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Performance and Clinical Utility of a Barcelona-Derived MRI Predictive Model for Clinically Significant Prostate Cancer

J. Smith[1*], A. Jones[1], M. Brown[1]

[1]Department of Radiation Oncology, School of Medicine, University of Liverpool, Liverpool, UK.

***E-mail** ✉ liverpool.radonc.34@yahoo.com

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ABSTRACT

An MRI-based predictive model (MRI-PM) for estimating the likelihood of clinically significant prostate cancer (csPCa) was created and independently validated across institutions in the Barcelona metropolitan region, accompanied by an online risk calculator (RC) that enables users to define their preferred csPCa probability cut-off. The model was derived from a cohort of 1486 men undergoing 3-tesla multiparametric MRI (mpMRI) and subsequent targeted and/or systematic biopsies at a single academic center. External validation was performed in 946 men evaluated with the same imaging and biopsy workflow at two additional academic hospitals. CsPCa was identified in 36.9% of the development cohort and 40.8% of the validation cohort ($p = 0.054$). Incorporation of the model increased the diagnostic AUC of mpMRI from 0.842 to 0.897 in the development dataset ($p < 0.001$) and from 0.743 to 0.858 in the validation dataset ($p < 0.001$). Using a 15% probability threshold would reduce biopsy procedures by 40.1%, with 5.4% of the 36.9% csPCa cases going undetected. For individuals with PI-RADS <3, biopsy would be recommended in 4.3% of cases, enabling detection of 32.3% of the 4.2% existing csPCa. Among those with PI-RADS 3, biopsy reduction would reach 62%, at the cost of missing 28% of the 12.4% csPCa. For PI-RADS 4, only 4% of biopsies would be avoided, and 0.6% of the 43.1% csPCa would remain undetected. In PI-RADS 5, 0.6% of biopsies would be avoided with no missed csPCa from the existing 42.0%. Although the Barcelona MRI-PM performed well overall, its clinical impact differed according to PI-RADS category. Allowing customization of csPCa probability thresholds in the RC may support more flexible external validation and potentially enhance performance of MRI-PMs within specific PI-RADS strata.

Keywords: Clinically significant prostate cancer, Predictive model, Magnetic resonance imaging, Risk calculator

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Introduction

Initial concerns about prostate cancer (PCa) usually stem from raised prostate-specific antigen (PSA) levels or an abnormal digital rectal examination (DRE), and confirmation still depends on tissue sampling through biopsy [1]. Reliance on systematic biopsy alone has long been criticized for driving up the number of avoidable procedures and increasing identification of insignificant PCa (iPCa) [2]. The adoption of magnetic resonance imaging (MRI) together with MRI-directed sampling has strengthened detection of clinically significant disease (csPCa) [3, 4], although decisions about who actually needs a biopsy after MRI remain far from perfect [5, 6]. Several tools have been suggested to refine that selection process, including PSA density (PSAD) [7], MRI-based predictive approaches (MRI-PMs) [8], and newer biomarker tests [9]. MRI-PMs typically combine PI-RADS scoring with independent variables such as PSAD [8-10]. Any model intended for use outside the population it was created in must undergo external validation to ensure reliable performance [11, 12].

At least fifteen MRI-PMs have been published so far [11–25]. Ten make use of PI-RADS version 2.0 or 2.1 [11, 13, 19–25]. Only five have been externally validated [20–22, 24, 25]. None have been paired with an openly available web- or smartphone-based risk calculator, and none have examined how model accuracy differs across PI-RADS categories.

This study aimed to create a web-based risk calculator (RC) for estimating csPCa probability, grounded in a newly built MRI-PM developed in the Barcelona metropolitan area. A notable feature of the RC is the ability to choose the csPCa probability cut-off, allowing easier comparison and future validation efforts. The project's objectives were: i) development of the Barcelona MRI-PM; ii) external validation in a metropolitan cohort; iii) construction of a freely accessible RC that permits selection of the probability threshold; and iv) assessment of model behavior across PI-RADS categories in both datasets.

Materials and Methods

Development cohort

The development cohort included 1987 men referred from primary care with suspicion of PCa, defined by PSA values above 3 ng/mL and/or an abnormal DRE. All were scheduled for a pre-biopsy multiparametric MRI (mpMRI) and subsequently underwent MRI-guided and/or systematic biopsy within one to four weeks, between 1 January 2016 and 31 December 2019, at a single academic hospital (VHH) in the Barcelona metropolitan area. Data entry followed the START reporting framework for MRI-targeted biopsy studies [26]. Written informed consent was obtained, and institutional ethics approval was secured (PR/AG-317/2017).

Patients were excluded if they were receiving 5-alpha reductase inhibitors for benign prostatic hyperplasia, had a prior PCa diagnosis, previously showed atypical small acinar proliferation or atypical prostate-intraepithelial neoplasia, or lacked required clinical or imaging information. Another 183 individuals did not undergo mpMRI for safety or technical reasons (claustrophobia: 56; pacemaker: 32; metallic implants: 95). The final development dataset consisted of 1486 men **(Figure 1)**.

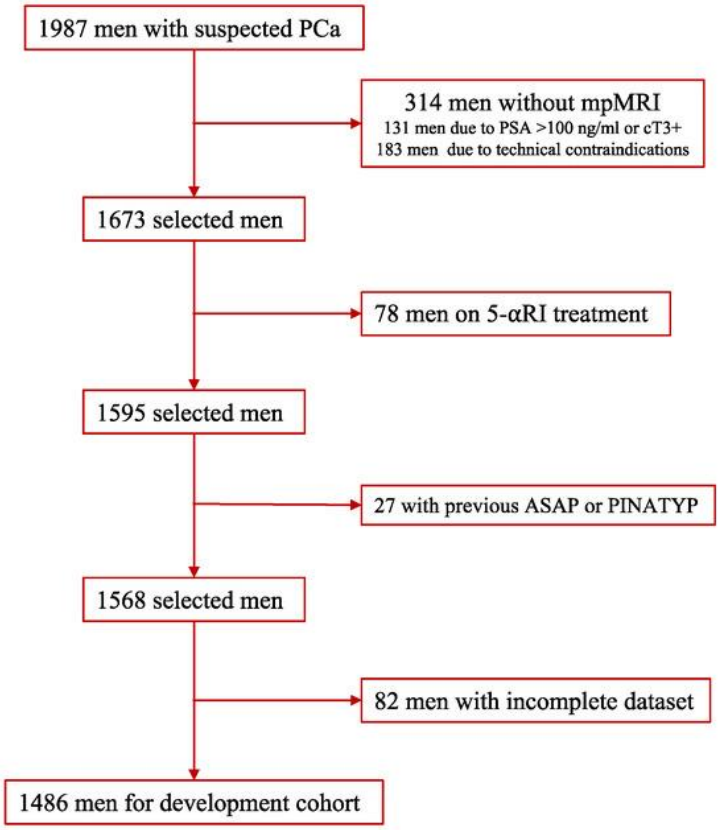


Figure 1. Flow chart of development cohort creation: inclusion and exclusion criteria.

External validation cohort

The external validation sample consisted of 946 men evaluated for possible PCa at two additional academic hospitals in the Barcelona metropolitan region (PSM and GTIPH). Participants were retrospectively selected. Criteria for suspicion of PCa, the recruitment timeframe, and the diagnostic workflow mirrored those applied in the development cohort.

MRI technique and interpretation

All MRI examinations were conducted using 3-tesla scanners equipped with surface phased-array coils. The development cohort was imaged on a Magneto Trio system (Siemens Corp., Erlangen, Germany), whereas the validation cohort was evaluated using Diamond Select Achieva 3.0-TX and Nova Dual platforms (Philips Corp., Eindhoven, The Netherlands). Protocols included T2-weighted, diffusion-weighted, and dynamic contrast–enhanced sequences, following European Society of Urogenital Radiology recommendations. Two senior radiologists at each participating center reviewed the images using PI-RADS v2.0 guidelines, and the highest PI-RADS category was used for men presenting with multiple lesions [27]. Prostate volume was measured by MRI at all three centers.

Prostate biopsy procedure

Biopsies were obtained using a uniform protocol across institutions. Men with PI-RADS > 3 underwent cognitive fusion, TRUS-guided sampling of 2–4 targeted cores in addition to a 12-core systematic biopsy. Men with PI-RADS < 3 received only the 12-core systematic sampling. One experienced urologist performed all biopsies at each site. TRUS units differed by cohort: the development center used the BK Focus 400 (BK Medical Inc., Herlev, Denmark), while the validation centers employed the Siemens Acuson 150 and the Sonolite Antares systems (Siemens Inc., Erlangen, Germany).

Pathological assessment and definition of csPCa

Biopsy specimens were processed individually and reviewed by two dedicated uropathologists at each institution. When PCa was detected, tumors were graded according to the International Society of Uro-Pathology (ISUP) system. Clinically significant disease (csPCa) was defined as ISUP grade > 2 [28].

Construction of the MRI-based predictive model

Candidate variables evaluated for their association with csPCa included PI-RADS v2.0 category (1–5), age, ethnicity (Caucasian vs. non-Caucasian), serum PSA, MRI-derived prostate volume, DRE findings, family history of PCa (none vs. first-degree relative), and biopsy setting (initial vs. repeat). PSAD was not added explicitly because it requires prior calculation and offered no meaningful gain in discrimination beyond PSA and prostate volume alone; the AUC for csPCa using these two predictors was 0.892 and 0.897, respectively (data not shown).

Model performance endpoints

The analysis focused on csPCa detection rates and the proportion of biopsies that could potentially have been avoided.

Statistical analysis

Baseline characteristics of the development and validation cohorts were summarized descriptively and compared using Chi-square and Mann–Whitney U tests. Model development involved stepwise binary logistic regression using variables associated with csPCa. Continuous predictors were examined for linearity and, when appropriate, modelled using restricted cubic splines. Calibration was evaluated in both datasets. Discriminative ability was quantified with ROC curves and corresponding AUC values. Clinical utility was assessed using clinical utility curves (CUCs), which estimate missed csPCa rates and avoidable biopsies, and by decision curve analysis (DCA) comparing the added value of mpMRI and the MRI-PM against a strategy of biopsying all men.

AUCs and specificities at 90% sensitivity for csPCa were compared between mpMRI and the MRI-PM using DeLong and Chi-square tests. After identifying the threshold corresponding to 95% sensitivity for csPCa, we compared overall model performance and conducted subgroup analyses stratified by PI-RADS <3, 3, 4, and 5. Metrics included sensitivity, specificity, positive and negative predictive values, accuracy, and estimated rates of biopsy avoidance and potentially missed csPCa. The external validation was performed in accordance with TRIPOD guidance. All statistical analyses were conducted using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS version 24 (IBM Corp., San Francisco, CA, USA).

Results and Discussion

Profiles of the development and validation cohorts

Table 1 provides an overview of the demographic and clinical features of both study cohorts. Compared with the external validation cohort, men in the development cohort were significantly younger and presented with lower PSA concentrations ($p < 0.001$). Conversely, abnormal DRE findings, a family history of PCa, and prior biopsy procedures were all more frequent among participants in the validation cohort ($p < 0.001$). Prostate volumes did not differ between groups ($p = 0.559$), and both cohorts consisted predominantly of Caucasian patients ($p = 0.738$). The distribution of PI-RADS categories varied significantly between the two populations ($p < 0.001$). Although the validation cohort showed a numerically higher prevalence of csPCa, this difference did not reach statistical significance ($p = 0.054$), whereas the rate of insignificant PCa was clearly higher ($p < 0.001$). In the development cohort, csPCa was identified in 36.9% of men overall, with detection frequencies of 4.1% for PI-RADS <3, 15.3% for PI-RADS 3, 52.4% for PI-RADS 4, and 83.4% for PI-RADS 5. In the validation cohort, the overall csPCa detection rate was 40.8%, and distribution by PI-RADS category was 10.9% for PI-RADS <3, 20.4% for PI-RADS 3, 51.9% for PI-RADS 4, and 84.0% for PI-RADS 5.

Table 1. Characteristics of men suspected to have PCa in development and external validation cohorts and comparisons between them.

Characteristic	Development Cohort	External Validation Cohort	p Value
Number of men	1486	946	-
Caucasian race, n (%)	1465 (98.6)	931 (98.4)	0.738
Median age at biopsy (IQR), years	69 (62–74)	67 (61–72)	<0.001
Median serum PSA (IQR), ng/mL	6.0 (4.4–9.2)	7.4 (5.5–10.9)	<0.001
Abnormal DRE, n (%)	329 (22.1)	283 (29.9)	<0.001
PCa family history, n (%)	127 (8.5)	34 (3.6)	<0.001
Median prostate volume (IQR), mL	55 (40–76)	55 (40–78)	0.559
Prior negative prostate biopsy, n (%)	388 (26.1)	293 (31.0)	0.010
PI-RADS v.2.0, n (%)			
1	242 (16.3)	185 (19.6)	<0.001
2	73 (4.9)	50 (5.3)	
3	444 (29.9)	201 (21.2)	
4	450 (30.3)	391 (41.3)	
5	277 (18.6)	119 (12.6)	
PCa detection, n (%)	693 (46.6)	521 (55.1)	<0.001
csPCa detection, n (%)	548 (36.9)	386 (40.8)	0.054
iPCa detection, n (%)	145 (9.8)	135 (14.3)	<0.001

IQR = interquartile range; n = number; PSA = prostate-specific antigen; DRE = digital rectal examination; PI-RADS = Prostate Imaging–Reporting and Data System; PCa = prostate cancer; csPCa = clinically significant PCa; iPCa = insignificant PCa.

Development and performance of the MRI-based predictive model

Multivariable logistic regression identified several variables—age, PSA level, DRE findings, prostate volume, family history of PCa, biopsy status (initial vs. repeat), and PI-RADS v2.0 classification—as independent contributors to the likelihood of csPCa **(Table 2)**.

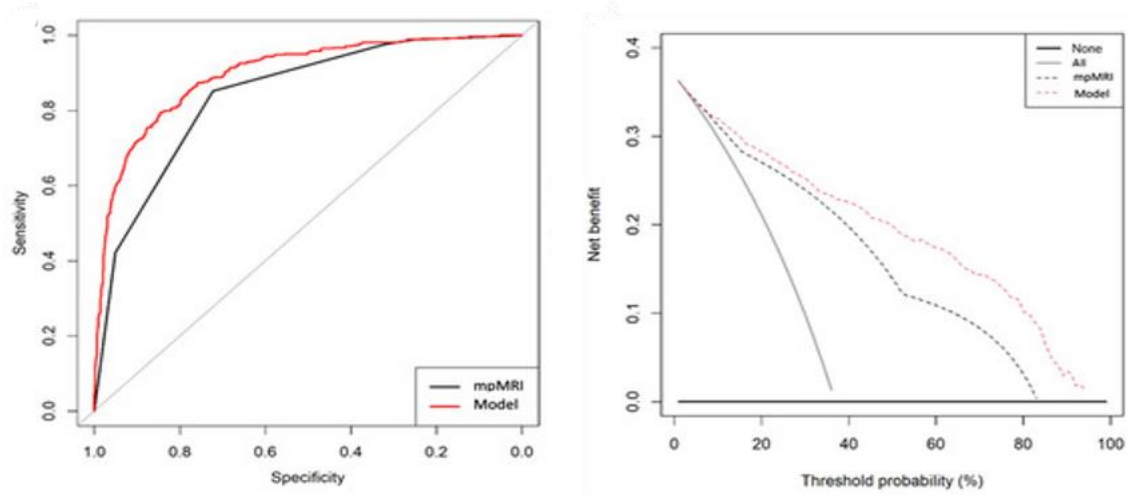
Table 2. Logistic regression analysis of independent significant predictors of csPCa in prostate biopsies.

Predictor	Odds Ratio (95% CI)	p Value
Age at prostate biopsy, ref. prior year	1.056 (1.036–1.077)	<0.001
Serum PSA, ref. prior ng/mL	1.085 (1.056–1.114)	<0.001
DRE, ref. normal.	1.730 (1.195–2.503)	0.004
Prostate volume, ref. prior mL	0.970 (0.964–0.977)	<0.001
Family history of PCa, ref. no	1.788 (1.066–3.002)	0.028
Biopsy type, ref. initial	0.668 (0.478–0.934)	0.018
PI-RADS v.2.0 score, 2 to ref. 1	3.311 (1.008–10.879)	0.048

3 to ref. 1	6.551 (2.740–15.661)	<0.001
4 to ref. 1	32.088 (13.660–75.377)	<0.001
5 to ref. 1	75.673 (30.738–186.311)	<0.001

CI = confidence interval; PSA = prostate-specific antigen; DRE = digital rectal examination; PI-RADSv.2 = Prostate Imaging-Reporting and Data System v.2.; ref. = referenced to.

Figure 2a illustrates the ROC curves for mpMRI and the MRI-PM within the development cohort. The MRI-PM provided additional clinical value compared with a strategy of biopsying every patient, beginning at a csPCa risk level of roughly 2%. A similar advantage of mpMRI over universal biopsy is shown in **Figure 2b**.



a) b)

Figure 2. ROC curves showing the efficiency of MRI and MRI-PM in the development cohort (a) DCAs evaluating the net benefit of MRI and MRI-PM over biopsying all men belonging to thedevelopment cohort (b)

Cohort characteristics

Table 3 summarizes the baseline characteristics of the development and external validation cohorts. Compared with the validation cohort, participants in the development cohort were slightly younger and had higher serum PSA levels ($p < 0.001$). Conversely, the validation cohort exhibited higher proportions of abnormal DRE findings, first-degree family history of PCa, and repeat biopsies ($p < 0.001$). Median prostate volumes were comparable between the two cohorts ($p = 0.559$), and both cohorts were predominantly Caucasian ($p = 0.738$). Distribution of PI-RADS categories differed significantly across cohorts ($p < 0.001$). While there was no statistically significant difference in csPCa prevalence between cohorts (36.9% vs. 40.8%, $p = 0.054$), the rate of iPCa was higher in the validation cohort ($p < 0.001$). Within the development cohort, PI-RADS categories were distributed as follows: <3: 4.1%, 3: 15.3%, 4: 52.4%, and 5: 83.4%. In the validation cohort, the corresponding distribution was: <3: 10.9%, 3: 20.4%, 4: 51.9%, and 5: 84.0%.

Abbreviations: IQR = interquartile range; n = number; PSA = prostate-specific antigen; DRE = digital rectal examination; PI-RADS = Prostate Imaging–Reporting and Data System; PCa = prostate cancer; csPCa = clinically significant PCa; iPCa = insignificant PCa.

Table 3. Efficacy of mpMRI and MRI-based predictive model analysed from the AUCs and specificitiescorresponding to the 85%, 90% and 95% sensitivity thresholds for csPCa, in development cohort (A) andexternal validation cohort (B).

Predictor	Development Cohort (A)				External Validation Cohort (B)			
	AUC (95% CI)	Specificities According to Sensitivity			AUC (95% CI)	Specificities According to Sensitivity		
		85%	90%	95%		85%	90%	95%

mpMRI	0.842 (0.822–0.861)	72.4 (69.4–75.2%)	56.8 (53.6–60.0)	40.7 (37.5–43.9)	0.743 (0.711–0.776)	45.5 (41.3–49.7)	41.3 (32.9–48.3)	14.3 (11.6–17.5)
MRI-PM	0.897 (0.880–0.914)	78.1% (75.3–80.7)	69.5 (66.4–72.4)	55.7 (52.5–58.9)	0.858 (0.833–0.883)	67.7 (63.6–71.5)	52.3 (48.1–56.5)	32.3 (28.5–36.4)
p Value	=0.011	p = 0.005	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

mpMRI = multiparametric magnetic resonance imaging; MRI-PM = MRI-based predictive model; AUC = area under the curve; CI = confidence interval.

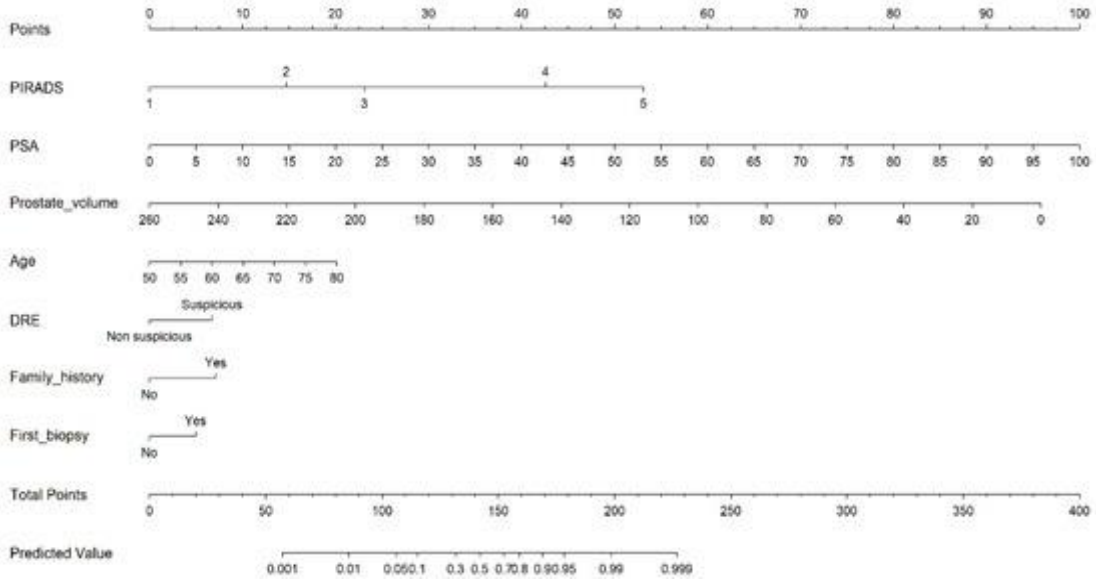


Figure 3. Nomogram derived from the developed MRI-PM model of csPCa in prostate biopsies.

CUCs showing the rate of avoidable biopsies and the corresponding rate of potentially missed csPCa, regarding the continuous csPCa probability threshold, are presented in **Figure 4**.

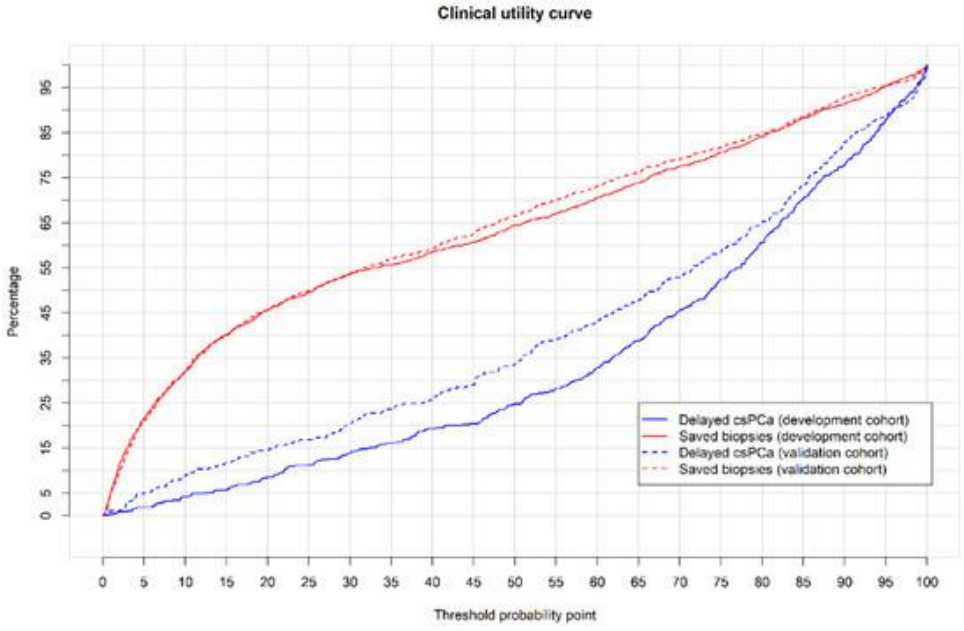


Figure 4. CUCs showing the rates of avoided biopsies (red lines) and corresponding missed csPCa(blue lines) regarding the continuous threshold of csPCa probability using MRI-PMs in developmentcohort (continuous lines) and external validation cohorts (interrupted lines).

Clinical implications and threshold-based biopsy reduction

The clinical utility curves (CUCs) for the MRI-based predictive model (MRI-PM) illustrate how varying csPCa probability thresholds influence both the number of biopsies that could be avoided and the proportion of csPCa cases potentially missed **(Figure 4)**. Solid lines represent the development cohort, while dashed lines correspond to the external validation cohorts.

For a hypothetical cohort of 1000 men, detailed estimates of avoidable biopsies and associated csPCa detection risk are provided. A threshold of 15% was selected because it preserved a 95% sensitivity for csPCa detection, which translates into a 40% reduction in biopsy procedures. Stratified by PI-RADS scores, the MRI-PM would yield the following outcomes: in PI-RADS 5, all csPCa cases would be correctly identified, with only 0.5% of biopsies avoided; in PI-RADS 4, 0.6% of csPCa cases would go undetected, while 4% of biopsies could be spared; in PI-RADS 3, 28.2% of csPCa cases would be missed, but 61.9% of biopsies would be unnecessary; and in PI-RADS <3, biopsy would be recommended for 4.3% of men, capturing 33.3% of the rare csPCa cases (4.2%) in this group **(Table 4)**.

The discrimination capacity of the MRI-PM across PI-RADS categories, highlighting its ability to differentiate between men with and without csPCa. Net benefit analyses stratified by PI-RADS categories further demonstrate that using the MRI-PM could improve decision-making compared with biopsying all men.

Table 4. Summary of the clinical impact of the MRI-based predictive model in a cohort of 1000 men, detailing the proportion of avoidable biopsies and potentially missed csPCa in the development (A) and external validation (B) cohorts, using a 15% csPCa probability threshold and stratified by PI-RADS scores.

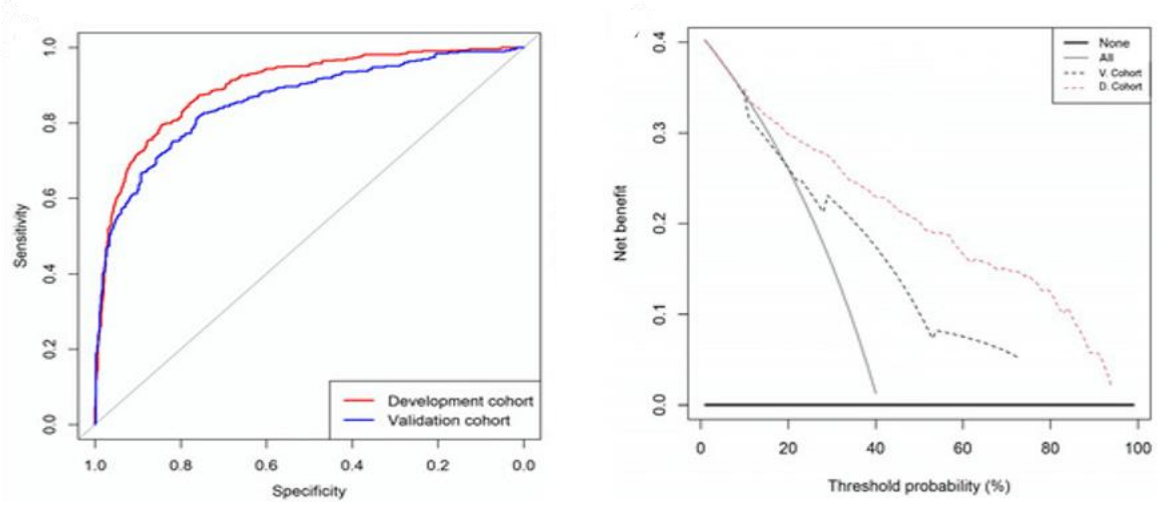
PI-RADS	Development Cohort (A)		External Validation Cohort (B)	
	Missed csPCa	Avoidable Biopsies	Missed csPCa	Avoidable Biopsies
1–2, n (%)	6/9 (66.7)	203/212 (95.7)	36/44 (81.8)	232/248 (93.5)
3, n (%)	13/46 (28.2)	185/299 (61.9)	6/43 (14.0)	134/212 (63.2)
4, n (%)	1/159 (0.6)	12/303 (4.0)	4/215 (1.9)	30/413 (7.3%)
5, n (%)	0/155 (0)	1/186 (0.5)	1/106 (0.9)	3/126 (2.4)
All, n (%)	20/369 (5.4)	401/1000 (40.1)	47/408 (11.5)	399/1000 (39.9)

Performance of MRI-PM in the external validation cohort

In the external validation dataset, the MRI-based predictive model (MRI-PM) slightly underestimated the actual risk of clinically significant prostate cancer (csPCa). For instance, a predicted probability of 20% corresponded to an observed csPCa rate of roughly 25%, suggesting a modest underprediction by the model. The calibration statistics, with an intercept of 0.261 and slope of 0.815, reflect this discrepancy, which may be explained by the higher overall prevalence of csPCa in the validation cohort (40.8%) compared with the development cohort (36.9%).

The discriminative performance of the MRI-PM was evaluated using ROC curves, as shown in **Figure 5a**. Decision curve analysis (DCA) further demonstrated that applying the MRI-PM could provide greater net benefit than performing biopsies on all men, both in the development and external validation cohorts **(Figure 5b)**. In the external validation group, mpMRI alone yielded an AUC of 0.743 (95% CI: 0.711–0.776), which was lower than the AUC observed in the development cohort (0.842, 95% CI: 0.822–0.861; $p < 0.001$). When the MRI-PM was applied, the AUC improved to 0.858 (95% CI: 0.833–0.883), compared with 0.897 (95% CI: 0.880–0.914) in the development cohort ($p = 0.009$) **(Tables 3A–3B)**.

At a sensitivity of 90% for csPCa detection, the specificity of the MRI-PM decreased in the external validation cohort to 41.3%, compared with 52.3% in the development cohort ($p < 0.001$) **(Table 3B)**. This reduction likely reflects differences in patient characteristics and csPCa prevalence between the two cohorts.



a) b)

Figure 5. (a) ROC curves comparing the discriminative performance of the MRI-based predictive model (MRI-PM) in the development and external validation cohorts. (b) Decision curve analyses (DCAs) illustrating the net clinical benefit of MRI-PM in the development cohort (red dashed line) and the external validation cohort (blue dashed line) relative to biopsying all men (solid grey line).

Clinical utility curves (CUCs) for MRI-PMs are shown in **Figure 4**, presenting results for both the development and external validation cohorts. Detailed estimates of the number of avoided biopsies and the corresponding risk of undetected csPCa for a hypothetical cohort of 1000 men in the external validation cohort are summarized. Using a 15% csPCa probability threshold, the model would reduce biopsies by 39.9% while missing 11.5% of csPCa cases. Stratified by PI-RADS category, in PI-RADS 5, 2.4% of biopsies could be avoided with 0.9% of csPCa undetected; in PI-RADS 4, 7.3% of biopsies could be spared at the cost of missing 18.6% of csPCa; in PI-RADS 3, 63.2% of biopsies could be avoided while 14% of csPCa cases would remain undetected; and in PI-RADS <3, 6.5% of men would be recommended for biopsy, capturing 18.2% of the limited csPCa present **(Table 4B)**.

Web-based risk calculator (RC)

The validated MRI-PM was implemented as an interactive web-based diagnostic tool using RStudio v.1.2.5001 and the shiny package (RStudio Team, 2015; URL: http://www.rstudio.com/; accessed 12 April 2020). This RC allows users to select a csPCa probability threshold, providing flexibility for clinical decision-making. The tool is freely accessible at https://mripcaprediction.shinyapps.io/MRIPCaPrediction/ (accessed 23 November 2020).

Discussion

Despite the widespread adoption of MRI and targeted biopsies, opportunities remain to improve early detection of csPCa through individualized biopsy selection [6]. Contemporary MRI-PMs incorporate PI-RADS scoring and MRI-derived prostate volume [11, 19, 20, 24]. Our model was constructed using PI-RADS v2.0 from 3-tesla mpMRI and includes age, serum PSA, and prostate volume as continuous, independent predictors, without imposing artificial ranges, to reflect real-world clinical practice [12].

Ethnicity was excluded because it was not predictive of csPCa in our largely homogeneous cohort, unlike other studies with more diverse populations [16]. PSA density (PSAD) is a well-recognized predictor that integrates serum PSA and prostate volume, providing a cost-effective metric without additional imaging. PSAD can be incorporated directly as a ratio or indirectly via PSA and prostate volume, with both approaches yielding similar odds ratios. We opted for the latter to simplify RC input and avoid pre-calculation. Previous studies have shown that PSAD-based models demonstrate robust performance and reliable calibration in external validations [29].

The type of biopsy (initial vs. repeat) was also included, enhancing clinical applicability compared with MRI-PMs limited to either biopsy-naïve men or those with prior negative biopsies [13, 19-21, 23, 24].

External validation is crucial for assessing model generalizability. In our study, it was conducted in two representative institutions using the same inclusion criteria and diagnostic workflow. Although csPCa prevalence

was slightly higher in the validation cohort (40.8% vs. 36.9%), the MRI-PM maintained strong discriminative ability with only minor underestimation.

The 15% probability threshold, selected in the development cohort for 95% sensitivity and a 40% reduction in biopsies, yielded similar outcomes in the external validation cohort, avoiding 39.9% of biopsies while missing 11.5% of csPCa.

When stratified by PI-RADS categories, the net benefit of MRI-PM over universal biopsy was modest in high PI-RADS groups. In PI-RADS 5, 0.5–2.4% of biopsies could be avoided, with less than 1% of csPCa missed; in PI-RADS 4, 4–7.3% of biopsies could be avoided while missing 0.6–18.6% of csPCa. In PI-RADS 3, more substantial reductions in biopsy rates were observed (61.9–62.3%) with 14–28.2% of csPCa undetected. For men with normal or near-normal mpMRI (PI-RADS <3), biopsy recommendations were limited (4.3–6.5%), detecting 18.2–33.3% of the few csPCa cases present. Overall, undetected csPCa in low and intermediate PI-RADS categories remained low due to their small absolute numbers (<5–10% of all csPCa).

External validation of predictive models in the populations where they are intended to be applied is critical, and providing accessible, user-friendly risk calculators (RCs) is essential to circumvent the cumbersome and time-intensive use of traditional nomograms [11, 12]. A key innovation of our web-based RC is the ability to customize the csPCa probability threshold for either the overall population or specific PI-RADS categories. This feature allows thresholds to be tailored to the csPCa prevalence of external validation cohorts [30] and enhances the model's utility in distinct PI-RADS subgroups. For example, if missing 28% of csPCa in men with PI-RADS 3 is considered unacceptable, the threshold can be lowered to 7%, which reduces the proportion of missed csPCa to 11% but also lowers the rate of avoided biopsies to 26% from 62%. Notably, this study represents the first systematic evaluation of MRI-PM performance stratified by PI-RADS categories. The findings indicate that MRI-PMs offer limited additional clinical benefit for men with PI-RADS >3, particularly those with PI-RADS 5, for whom biopsy should be consistently performed due to the high prevalence and aggressiveness of csPCa in this group [27, 31–35].

We successfully developed a novel MRI-PM for csPCa and validated it externally within the same metropolitan area. The associated web-based RC provides an intuitive interface for widespread adoption, and the option to adjust csPCa probability thresholds enables clinicians to optimize sensitivity for each PI-RADS category. Rather than representing limitations, the involvement of experienced local radiologists following PI-RADS v2 [27], pathologists reporting ISUP grades [28], and urologists performing biopsies according to EAU guidelines [1] reflects real-world practice and strengthens the generalizability of our results. One inherent limitation is that csPCa prediction relies on biopsy findings, which may not fully reflect the pathology of the entire prostate gland [36]. Moreover, the model's applicability is restricted in populations where ethnicity significantly modifies csPCa risk. Future studies should explore its performance in diverse clinical settings, including non-academic centers or institutions with different PI-RADS distributions and csPCa prevalence. While cognitive-fusion guided biopsies were used in both development and validation cohorts, prior studies suggest that outcomes are comparable to software-based fusion techniques [37]; nevertheless, additional validation in cohorts using different biopsy schemes is warranted. Advances in genomics may refine the understanding of PCa aggressiveness, and future integration of radiomics could allow MRI-PMs to predict newly redefined csPCa [38].

Conclusion

A new MRI-based predictive model for csPCa was developed to support individualized decision-making for prostate biopsy in the metropolitan area of Barcelona. The associated web-based RC allows clinicians to select the csPCa probability threshold, facilitating external validation and enabling performance optimization for specific PI-RADS categories. In our overall population, the model detected 95% of csPCa while reducing prostate biopsies by 40%. Stratified analyses indicate that the MRI-PM provides the greatest clinical benefit in men with PI-RADS <3, highlighting its value for low- and intermediate-risk patients.

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