# PROGNOSTIC AND CLINICAL UTILITY CAPABILITIES OF CELL CYCLE PROGRESSION TESTING, PROSTATE IMAGING-REPORTING AND DATA SYSTEM SCORING, AND CLINICOPATHOLOGIC DATA IN MANAGEMENT OF LOCALIZED PROSTATE CANCER

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## BACKGROUND

- Though guidelines support MRI as a diagnostic tool, evidence that PI-RADs are prognostic remains limited.
- We compared prognostic and clinical utility capabilities among cell cycle progression (CCP) testing, mpMRI with PI-RADS, and clinicopathologic data in select medical management scenarios. We assessed:
  - Distributions of CCP scores, clinical cell-cycle risk (CCR) scores, and clinicopathologic data relative to PI-RADS.
  - Ability to predict tumor grade post-radical prostatectomy.
  - Impact on treatment selection.

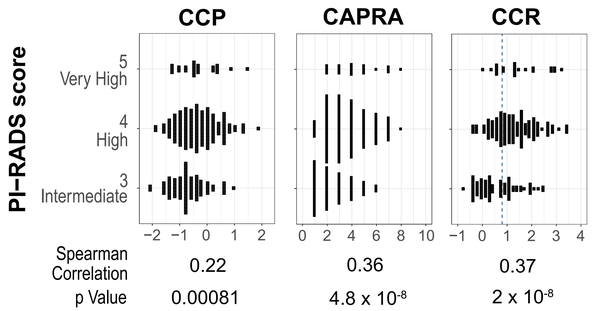
## METHODS

- Retrospective, observational analysis of data from sequential patients (N=222, two cohorts) from a single Urology community practice (January 2015-June 2018).
  - Cohort 1 (n=156): Newly diagnosed with localized prostate cancer (PrCA).
  - Cohort 2 (n=66): Already on active surveillance (AS).
- Inclusion criteria: Diagnosed with localized PrCa; had PI-RADS version 2 score >2 derived from mpMRI-ultrasound fusion targeted biopsy; and had a biopsy CCP test result.
- CCP test measured the expression of 31 CCP genes and 15 housekeeper genes in FFPE tissue using RT-PCR. CCP score was calculated as the normalized expression of 31 CCP genes and was combined in a validated model with the UCSF Cancer of the Prostate Risk Assessment (CAPRA) score (0.57×CCP + 0.39×CAPRA) (Cuzick et al., *Br J Cancer*, 2015).

## RESULTS

- In combined Cohorts, weak but significant correlations were seen between PI-RADS and CCP, CAPRA, or CCR, suggesting that much prognostic information captured by these measures is independent (Figure 1).
- On multivariate analysis, CCP was a significant predictor of higher-grade tumor (Gleason score ≥4+3) after radical prostatectomy, with the resected tumor ~4 times more likely to harbor a higher-risk Gleason score with every 1-unit increase in CCP (Table 1).
- On multivariate analysis, both CCP and CCR were significant and independent predictors of AS versus curative therapy in Cohort 1. Each 1-unit increase in CCP corresponded to ~2-fold greater likelihood of selecting curative therapy (Table 2).
- CCR score at or below the AS threshold significantly reduced the probability of selecting curative therapy over AS [OR 0.28 (95% CI 0.13, 0.57), p=0.00044].

***Figure 1. CCP, CAPRA, and CCR Score Distributions Across PI-RADS Score Groups in Combined Cohorts 1 + 2 (N=222)***




CCR 0.8 active surveillance threshold (Men below threshold: Intermediate 50.0%, High 43.3%, Very High 6.7%) (Men above threshold: Intermediate 21.2%, High 66.7%, Very High 12.1%)

***Table 1. Prediction of Gleason Score Category: Multivariate Analysis***

| Cohort 1, Newly Diagnosed (n=55/156) | | |
|---|---|---|
| **Predictor** | **Odds Ratio (95% CI)** | **p-value** |
| CCP | 4.33 (1.58, 14.65) | **0.0033** |
| CAPRA | 2.06 (1.24, 3.81) | **0.0039** |
| PI-RADS | 0.42 (0.09, 1.65) | 0.22 |
| **Combined Cohorts (n=68/222)** | | |
| **Predictor** | **Odds Ratio (95% CI)** | **p-value** |
| CCP | 4.01 (1.54, 12.59) | **0.0035** |
| CAPRA | 2.43 (1.50, 4.44) | **0.00011** |
| PI-RADS | 0.35 (0.08, 1.31) | 0.12 |

CAPRA, UCSF Cancer of the Prostate Risk Assessment; CCP, cell cycle progression; CI, confidence interval; PI-RADS, Prostate Imaging and Reporting Data System; PSA, prostate specific antigen; RP, radical prostatectomy

***Table 2. Impact on Management Selection Among Newly Diagnosed Patients (Cohort 1) (N=150)***

| Predictor | Odds Ratio (95% CI) | p-value |
|---|---|---|
| **Univariate Models** | | |
| CCP | 2.64 (1.53, 4.85) | **0.00033** |
| CAPRA | 1.44 (1.16, 1.82) | **0.00071** |
| CCR | 2.41 (1.56, 3.92) | **3.7 x $10^{-5}$** |
| PI-RADS | 1.49 (0.84, 2.68) | 0.17 |
| **CCP, CAPRA, PI-RADS Multivariate Model** | | |
| CCP | 2.1 (1.17, 3.96) | **0.012** |
| CAPRA | 1.3 (1.02, 1.68) | **0.035** |
| PI-RADS | 1.08 (0.58, 2.01) | 0.82 |
| **CCR, PI-RADS Multivariate Model** | | |
| CCR | 2.38 (1.51, 3.94) | **9.7 x $10^{-5}$** |
| PI-RADS | 1.06 (0.57, 1.97) | 0.86 |

CAPRA, UCSF Cancer of the Prostate Risk Assessment; CCP, cell cycle progression; CCR, Clinical Cell-Cycle Risk; CI, confidence interval; PI-RADS, Prostate Imaging and Reporting Data System

Multivariate models adjusted for CCP, CAPRA, CCR, and PI-RADS.

## CONCLUSIONS

- The CCP score was a better predictor of both tumor grade and treatment selection than were PI-RADS scores.
- A broad portfolio of clinical, imaging, and molecular measures remains essential to ensure the most accurate and precise risk assessment to inform treatment selection.