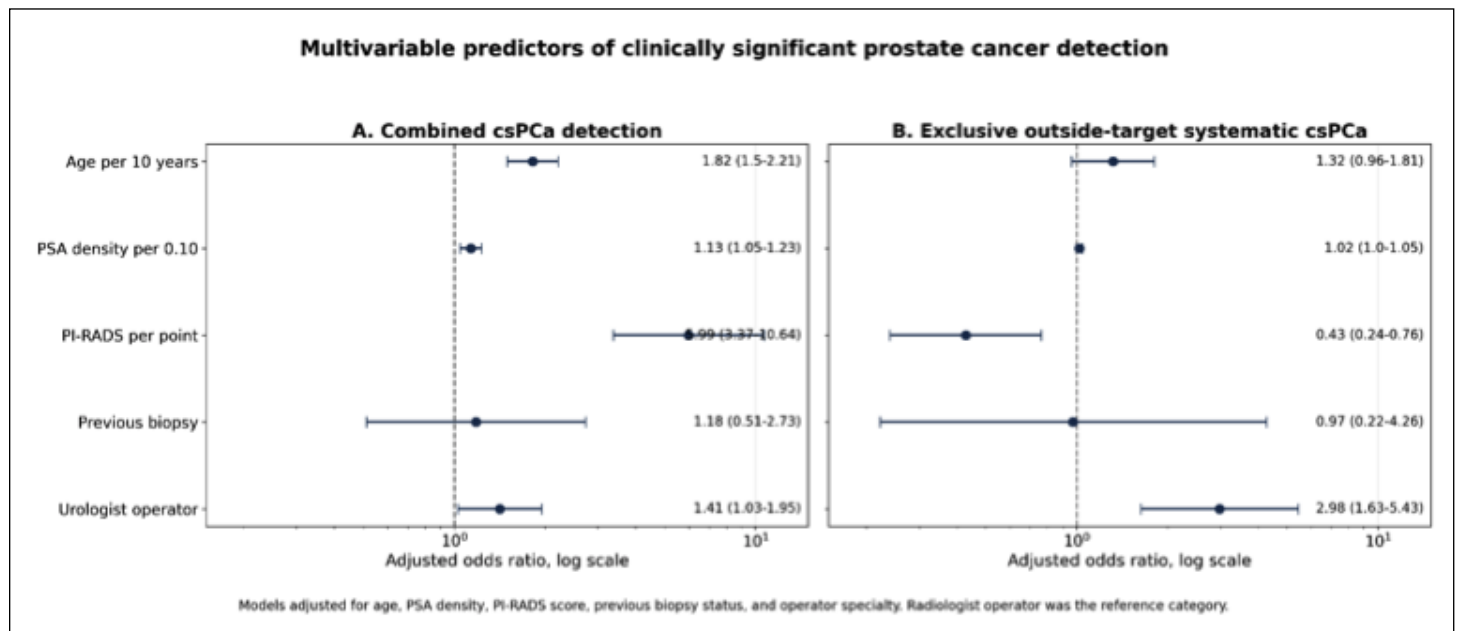
This finding may reflect intrinsic limitations of mpMRI sensitivity for smaller, multifocal, low-volume, or non-index clinically significant lesions. Alternatively, it may reflect biological heterogeneity in prostate cancer spatial distribution, where dominant MRI-visible lesions coexist with anatomically separate clinically significant tumour foci.

This observation has important implications for MRI-target-



**Figure 3.**  
ROC curves for  
multivariable  
prediction  
models

**Figure 4.**  
Forest plot for predictors of csPCa detection.



ed biopsy pathways and focal therapy planning. If additional significant lesions are frequently anatomically distinct from the MRI-visible lesion, omission of systematic sampling may underestimate tumour multifocality and disease burden.

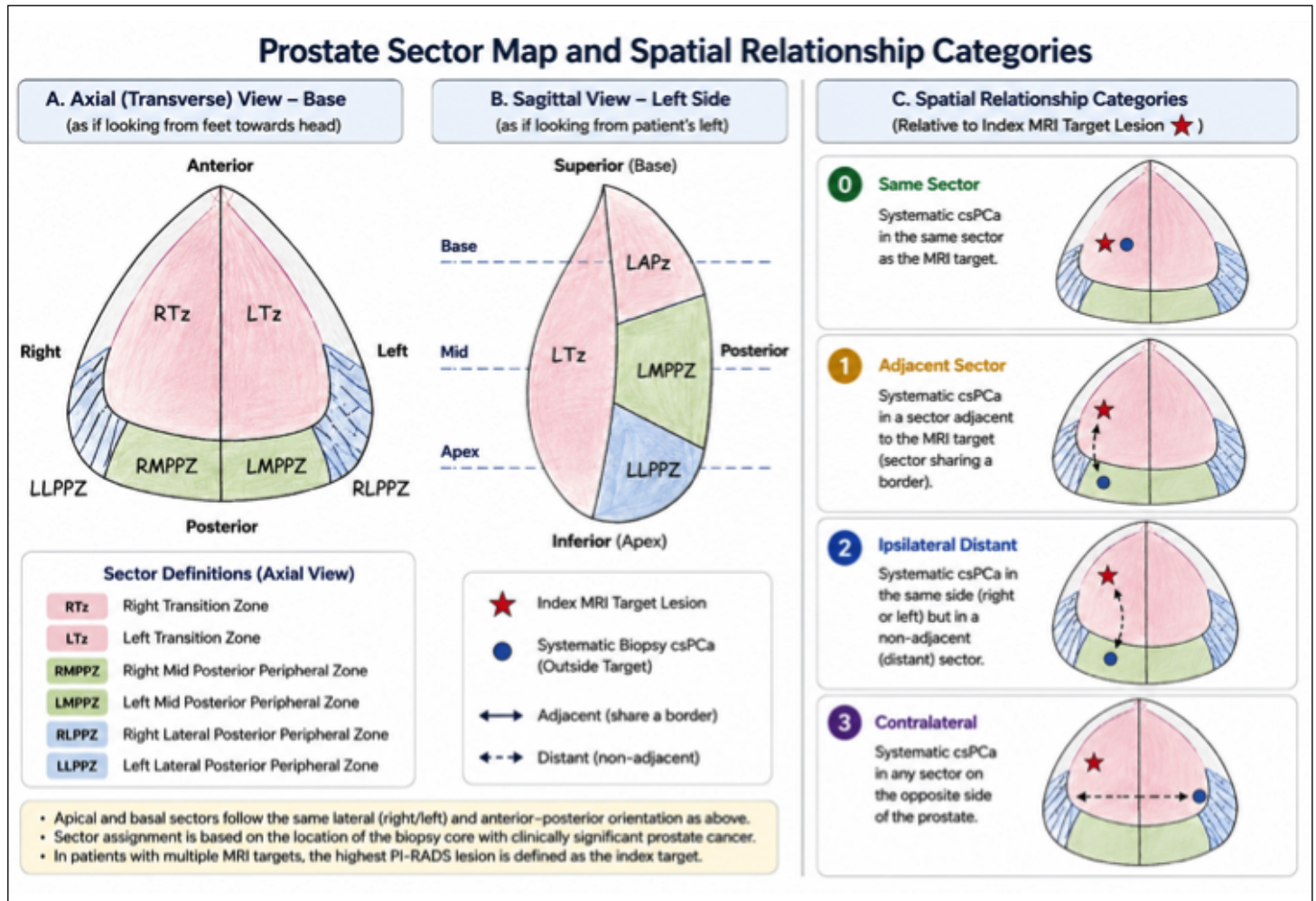
#### *Interpretation in the context of existing evidence*

PROMIS and PRECISION established MRI-targeted pathways as standard practice for prostate cancer diagnosis (5, 6), unlike TRUS biopsies, which tend to miss clinically significant disease (6, 12, 13) and have other limitations

**Figure 5.**

Schematic prostate sector map used for spatial relationship analysis.

The index MRI-visible lesion and systematic-only clinically significant prostate cancer lesions were categorised according to predefined transperineal prostate sectors and classified as same-sector, adjacent-sector, ipsilateral distant, or contralateral relationships.



(14-17). Few previous studies have specifically evaluated the anatomical relationship between systematic-only csPCa lesions and MRI-visible targets, making direct comparison with existing literature difficult (18).

However, MRI-targeted biopsy does not eliminate the need for systematic sampling. In the large paired-biopsy study by *Ahdoot et al.* (3), combined targeted and systematic biopsy detected more cancers than either method alone, and targeted biopsy alone underestimated grade in a proportion of patients. In that study, combined biopsy also resulted in fewer upgrades to grade group 3 or higher at radical prostatectomy compared with either targeted or systematic biopsy alone.

The current study expands on this evidence by concentrating especially on malignancies discovered outside of MRI-targeted lesions, rather than simply comparing targeted and systematic biopsies as competing techniques. The finding that 8.3% of men had csPCa detected only by systematic biopsy outside the target suggests that MRI-targeted biopsy alone may not be sufficient in all patients, particularly where the clinical objective is maximal detection of clinically significant disease.

### PI-RADS subgroup findings

The incremental value of systematic biopsy was greatest in PI-RADS 3 lesions and decreased with increasing MRI suspicion. This likely reflects the lower sensitivity of targeted biopsy in equivocal MRI lesions compared with highly suspicious PI-RADS-5 disease. These findings support continued consideration of systematic sampling in selected patients with indeterminate MRI findings (19).

### Predictors of csPCa

On multivariable analysis, detection of csPCa by either biopsy method was independently associated with older age, higher PSA density, and higher PI-RADS score. PI-RADS score was the strongest predictor, with an adjusted odds ratio of 5.99 per 1-point increase, reinforcing the central role of MRI suspicion in contemporary prostate cancer diagnosis. PSA density also remained independently associated with csPCa, supporting its use as a complementary clinical risk marker alongside MRI.

The model evaluating the primary outcome showed a different pattern. Higher PI-RADS score was inversely associated with csPCa detected exclusively by systematic

biopsy outside the target, with an adjusted odds ratio of 0.43 per 1-point increase. This is consistent with the subgroup results, where the exclusive systematic yield was greatest in PI-RADS 3 disease and lowest in PI-RADS 5 disease. In other words, as MRI suspicion increases, csPCa is more likely to be captured by targeted biopsy; when MRI findings are less definitive, systematic sampling appears to contribute proportionally more.

Operator type was also associated with exclusive systematic outside-target csPCa detection, with higher odds among procedures performed by urologists. This finding should be interpreted cautiously. It may reflect differences in biopsy technique, case selection, sampling intensity, lesion targeting, operator experience, or unmeasured institutional workflow factors rather than a direct causal effect of operator speciality.

### Clinical implications

The key clinical implication is that targeted biopsy alone would have missed 64 csPCa cases in this cohort, supporting combined biopsy strategies when minimising missed clinically significant disease is prioritised. The findings were particularly relevant in PI-RADS 3 lesions, where targeted biopsy detected csPCa in only 13.3%, compared with 40.0% using combined biopsy, suggesting systematic biopsy should not routinely be omitted in equivocal MRI lesions, especially in higher-risk patients. The predominance of contralateral and anatomically distinct systematic-only csPCa lesions may have implications for focal therapy planning and tumour burden assessment. The high proportion of contralateral systematic-only csPCa lesions may also have implications for hemiablativ

focal therapy strategies, where unrecognised contralateral disease could influence oncological safety.

### Strengths

The principal strength of this analysis is its direct focus on the incremental value of systematic biopsy outside MRI-targeted lesions, which is the clinically relevant question when considering whether systematic cores can safely be omitted from an MRI-targeted pathway. The cohort was relatively large, with 767 evaluable men for the primary paired csPCa analysis, allowing estimation of the absolute yield of systematic outside-target sampling with reasonable precision. Another strength is the availability of paired targeted and systematic biopsy outcomes within the same patients. This design reduces between-patient confounding when comparing biopsy strategies and allows the clinically important subgroup of patients with systematic-only csPCa to be identified directly.

### Limitations

Several limitations should be acknowledged. This retrospective single-centre analysis of routinely collected data is subject to missing values, coding inconsistencies, and selection bias. No whole-mount or template biopsy reference standard was available, limiting assessment of true sensitivity. PI-RADS subgroup analyses, particularly for PI-RADS 3 lesions, were underpowered. Observed operator-related differences should therefore be considered hypothesis-generating.

Spatial analysis was based on sector mapping rather than true three-dimensional lesion distance and may therefore incompletely reflect anatomical proximity. Spatial localisation analysis was retrospective and dependent on procedural documentation and sector-based anatomical coding.

### DECLARATIONS

**Ethical approval and consent for participate:** Ethical approval was waived by the local Ethics Committee of Kingston and Richmond Hospital NHS in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

**Authors declare no financial or non-financial interests that are directly or indirectly related to the work submitted for publication.**

**Availability of data and material:** The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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**Authors' contributions:** Emeka I Udeh: Protocol/project development, Data collection or management, Data analysis, Manuscript writing/editing; Nadine Coull: Protocol/project development, Data collection or management, Data analysis, Manuscript writing/editing; Abdussalam Musbahi: Protocol/project development, Data management, Data analysis, Manuscript writing/editing; Rotimi David: Protocol/project development, Data management, Data analysis, Manuscript writing/editing; Richard Akiboye: Protocol/project development, Data management, Data analysis, Manuscript writing/editing.

### CONCLUSIONS

In this cohort, systematic biopsy outside MRI-targeted lesions identified csPCa that would have been missed by targeted biopsy alone in 64/767 men (8.3%), representing 16.7% of all detected csPCa. Its incremental yield was greatest in men with PI-RADS 3 lesions and declined with increasing PI-RADS score. These findings support systematic sampling alongside MRI-targeted biopsy when minimising missed csPCa is prioritised, particularly in men with equivocal MRI findings or persistent clinical suspicion. The predominance of anatomically distinct systematic-only lesions suggests that omitting systematic sampling may underestimate tumour multifocality and clinically significant disease burden.

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