

Title: Beyond the Cores: MRI-Defined Extension and PSA Density Refine Risk in Gleason 7 Prostate Cancer

Authors

1. James Janopaul-Naylor, MD, janopaj@mskcc.org¹
2. Stephanie Lobaugh¹
3. Sankalp Pandya¹
4. Daniel J. Gorovets¹
5. Marisa A. Kollmeier¹
6. Sean A. McBride¹
7. Michael B. Bernstein¹
8. Justin Haseltine¹
9. Thomas P. Kole¹
10. Victoria Brennan¹
11. Carson Callahan²
12. Zachary R. Moore¹
13. Borys R. Mychalczak¹
14. Boris A. Mueller¹
15. David M. Guttman¹
16. Andrew R. Barsky¹
17. Zachary Zumsteg³
18. Daniel Spratt⁴
19. Zhigang Zhang¹
20. Shuang George Zhao⁵
21. Himanshu Nagar¹

Affiliations

¹Memorial Sloan Kettering Cancer Center

²University of Wisconsin

³Cedars-Sinai Medical Center

⁴University Hospitals Seidman Cancer Center

⁵MD Anderson Cancer Center

Funding Acknowledgements: JJN is a PCF YIA 2026

Conflicts of Interest Disclosure Statement: None

Background: Contemporary intermediate-risk prostate cancer (IR PCa) classifications rely on digital rectal examination and omit MRI-defined disease extent or PSA density, despite the routine availability of both. This project evaluates whether MRI-defined local disease extent and PSA density provide prognostic information beyond established risk stratification for distant metastasis (DM) and biochemical recurrence (BCR) among men with IR PCa.

Methods: We conducted a multi-site, single institution retrospective study including 1,425 men with cT1-2, Grade Group (GG) 2-3, PSA <20, staging MRI, and who were treated with dose-escalated

radiotherapy between 1998-2020 with median follow-up 7 years. Composite Radiographic Risk (CRR) stratified as high (definite ECE or SVI), intermediate (possible/probable findings), or low. PSA density incorporated into three tiers: high PSA (≥ 10 ng/mL) and high density (≥ 0.15 ng/mL/cc), low PSA and high density, and low density. DM, BCR, and overall survival (OS) assessed with Fine-Gray competing risk regression for associations. Risk prediction models using different risk features assessed using AUC and Brier Scores. Data analysis completed July 2026.

Results: This cohort had median PSA density 0.20 (IQR 0.14-0.30), with 16% and 35% CRR high and intermediate respectively. Ten-year OS, DM, and BCR were 76%, 9%, and 21% respectively. Percent core involvement was significantly associated with DM and BCR on UVA. There was no significant difference (AUC $p=0.41$, Brier $p=0.42$) between percentage core involvement as binary ($\geq 50\%$ vs $<50\%$) and every 10% (e.g. 0-10% vs 10-20% vs 20-30%, etc.). On MVA with standard variables, GG, absolute PSA, core percentage, and ADT were significantly associated with DM. When incorporating CRR and PSA density tiers, GG, ADT, CRR, and PSA density tiers were associated with DM and BCR but core percentage was not. The only significant association with OS was GG. The MVA with CRR and PSA density tiers had the lowest Brier score for DM and BCR.

Conclusions: MRI-derived CRR and PSA density tiers were independently associated with DM and BCR. After incorporating MRI-informed features, percentage core involvement was no longer independently associated with outcomes, supporting reassessment of core-based intermediate-risk classification and prospective validation of MRI-informed prognostic models.