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**Article**

# Prostate cancer risk stratification using magnetic resonance imaging–ultrasound fusion vs systematic prostate biopsy

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## Abstract

**Background:** Image-guided approaches improve the diagnostic yield of prostate biopsy and frequently modify estimates of clinical risk. To better understand the impact of magnetic resonance imaging–ultrasound fusion targeted biopsy (MRF-TB) on risk assessment, we compared the distribution of National Comprehensive Cancer Network (NCCN) risk groupings, as calculated from MRF-TB vs systematic biopsy alone.

**Methods:** We performed a retrospective analysis of 713 patients who underwent MRF-TB from January 2017 to July 2021. The primary study objective was to compare the distribution of National Comprehensive Cancer Network risk groupings obtained using MRF-TB (systematic + targeted) vs systematic biopsy.

**Results:** Systematic biopsy alone classified 10% of samples as very low risk and 18.7% of samples as low risk, while MRF-TB classified 10.5% of samples as very low risk and 16.1% of samples as low risk. Among patients with benign findings, low-risk disease, and favorable/intermediate-risk disease on systematic biopsy alone, 4.6% of biopsies were reclassified as high risk or very high risk on MRF-TB. Of 207 patients choosing active surveillance, 64 (31%), 91 (44%), 42 (20.2%), and 10 (4.8%) patients were classified as having very low-risk, low-risk, and favorable/intermediate-risk and unfavorable/intermediate-risk criteria, respectively. When using systematic biopsy alone, 204 patients (28.7%) were classified as having either very low-risk and low-risk disease per NCCN guidelines, while 190 men (26.6%) received this classification when using MRF-TB.

**Conclusion:** The addition of MRF-TB to systematic biopsy may change eligibility for active surveillance in only a small proportion of patients with prostate cancer. Our findings support the need for routine use of quantitative risk assessment over risk groupings to promote more nuanced decision making for localized cancer.

Active surveillance is increasingly selected as the initial management for patients with Gleason grade group 1 and 2 prostate cancer (1). Multidimensional assessments of risk are commonly used to inform clinical decisions, including the appropriateness of active surveillance or definitive treatment (2,3). Although risk prediction tools derived from multivariable models offer improved prognostic performance, clinical risk groupings are commonly used, particularly those affiliated with major guideline-issuing bodies (eg, the National Comprehensive Cancer Network [NCCN], American Urological Association, and Society of Urologic Oncology) (4,5).

Within the past 10 years, prostate cancer diagnosis has been transformed by the availability of increasingly reliable imaging for disease localization, particularly multiparametric magnetic resonance imaging (MRI) (6,7). Although direct image-guided biopsy (generally multiparametric MRI–guided fusion biopsy) improves the diagnostic yield of prostate biopsy, this approach generally increases appraisals of clinical risk (8). Despite benefits to identification of higher-grade disease, multiparametric MRI-ultrasound fusion targeted biopsy (MRF-TB) increases cost, is subject to variation in quality (9), and may lead to overtreatment through the overdetection of indolent cancer (10). To better understand the impact of MRF-TB on risk assessment, we compared the distribution of NCCN risk groupings, as calculated from both MRF-TB and 12-core systematic biopsy alone.

## Methods

We retrospectively queried an institutional review board–approved database to perform a retrospective review of patients who underwent prostate MRF-TB from January 2017 to July 2021.

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Baseline data included age; race; serum prostate-specific antigen (PSA); PSA density; maximum Prostate Imaging Reporting & Data System (PI-RADS), version 2, score; number of positive biopsy cores; and greatest extent of core positivity.

Multiparametric MRI scans were generated using 3.0 T scanners (Verio, Trio, or Skyra; Siemens Healthineers, Erlangen, Germany). Interpreted by experienced genitourinary MRI radiologists, each scan was assessed using PI-RADS, version 2, for T2-weighted, diffusion-weighted MRI and dynamic contrast-enhanced sequences. Before the biopsy procedure, the prostate was segmented on T2-weighted images, and regions of interest were contoured (ProFuse; Eigen Health, Grass Valley, CA). MRF-TB of regions of interest and concurrent 12-core systematic biopsy were carried out using the Artemis system (Eigen Health, Grass Valley, CA). MRF-TB was performed by 1 of 3 experienced urologists, with an average of 5 biopsy cores taken from each region of interest, followed by a 12-core template systematic biopsy under local anesthesia (11). The biopsy cores were subsequently graded by genitourinary pathologists in accordance with International Society of Urological Pathology guidelines (12).

The primary study objective was to compare the distribution of NCCN risk groupings obtained using MRF-TB (systematic + targeted) vs systematic biopsy. We calculated NCCN risk classifications (very low, low, favorable intermediate, unfavorable intermediate, high, and very high) based on constituent components (PSA, PSA density, number of positive biopsy cores, and greatest extent of core positivity) (1). We also compared the distribution of condensed NCCN risk status using MRF-TB vs systematic biopsy (Supplementary Table 1 and Supplementary Figure 1, available online). The condensed NCCN risk groupings were benign, low risk (including very low and low strata), favorable/intermediate risk, unfavorable/intermediate risk, and high risk (including high and very high strata).

We conducted comparisons within patients based on findings obtained through MRF-TB vs systematic biopsy only. When considering targeted biopsies, separate cores within a single lesion were considered to be 1 site, as stipulated by the NCCN risk groupings (1). Continuous variables were reported as median (interquartile range). Categorical variables were reported as count and proportion.

## Results

We identified 713 patients who underwent first-time prostate biopsy for clinical suspicion of prostate cancer (Table 1). The median (interquartile range) age was 67 (61-72) years. The median PSA value was 7.2 ng/mL (interquartile range = 5.3-10.9). Using data obtained through systematic biopsy alone, 71 (10%) and 133 (18.7%) patients were classified as having very low-risk and low-risk disease per NCCN guidelines, respectively. Incorporating data from MRF-TB, 75 (10.5%) and 115 (16.1%) patients were classified as having very low-risk and low-risk disease per NCCN guidelines, respectively (Table 2).

Of 434 patients with benign or favorable disease on systematic biopsy alone (ie, benign, very low, low, and favorable/intermediate NCCN risk), 71 (16.3%) were reclassified as having unfavorable/intermediate-risk, high-risk, and very high-risk prostate cancer on MRF-TB (Figure 1). Among 207 patients electing active surveillance as management, 64 (31%) met very low risk criteria, 91 (44%) met low risk criteria, 42 (20.2%) met favorable/intermediate risk criteria, and 10 (4.8%) met unfavorable/intermediate risk criteria.

**Table 1.** Characteristics of the study cohort[a]

| Variable | Value |
|---|---|
| Age, median (interquartile range) | 67 (61-72) |
| African American race, No. (%) | 97 (13.6) |
| PSA value, median (interquartile range) | 7.2 (5.3-10.9) |
| PSA density, median (interquartile range) | 0.14 (0.10-0.23) |
| Maximum PI-RADS score, No. (%) | |
| 2-3 | 133 (18.7) |
| 4 | 326 (45.7) |
| 5 | 254 (35.6) |
| Systematic biopsy grade group, No. (%) | |
| Benign | 79 (11) |
| 1 | 249 (35) |
| 2 | 199 (28) |
| 3 | 81 (11.3) |
| 4 | 62 (8.7) |
| 5 | 43 (6) |
| Targeted biopsy grade group, No. (%) | |
| Benign | 89 (12.5) |
| 1 | 204 (28.6) |
| 2 | 208 (29.2) |
| 3 | 94 (13.2) |
| 4 | 62 (8.7) |
| 5 | 56 (7.8) |

[a] PI-RADS = Prostate Imaging Reporting & Data System; PSA = prostate-specific antigen.

**Table 2.** NCCN risk classification (very low, low, favorable/intermediate, unfavorable/intermediate, high, very high) based on targeted + systematic biopsy vs systematic biopsy alone[a] (N = 713)

| NCCN risk status | Systematic biopsy alone, No. (%) | Targeted + systematic biopsy, No. (%) |
|---|---|---|
| Benign | 79 (11) | 0 (0) |
| Very low | 71 (10) | 75 (10.5) |
| Low | 133 (18.7) | 115 (16.1) |
| Favorable/intermediate | 151 (21.2) | 173 (24.3) |
| Unfavorable/intermediate | 146 (20.5) | 173 (24.3) |
| High | 110 (15.4) | 147 (20.6) |
| Very high | 23 (3.2) | 30 (4.2) |

[a] NCCN = National Comprehensive Cancer Network.

Supplementary Table 1 and Supplementary Figure 1 (available online) present data on condensed NCCN risk status. When using systematic biopsy alone, 204 patients (28.7%) were classified as having combined very low and low NCCN risk, while 190 men (26.6%) received this classification when using MRF-TB. Furthermore, among the 297 men categorized as having combined intermediate (favorable and unfavorable) NCCN risk using systematic biopsy alone, 29 patients (9.8%) were subsequently upgraded to a combined high NCCN risk status (high and very high risk) based on MRF-TB.

## Discussion

With the increased use of image-guided prostate biopsy, the results of our study highlight the potential impact on risk assessment and management. Notably, we show that MRF-TB and systematic biopsy resulted in similar distributions of low NCCN risk classifications (ie, very low and low NCCN risk) (26.6% vs 28.7%). Practically, these findings suggest that the addition of multiparametric MRI to systematic biopsy may change eligibility for active surveillance in only a small minority of patients with prostate cancer. These findings are in contrast with results of other

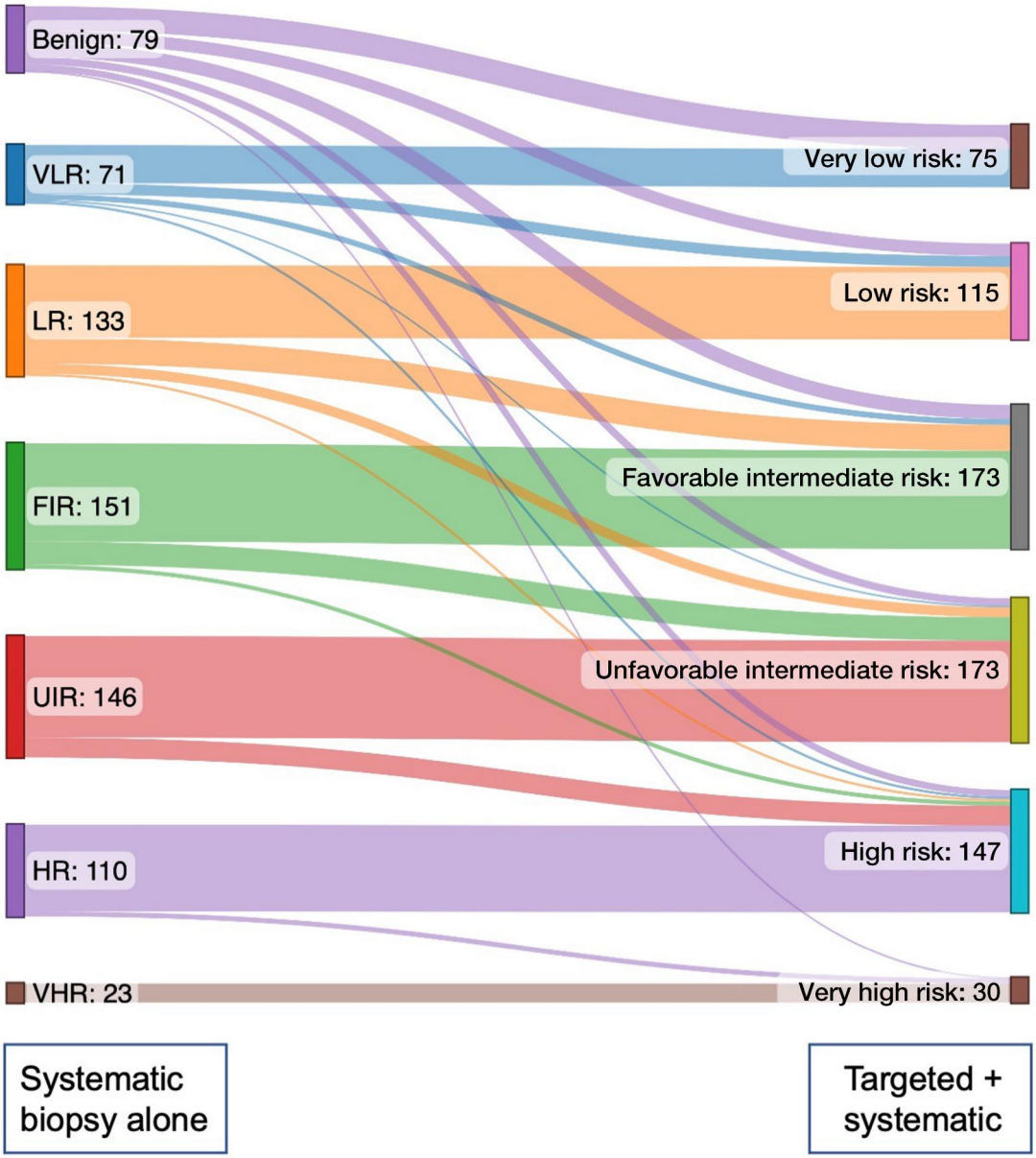


**Figure 1.** Sankey diagram depicting shifts in National Comprehensive Cancer Network risk classifications on systematic biopsy alone (**left**) to targeted + systematic biopsy (**right**). FIR = favorable/intermediate risk; HR = high risk; LR = low risk; UIR = unfavorable/intermediate risk; VHR = very-high risk VLR = very low risk.

studies, including 1 demonstrating a notable reduction in the rate of low-risk disease from 30% to 4% with the addition of MRF-TB to systematic biopsy (13). As a result, this work can add depth to discussions of how best to apply clinical risk stratification systems in the contemporary era of MRF-TB and their implications for active surveillance candidacy (14). Increases in clinical risk estimates may be most relevant for patients found to have small volumes of Gleason grade group 2 prostate cancer, for whom a large number of patients will require treatment to avert death from prostate cancer (15).

We found that adding multiparametric MRI to systematic biopsy yielded upstaging from intermediate NCCN risk (favorable or unfavorable) to high NCCN risk in 9.8% of patients. This finding aligns with previous studies that reported similar upstaging from intermediate to high risk when MRF-TB was added to systematic biopsy (13,16). The consistent observation of such upstaging underscores the substantial impact that MRF-TB can have on prostate cancer management.

Our study has notable limitations. This analysis was conducted as a retrospective study within a single institution. Our cohort consisted of patients with biopsy-proven prostate cancer, confirmed either through systematic biopsy or MRF-TB. As such, the findings of this study should not be extrapolated to patients undergoing prostate cancer screening. We also excluded men with negative multiparametric MRI findings and included patients who showed a visible lesion on their multiparametric MRI scans, with a range of maximum PI-RADS scores from 2 to 5, resulting in varying probabilities of detecting clinically significant prostate cancer. As with any radiologic interpretation, there might have been some degree of variability in multiparametric MRI readings, even though our study involved assessment of all cases by an experienced prostate multiparametric MRI radiologist. Moreover, determination of disease risk

status relied on biopsy specimens rather than radical prostatectomy specimens.

The findings from this study indicate an ongoing opportunity to further refine the initial approach to prostate cancer diagnosis. Given the diagnostic advantages of prostate multiparametric MRI for identifying occult, high-grade prostate cancers missed on systematic biopsy, the prospect of eschewing imaging to limit overdetection is likely impractical. There is promise, however, in using multiparametric MRI more widely as a triage strategy for selecting patients for biopsy, an approach associated with high rates of detecting high-grade cancer, while reducing the identification of low-grade disease (8,17). To decrease overtreatment, more inclusive approaches based on dynamic estimates of risk represent a promising middle ground to expand initial eligibility (18).

## Data availability

The data underlying this article cannot be shared because of the need to protect the privacy of individuals who participated in the study. All summary-level data are included within the manuscript.

## Author contributions

Ghazal Khajir, MD (Data curation; Formal analysis; Investigation; Software; Writing—original draft), Benjamin Press, MD (Data curation; Investigation; Methodology; Writing—original draft), Soum Lokeshwar, MD (Data curation; Investigation; Methodology; Writing—original draft), Kamyar Ghabili, MD (Formal analysis; Investigation; Software; Writing—original draft), Syed Rahman, MD (Data curation; Investigation; Methodology; Writing—original draft), Mursal Gardezi, MD (Data curation; Investigation; Methodology; Writing—original draft), Samuel Washington, MD (Conceptualization; Methodology; Supervision; Writing—review & editing), Matthew R. Cooperberg, MD (Conceptualization; Methodology; Supervision; Writing—review & editing), Preston Sprenkle, MD (Conceptualization; Investigation; Software; Supervision; Writing—original draft), Michael S. Leapman, MD (Conceptualization; Investigation; Methodology; Supervision; Validation; Writing—original draft).

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## Conflicts of interest

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