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Establishing the distribution of satellite lesions in intermediate- and high-risk prostate cancer: implications for focused radiotherapy

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Abstract

BACKGROUND: In focused radiotherapy for prostate cancer (PC), a full dose of radiation is delivered to the index lesion while reduced dose is delivered to the remaining prostate to reduce morbidity. As PC is commonly multifocal, we investigated whether baseline clinical characteristics or multiparametric magnetic resonance imaging (mpMRI) may be useful to predict the actual pathologic distribution of PC in men with intermediate- or high-risk PC, which may better inform how to deliver focused radiotherapy.

METHODS: A retrospective single-institutional study was performed on 71 consecutive men with clinically localized, intermediate-or high-risk PC who underwent mpMRI followed by radical prostatectomy (RP) from January 2012 to December 2012. Logistic regression analysis was performed to evaluate preoperative predictors for satellite lesions. Performance characteristics of mpMRI to detect satellite lesions and the extent of prostate disease (one hemi-gland vs both) were also evaluated.

RESULTS: In all, 50.7% had satellite lesions on mpMRI. On RP specimen analysis, 66.2% had satellite lesions and 55.3% of these satellite lesions had pathologic Gleason score (pGS) ⩾ 3+4. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy for mpMRI detecting a satellite lesion being present in the RP specimen were 59.6%, 66.7%, 77.8%, 45.7% and 62.0%, respectively. The presence of MRI satellite lesions was the only preoperative predictor significantly associated with finding satellite lesions on final pathology (hazard ratio (HR), 2.95, P= 0.040). There was agreement in 76.1% of the entire cohort for unilateral vs bilateral disease when incorporating both biopsy and mpMRI information and comparing with the RP specimen.

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CONFLICT OF INTEREST

Dr Margolis reports personal fees from Blue Earth Diagnostics, outside the submitted work. The remaining authors declare no conflicts of interest.

CONCLUSIONS: In intermediate risk or greater PC, only the presence of mpMRI satellite lesions could predict for pathologic satellite lesions. While combining biopsy and mpMRI information may improve preoperative disease localization, the relatively high incidence of bilateral hemi-gland involvement with pGS ⩾ 7 satellite lesions makes it challenging to appropriately select men eligible for hemi-gland therapy.

INTRODUCTION

Some clinical experts have proposed that in low- and favorable intermediate-risk prostate cancer (PC), limiting treatment to the index lesion alone with focal therapy may be appropriate.[1] These clinicians argue that while PC is usually multifocal, 'active surveillance' of small-sized lesions (≤ 5 mm in biopsy core length) with Gleason score (GS) 3+3 disease, or even potentially GS 3+4 disease, may be reasonable.[1] Indeed, in low-risk cohorts, virtually all satellite lesions appear to be GS < 3+ 4.[2] For men with intermediate- and high-risk disease, however, there is more limited data regarding whether satellite lesions harbor predominantly nonsignificant PC. Therefore, it remains unclear whether this subgroup should be considered for focal therapy.

Focal treatment to the index lesion alone is appealing for potential reductions in morbidity. An alternative strategy could harness an advantage of radiotherapy—the ability to 'dose paint,' or prescribe differing doses of radiation to regions at higher or lower risk of harboring disease. While delivering different doses to various parts of the prostate gland is relatively straightforward with modern radiotherapy planning, it is more complicated for other types of ablative strategies like high-intensity focused ultrasound (US) and cryotherapy. Ultimately, a dose painting approach may allow for similar long-term biochemical control as uniform, whole-gland therapy, while possibly reducing the risk for acute and longer-term toxicities.

A dose painting strategy would not utilize focal treatment to the dominant lesion alone; rather this strategy would involve focused radiotherapy, where full dose is delivered to the index lesion but a reduced dose is delivered to the remaining prostate gland. A major obstacle to this is that most PC cases are multifocal.[3] As such, it is unknown whether a reduced dose is able to control the commonly found satellite lesions or whether they should also be treated to a full, minimum dose.

Regardless, a focused radiotherapy approach is achievable only if more confident characterization of the distribution of disease within the prostate gland can be performed. In this study, we evaluated the predictive capabilities of pre-treatment clinical characteristics, biopsy information and multiparametric magnetic resonance imaging (mpMRI) findings in men with intermediate- or high-risk PC to determine the actual distribution of PC in the radical prostatectomy (RP) specimen.

MATERIALS AND METHODS

Patient selection

This was a retrospective study approved by the University of California, Los Angeles (UCLA) Medical Center Institutional Review Board. The Institutional Review Board designated this study exempt from informed consent. One hundred and thirty-seven men who had PC and underwent RP from January 2012 to December 2012 were consecutively studied. Within this population, 71/137 men (51.8%) had previously untreated intermediate-, high- or very high-risk PC as defined by the National Comprehensive Care Network Guidelines[4] and had a preoperative mpMRI. Intermediate-risk PC was further divided into favorable versus unfavorable intermediate-risk disease in this study, as defined by Zumsteg *et al.*[5] No patients had been previously treated for PC.

MRI protocol and imaging interpretation

Pelvic MRIs were ordered on all patients preoperatively. An mpMRI was performed with a Siemens SOMATOM Trio Tim or Skyra scanner (Siemens Medical Solutions USA, Malvern, PA, USA) at 1.5 or 3 Tesla using a multichannel external phased-array body coil with or without an endorectal coil. mpMRI sequence parameters included multiplanar T2-weighted, diffusion-weighted and dynamic contrast-enhanced (DCE) imaging. T2-weighted images were used for morphologic image interpretation of pelvic anatomy. Apparent Diffusion Coefficient (ADC) maps of the prostate were created from diffusion-weighted imaging acquisitions for interpretation. DCE imaging was performed using intravenous (IV) gadolinium contrast injected prior to image acquisition. K^{trans} maps generated from the DCE data acquisitions were used for image interpretation. Images were interpreted by one of three experienced radiologists, all of whom are fellowship-trained in abdominal imaging and had a minimum of 8 years of experience in prostate MRI interpretation. Each region of interest (target) identified was assigned an overall suspicion score on a scale of 1 (significant cancer is highly unlikely to be present) to 5 (significant cancer is very likely to be present). This was the system utilized in 2012 prior to the implementation of Prostate Imaging Reporting and Data System (PI-RADS) at our institution, and it is based on a combination of the individual assessment of T2-weighted images, ADC and DCE. Similar accuracy for PC tumor localization between this system and PI-RADS has been reported previously.[6] For this study, the preoperative index lesion on MRI was defined as the largest lesion seen, as the largest lesion would be treated as an index lesion in a focused radiotherapy setting, since full pathologic analysis (including pGS from the RP specimen) would obviously be unavailable. The index lesion has been defined as the largest lesion in several other studies.[7–9]

Transrectal US-guided prostate biopsy procedure

Transrectal US-guided systematic biopsies of the prostate were performed for all patients, aside from one patient who instead had a computed tomography-guided trans-perineal approach for biopsy due to the absence of his rectum from a previous procedure. Notably, 29.6% (21/71) of men had MRI-US fusion targeted biopsies of suspicious mpMRI lesions using the Artemis device (Eigen, Grass Valley, CA, USA) in addition to conventional transrectal US-guided core biopsies. Patients were recommended for MRI-US fusion targeted biopsy due to elevated PSA with a negative previous systematic biopsy or better

characterization of known PC for management recommendations, including the consideration of active surveillance. For the MRI-US fusion targeted biopsy procedure, the mpMRI was fused to the transrectal US imaging to properly localize and sample the mpMRI lesions of interest. For the systematic biopsy component of the procedure, mpMRI was not used for biopsy planning. For patients undergoing a targeted and systematic biopsy, a mean (± standard deviation (s.d.)) of 17 (±4) cores were taken, while for patients undergoing systematic biopsy alone, a mean (±s.d.) of 12 (±1) was taken.

Radical prostatectomy

Board-certified academic urologic surgeons with greater than 10 years of practice in urologic oncology performed consecutive RPs for a primary diagnosis of PC over a 1-year period (January 2012-December 2012). In all, 93.0% (66/71) of patients had a robotic-assisted RP, while 7.0% (5/71) had a radical retropubic prostatectomy. One of six academic pathologists who were fellowship-trained and/or had greater than 20 years of experience in genitourinary pathology evaluated all 71 RP specimens.

Comparison of preoperative mpMRI with the RP specimen

The locations of the index lesion and satellite lesions on mpMRI were compared to the locations of the index and satellite lesions found in the RP specimen for each patient. Lesions on mpMRI were also oriented in the cranio-caudal (where they were located relative to the base and apex) and radial (clockwise) directions. A true positive lesion was defined as one existing in the same sextant (or sextants if there was overlap) on both mpMRI and RP. If a lesion was only present on mpMRI or only in the RP specimen, these cases were considered a false positive and false negative, respectively.

Statistical analysis

Logistic regression analyses were performed to evaluate potential preoperative predictors of satellite lesions and number of tumors found at RP. All assumptions required for logistic regression analysis were met. Potential predictors tested included preoperative predictors of adverse pathology at RP, including age, PSA, clinical T-category, biopsy Gleason score, and percent positive biopsies, as well as MRI characteristics, including T-category, presence of satellite lesions, index lesion greatest dimension, overall MRI suspicion score, ADC, and the DCE kinetics parameters K^{trans} and k^{ep}. A mean and s.d. were calculated for all continuous variables. A P-value < 0.05 was considered statistically significant. Performance characteristics were calculated for mpMRI detecting any satellite lesion as well as only satellite lesions with clinically significant disease. Clinically significant disease was defined as a focus of cancer with GS ≥ 3+4 and a volume ≥ 0.5 cm^3 or any lesion with a volume ≥ 1.0 cm^3, similar to definitions used in previous studies, although there is still controversy and further optimization needed for accurately defining clinically significant and insignificant disease.[10]

RESULTS

Preoperative clinical characteristics

Baseline patient clinical and pathologic characteristics are listed in Table 1. The percentages of men with favorable intermediate risk, unfavorable intermediate risk and high-risk PC based on their baseline characteristics were 38.0%, 43.7%, and 18.3%, respectively.

Preoperative multiparametric MRI results

Table 2 reports on preoperative mpMRI findings. In all, 94.4% of mpMRIs were performed with a 3-Tesla magnet and 66.2% with an endorectal coil. Sixty-seven out of 71 patients (94.4%) had an index lesion present on mpMRI. For mpMRI-detected index lesions, overall mpMRI suspicion scores were higher and ADC scores were lower as preoperative clinical risk score increased. In all, 49.3% (35/71) of men had no mpMRI evidence of satellite lesions. The trends in MRI suspicion score and ADC seen for the index lesions were not seen for satellite lesions. In total, 11.3% (8/71) had evidence of satellite lesions in the ipsilateral hemi-gland on which the index lesion was located, while 36.6% (26/71) had evidence of satellite lesions contralateral to the hemi-gland of the MRI index lesion.

Pathologic findings at RP

Table 3 contains characteristics of the RP specimens. In total, 32.4% of the cohort had pathologic upstaging to pT3 at RP, while 33.8% had pGS upgrading at RP. Pathologic upstaging was more common in men with high-risk PC preoperatively (69.2%) than with favorable intermediate-risk PC (7.4%). Pathologic upgrading was more common in the favorable intermediate risk (33.3%) and unfavorable intermediate risk (41.9%) cohorts than in the high-risk cohort (15.4%).

At RP, 33.8% (24/71) had a single index lesion without satellite lesions, while 66.2% of men had multiple lesions. In patients with a satellite lesion, 55.3% (26/47) had GS ≥ 3+4, including 19.1% with GS ≥ 4+3. In all, 11.3% of patients had a higher GS in a satellite lesion compared with the index lesion. 60.6% (43/71) had multifocal disease involving both hemi-glands.

In Table 4, the pathologic characteristics of mpMRI-detected and mpMRI-occult (non-detected) index and satellite lesions are presented. Of the 67 index lesions detected on mpMRI (4 patients had no index lesion detected on mpMRI), 53/67 (79.1%) of these lesions were found to have a pathologic index lesion localized to the same hemi-gland(s). Conversely, 18/71 index lesions (25.4%) found at RP were not detected by mpMRI. For the 36 men with mpMRI satellite lesions detected, 28/36 (77.8%) had satellite lesions at RP. It was difficult to establish any trends for mpMRI-detected and occult index and satellite lesions given the small sample sizes available for comparison between risk groups.

Logistic regression analyses for the prediction of satellite lesions and number of tumors

On univariate analysis (Table 5), only the presence of mpMRI satellite lesions was significantly associated with finding satellite lesions on final pathology (hazard ratio, HR, 2.95, 95% confidence interval 1.05–8.25, $P = 0.040$). No clinical, biopsy or mpMRI

characteristic was significant on univariate analysis for predicting the number of tumors present in the RP specimen.

Performance characteristics of finding satellite lesions and localization of disease laterality

Table 6 presents the performance characteristics of mpMRI to detect satellite lesions, as well as the accuracy of determining laterality when evaluating mpMRI alone and when integrating mpMRI and biopsy data. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for any mpMRI-detected satellite lesion being present in the RP specimen were 59.6%, 66.7%, 77.8%, 45.7% and 62.0%, respectively. For clinically significant satellite lesions, these values were 59.5%, 58.8%, 61.1%, 57.1% and 59.2%, respectively. Comparatively, the accuracy of determining RP index lesion laterality was 53/71 (74.6%) using mpMRI alone (74.1% in men with favorable intermediate risk, 67.7% with unfavorable intermediate risk and 92.3% with high-risk disease).

Given the relatively low accuracy for mpMRI to identify satellite lesions, we evaluated whether mpMRI findings combined with biopsy information could improve the accuracy of localizing all disease to at least the correct hemi-gland. When comparing a combined biopsy and mpMRI assessment of disease laterality (one hemi-gland or both) to the laterality findings at RP, 76.1% (54/71) of men had agreement between the two sets of data, while 23.9% (17/71) did not (Table 6). Among the 17 patients who did not have agreement, mean (s.d.) age was 65.5 years (±7.9), mean (s.d.) PSA was 10.3 ng ml^{-1} (±11.5), T-category was T1 in 82.4% and T2 in 17.6%, and biopsy GS was ≤3+4 in 76.5%, while it was ≥4+3 in 23.5%. Mean (s.d.) percent positive biopsies were 23.0% (±11.0%), while mean (s.d.) length of biopsy involved with cancer was 5.1 mm (±2.8). These preoperative factors for adverse RP pathology were very similar to the values seen for the entire cohort, consistent with the finding on logistic regression analysis that no preoperative clinical or biopsy characteristics significantly predicted for RP satellite lesions.

The positive predictive value of finding bilateral disease with combined biopsy and mpMRI assessment on final pathology was 87.8%, while the positive predictive value of finding unilateral disease with combined assessment was 50%. In the six men who were predicted to have bilateral disease but were found to have unilateral disease, one patient had a biopsy indicating bilateral disease which was not found at RP. The other 5/6 patients had mpMRI lesions seen on a hemi-gland not involved in malignancy at RP. In the 11 men who were predicted to have unilateral disease but were found to have bilateral disease, pGS 3+4 or higher disease was found in the satellite lesions in 6/11 patients.

When evaluating only the 21 patients who had MRI-US fusion targeted biopsy in addition to standard systematic transrectal US-guided biopsy, 95.2% had agreement on laterality, with the positive predictive value of finding bilateral disease being 100% and unilateral disease being 85.7%.

DISCUSSION

For men with intermediate- and high-risk PC, definitive treatment with either whole-gland radiotherapy or surgery is the standard-of-care. Conventionally, a uniform radiotherapy dose is prescribed to the entire prostate regardless of the number or distribution of positive biopsy cores. However, imaging with mpMRI allows for improved identification of intraprostatic lesions, especially the index lesion.[11] This information is being used to escalate dose to the index lesion through dose painting.[12,13] While this is one way to utilize the information from mpMRI, another consideration is to de-escalate portions of the prostate that are only at risk for harboring microscopic deposits of disease with a focused radiotherapy technique. However, to optimize such a technique, we would need to accurately identify both the location and aggressiveness of intraprostatic disease in a preoperative setting. mpMRI, potentially with the use of MRI-US fusion targeted biopsy, to evaluate index lesions may be one way to better achieve this.

We investigated whether we could predict if all disease was limited to one hemi-gland. If all disease, including any satellite lesion, is limited to one hemi-gland, then it is conceivable to treat the involved hemi-gland to full dose while reducing the dose to the contralateral hemi-gland. In 76.1% of our cohort, the combined biopsy and mpMRI findings regarding laterality agreed with the RP specimen findings (Table 6). The discrepancy in the other 23.9% of the cohort appeared to be primarily due to the insensitivity of finding satellite lesions on biopsy or mpMRI which were later found at RP.

Importantly, satellite lesions are not necessarily directly adjacent to the index lesion, with the median distance being 1.0 cm away and up to 4.4 cm in one study.[14] Furthermore, mpMRI appears to substantially underestimate the size and extent of PC tumors.[15] While these distinctions are less important when treating the entire prostate to the same dose, with a focused radiotherapy approach proper tumor localization carries higher importance. The results of novel imaging techniques like combined gallium 68-prostate-specific membrane antigen (^{68}Ga-PSMA) positron emission tomography-MRI, which showed significantly improved imaging localization compared with either technique alone, may help reduce this concern.[16] However, positron emission tomography alone has resolution limitations which somewhat temper enthusiasm for this being the whole solution in prostate imaging.

Further improvement of both biopsy and mpMRI techniques, perhaps with MRI-US fusion targeted biopsy, may better optimize localization as well.[1] Indeed, in the 21 men in our study who had MRI-US fusion targeted biopsy, only 1 patient (4.8%) had a discrepancy between laterality findings for the combined biopsy and mpMRI information with the RP specimen. This result, while quite encouraging, may be due to a small sample size. Another explanation may be that at our institution, mpMRI interpretation is somewhat different depending if the study is ordered for MRI-US fusion targeted biopsy planning or for surgical planning. Indeed, for targeted biopsy planning, the lesions most suspicious for malignancy are highlighted, while less suspicious lesions are of less interest. In contrast, for surgical planning, attention is paid especially to lesions involving the prostatic capsule. This is because extracapsular lesions may affect surgical planning, even if these lesions appear to be relatively low risk, given the surgical emphasis of achieving negative surgical margins.

Of note, our understanding of the clinical significance of satellite lesions is still limited. Some have proposed that only the index lesion is responsible for dictating the natural history of PC; however, this is still controversial.[17] There is also no consensus about the index lesion being defined strictly as the largest lesion or whether it is the lesion with the highest GS. In our cohort, for example, 11.3% of patients had a higher pGS in a smaller satellite lesion than in the larger index lesion (Table 3). Nonetheless, since with definitive radiotherapy treatment no pathologic specimen will be obtained, selecting the largest lesion as the index lesion would appear appropriate until preoperative lesion analysis further improves.

We also found that in the subset of men with satellite lesions, 55.3% of the satellite lesions had pGS 3+4 or greater disease (Table 3). This is in contrast to a previous study showing that almost all satellite foci (99.4%) harbor clinically insignificant GS 6 disease.[2] This discrepancy is likely a result of the previous data coming from a lower-risk cohort. Based on our data, it appears that satellite lesions are more likely to have a potential clinical impact and should not necessarily be ‘ignored.’

Pre-treatment predictive tools for the presence of satellite lesions are clearly necessary to select patients for more tailored therapy. In our study, the sensitivity for finding any satellite lesion on MRI was only 59.6% (Table 6). This is consistent with two recent studies using modern mpMRI showing 50–96% of satellite lesions being missed on mpMRI, often attributable to the lesions being small and/or low-grade in appearance.[18,19] The far different detection rate between even these two studies may be the result of different thresholds for identifying suspicious lesions.

We found on univariate analysis that the presence of satellite lesions on mpMRI was associated with finding satellite lesions at RP (HR 2.95, P = 0.040) (Table 5). While several variables have been previously established as pre-treatment predictors of unilateral (but not necessarily unifocal) PC, more limited data exist to predict for satellite lesions.[20–22] Importantly, these studies identified predictors of unilateral disease in cohorts with predominantly lower-risk PC, so these findings may not be applicable to intermediate- and high-risk men, in which focused/focal therapy trials are becoming increasingly popular.[1]

One limitation to this study is that it is retrospective in nature. Therefore, there is the potential for selection bias, especially since this is a cohort of men who exclusively selected RP for treatment. A second important limitation is that in men who are having preoperative mpMRI for staging and surgical planning (in contrast to having mpMRI for targeted biopsy planning), the interpreting radiologist may have been less inclined to identify small, low-suspicion lesions that are not abutting the prostate capsule. These lesions will be resected along with the rest of the prostate, so they would not affect the procedure. A third limitation is that whole-mount histopathology was not used for pathologic analysis. Whole-mount histology may have detected additional satellite lesions, so the current study may have underestimated (or overestimated) the sensitivity of mpMRI detection. A fourth important consideration is that while a lesion may have been found in the same sextant, hemi-gland, etc., on mpMRI/biopsy and in the RP specimen, these may be in fact different lesions. This may have resulted in an overestimation of the true sensitivity of mpMRI. A fifth limitation is

that this is a small patient cohort and may be underpowered to detect other predictors of satellite lesions. Within this cohort, only 21/71 patients had an MRI-US targeted biopsy in addition to a systematic biopsy. A recent meta-analysis noted that MRI-US fusion biopsy did not detect more PC as compared with cognitive registration alone.[23] Therefore, while we found in the 21-patient subset that laterality determination may be improved with MRI-US fusion targeted biopsy, cognitive evaluation may perform similarly. Lastly, experience in prostate imaging for accurate interpretation is very important, with poorer performance reported in community practice.[24] As such, the findings of this study, performed in a high-volume academic center, may not be broadly generalizable to lower-volume, community settings.

In conclusion, in men with intermediate- or high-risk PC, satellite lesions with pGS ≥3+4 are common, and the presence of mpMRI satellite lesions could significantly predict for satellite lesions at RP. Both of these findings are of interest for further studies involving focused radiotherapy for PC.

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Table 1.

Baseline patient clinical characteristics

	Entire cohort (*N* = 71)	Favorable intermediate risk (*N* = 27/71)	Unfavorable intermediate risk (*N* = 31/71)	High risk (*N* = 13/71)
Age at diagnosis, mean, in years (s.d.)	62.3 (±7.4)	60.3 (±8.0)	62.5 (±7.0)	66.1 (±4.7)
PSA, mean in ng ml^{-1} (s.d.)	8.8 (±6.8)	7.0 (±3.0)	8.4 (±4.4)	13.3 (±12.5)
Clinical T-category				
Unknown	1.4% (1/71)	0 (0/27)	3.2% (1/31)	0 (0/13)
T1	76.1% (54/71)	85.2% (23/27)	71.0% (22/31)	69.2% (9/13)
T2	22.5% (16/71)	14.8% (4/27)	25.8% (8/31)	30.8% (4/13)
Biopsy Gleason score				
3+3	2.8% (2/71)	7.4% (2/27)	0 (0/31)	0 (0/13)
3+4	54.9% (39/71)	92.6% (25/27)	41.9% (13/31)	7.7% (1/13)
4+3	26.8% (19/71)	0 (0/27)	58.1% (18/31)	7.7% (1/13)
8–10	15.5% (11/71)	0 (0/27)	0 (0/31)	84.6% (11/13)
Percent positive biopsies, mean (s.d.)	33.9% (±17.5)	24.3% (±11.0)	42.7% (±18.5)	32.4% (±15)

One patient was clinically unstageable due to the absence of a rectum from a prior abdominoperineal resection. His risk category was determined by his other clinical factors. Please note that the ‘high-risk’ group encompasses both ‘high-risk’ and ‘very high-risk’ patients per National Comprehensive Care Network guidelines.

Table 2.

Preoperative multiparametric MRI findings

	Entire cohort (*N* = 71)	Favorable intermediate risk (*N* = 27)	Unfavorable intermediate risk (*N* = 31)	High risk (*N* = 13)
MRI T-category				
T1	5.6% (4/71)	3.7% (1/27)	9.7% (3/31)	0 (0/13)
T2	83.1% (59/71)	96.3% (26/27)	80.6% (25/31)	61.5% (8/13)
T3	11.3% (8/71)	0 (0/27)	9.7% (3/31)	38.5% (5/13)
MRI greatest tumor diameter of index lesion, mean in mm (s.d.)	12.2 (±5.5)	10.3 (±3.2)	12.5 (±5.5)	15.6 (±7.1)
MRI suspicion sore of index lesion				
2	14.1% (10/71)	25.9% (7/27)	9.7% (3/31)	0 (0/13)
3	28.2% (20/71)	40.7% (11/27)	22.6% (7/31)	15.4% (2/13)
4	29.6% (21/71)	18.5% (5/27)	38.7% (12/31)	30.8% (4/13)
5	22.5% (16/71)	11.1% (3/27)	19.4% (6/31)	53.9% (7/13)
No MRI index lesion	5.6% (4/71)	3.7% (1/27)	9.7% (3/31)	0 (0/13)
ADC value for index MRI lesion, mean in μ^2 s^{-1} (s.d.)	973.4 (±194.6)	1025.8 (±202.0)	981.7 (±193.1)	855.5 (±105.7)
K^{trans} value for index MRI lesion, mean in 1/minute (s.d.)	0.54 (±0.29)	0.52 (±0.30)	0.61 (±0.29)	0.49 (±0.18)
K^{ep} value for index MRI lesion, mean in 1/minute (s.d.)	1.64 (±0.88)	1.63 (±0.94)	1.51 (±0.70)	1.89 (±0.94)
iAUC value for index MRI lesion, mean (s.d.)	10.7 (±5.7)	9.5 (±5.3)	13.0 (±6.5)	9.5 (±3.5)
Presence of MRI satellite lesions				
No	49.3% (35/71)	59.3% (16/27)	51.6% (16/31)	23.1% (3/13)
Yes	50.7% (36/71)	40.7% (11/27)	48.39% (15/31)	76.9% (10/13)
MRI greatest tumor diameter of satellite lesion, mean in mm (s.d.)	9.7 (±3.4)	9.0 (±2.6)	10.2 (±4.2)	9.8 (±2.8)
MRI suspicion score of satellite lesion				
2	33.3% (12/36)	63.6% (7/11)	0 (0/15)	50.0% (5/10)
3	47.2% (17/36)	36.4% (4/11)	66.7% (10/15)	30.0% (3/10)
4	16.7% (6/36)	0 (0/11)	26.7% (4/15)	20.0% (2/10)
5	2.8% (1/36)	0 (0/11)	6.7% (1/15)	0 (0/10)
ADC value for satellite MRI lesion, mean in μ^2 s^{-1} (s.d.)	1093.6 (±252.9)	1249.1 (±75.3)	994.7 (±322.4)	1086.6 (±153.0)
K^{trans} value for satellite MRI lesion, mean in 1/minute (s.d.)	0.50 (±0.45)	0.48 (±0.37)	0.62 (±0.57)	0.39 (±0.35)
K^{ep} value for satellite MRI lesion, mean in 1/minute (s.d.)	1.36 (±0.95)	1.72 (±1.26)	1.14 (±0.44)	1.08 (±0.66)
iAUC value for satellite MRI lesion, mean (s.d.)	8.8 (±4.9)	8.5 (±4.5)	9.8 (±3.6)	7.9 (±6.2)

	Entire cohort (*N* = 71)	Favorable intermediate risk (*N* = 27)	Unfavorable intermediate risk (*N* = 31)	High risk (*N* = 13)
Location of MRI satellite lesions				
No MRI satellite lesions	49.3% (35/71)	59.3% (16/27)	51.6% (16/31)	23.1% (3/13)
No, only ipsilateral disease	11.3% (8/71)	11.1% (3/27)	3.2% (1/31)	30.8% (4/13)
No, MRI satellite lesion at midline	2.8% (2/71)	0 (0/27)	6.5% (2/31)	0 (0/13)
Yes, MRI satellite lesion present in hemi-gland contralateral to MRI index lesion	36.6% (26/71)	29.6% (8/27)	38.7% (12/31)	46.2% (6/13)

Abbreviations: ADC, Apparent Diffusion Coefficient; MRI, magnetic resonance imaging. Please note that the ‘high-risk’ group encompasses both ‘high-risk’ and ‘very high-risk’ patients per National Comprehensive Care Network guidelines.

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Table 3.

Pathologic characteristics of the radical prostatectomy specimens

	Entire cohort (*N* = 71)	Favorable intermediate risk (*N* = 27)	Unfavorable intermediate risk (*N* = 31)	High risk (*N* = 13)
Pathologic T-category				
T2a	16.9% (12/71)	33.3% (9/27)	6.5% (2/31)	7.7% (1/13)
T2b	4.2% (3/71)	7.4% (2/27)	3.2% (1/31)	0 (0/13)
T2c	46.5% (33/71)	51.9% (14/27)	51.6% (16/31)	23.1% (3/13)
T3a	22.5% (16/71)	7.4% (2/27)	29.0% (9/31)	38.5% (5/13)
T3b	9.9% (7/71)	0 (0/27)	9.7% (3/31)	30.8% (4/13)
Pathologic GS of index lesion				
3+3	5.6% (4/71)	11.1% (3/27)	3.2% (1/31)	0 (0/13)
3+4	54.9% (39/71)	63.0% (17/27)	61.3% (19/31)	23.1% (3/13)
4+3	16.9% (12/71)	14.8% (4/27)	12.9% (4/31)	30.8% (4/13)
4+4	14.1% (10/71)	11.1% (3/27)	12.9% (4/31)	23.1% (3/13)
4+5	7.0% (5/71)	0 (0/27)	9.7% (3/31)	15.4% (2/13)
5+4	2.8% (1/71)	0 (0/27)	0 (0/31)	7.7% (1/13)
Maximal diameter of index lesion in mm (s.d.)	21.2 (±8.1)	17.5 (+7.0)	23.4 (±7.2)	23.6 (±9.4)
Perineural invasion				
No	23.9% (17/71)	33.3% (9/27)	9.7% (3/31)	38.5% (5/13)
Yes	76.1% (54/71)	66.7% (18/27)	90.3% (28/31)	61.5% (8/13)
Lymphovascular invasion				
No	94.4% (67/71)	100% (27/27)	93.6% (29/31)	84.6% (11/13)
Yes	5.6% (4/71)	0 (0/27)	6.5% (2/31)	15.4% (2/13)
Positive margin				
No	83.1% (59/71)	85.2% (23/27)	77.4% (24/31)	92.3% (12/13)
Yes	16.9% (12/71)	14.8% (4/27)	22.6% (7/31)	7.7% (1/13)
Lymph node involvement				
No	69.0% (49/71)	51.9% (14/27)	80.6% (25/31)	76.9% (10/13)
Yes	4.2% (3/71)	0 (0/27)	6.5% (2/31)	7.7% (1/13)
Not assessed	26.8% (19/71)	48.2% (13/27)	12.9% (4/31)	15.4% (2/13)
Number of tumors				

	Entire cohort (*N* = 71)	Favorable intermediate risk (*N* = 27)	Unfavorable intermediate risk (*N* = 31)	High risk (*N* = 13)
1	33.8% (24/71)	33.3% (9/27)	32.3% (10/31)	38.5% (5/13)
2	38.0% (27/71)	44.4% (12/27)	32.3% (10/31)	38.5% (5/13)
3	12.7% (9/71)	3.7% (1/27)	16.1% (5/31)	23.1% (3/13)
4	9.9% (7/71)	7.4% (2/27)	16.1% (5/31)	0 (0/13)
5 or more	5.6% (4/71)	11.1% (3/27)	3.2% (1/31)	0 (0/13)
Pathologic satellite lesions present				
No	33.8% (24/71)	33.3% (9/27)	32.3% (10/31)	38.5% (5/13)
Yes	66.2% (47/71)	66.7% (18/27)	67.7% (21/31)	61.5% (8/13)
Maximal diameter of RP satellite lesions in mm (s.d.)	11 (±6)	11 (±5)	12 (±7)	11 (±6)
Pathologic Gleason score of satellite lesions				
⩽ 3+3	44.7% (21/47)	33.3% (6/18)	47.6% (10/21)	62.5% (5/8)
3+4	36.2% (17/47)	50.0% (9/18)	33.3% (7/21)	12.5% (1/8)
4+3	10.6% (5/47)	16.7% (3/18)	4.8% (1/21)	12.5% (1/8)
4+4	6.4% (3/47)	0 (0/18)	14.3% (3/21)	0 (0/8)
5+4	2.1% (1/47)	0 (0/18)	0 (0/21)	12.5% (1/8)
Difference between largest tumor (index lesion) and highest GS tumor in RP specimen				
No	88.7% (63/71)	85.2% (23/27)	90.3% (28/31)	92.3% (12/13)
Yes	11.3% (8/71)	14.8% (4/27)	9.7% (3/31)	7.7% (1/13)
Pathologic upstaging to ⩾ T3 at RP				
No	67.6% (48/71)	92.6% (25/27)	61.3% (19/31)	30.8% (4/13)
Yes	32.4% (23/71)	7.4% (2/27)	38.7% (12/31)	69.2% (9/13)
Pathologic GS upgrading at RP				
No	66.2% (47/71)	66.7% (18/27)	58.1% (18/31)	84.6% (11/13)
Yes	33.8% (24/71)	33.3% (9/27)	41.9% (13/31)	15.4% (2/13)
Laterality/focality of disease				
Unilateral without satellite lesions	18.3% (13/71)	29.6% (8/27)	9.7% (3/31)	15.4% (2/13)
Unifocal (both hemi-glands) w/o satellite lesions	15.5% (11/71)	3.7% (1/27)	53.8% (7/31)	23.1% (3/13)
Unilateral disease with satellite lesions ⩽ pGS 6	2.8% (2/71)	3.7% (1/27)	3.2% (1/31)	0 (0/13)
Unilateral disease with satellite lesions > pGS 6	2.8% (2/71)	7.4% (2/27)	0 (0/31)	0 (0/13)
Bilateral disease with satellite lesions ⩽ pGS 6	22.5% (16/71)	25.9% (7/27)	19.4% (6/31)	23.1% (3/13)
Bilateral disease with satellite lesions > pGS 6	38.0% (27/71)	29.6% (8/27)	45.2% (14/31)	38.5% (5/13)

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Abbreviations: GS, Gleason score; pGS, pathologic GS; RP, radical prostatectomy. Please note that the 'high-risk' group encompasses both 'high-risk' and 'very high-risk' patients per National Comprehensive Care Network guidelines.

Table 4.

Characteristics of mpMRI-detected and mpMRI-occult index and satellite lesions in the RP specimen

	Entire cohort (*N* = 71)	Favorable intermediate risk (*N* = 27)	Unfavorable intermediate risk (*N* = 31)	High risk (*N* = 13)
mpMRI detection of an index lesion				
No	5.6% (4/71)	3.7% (1/27)	9.7% (3/31)	0 (0/13)
Yes	94.3% (67/71)	96.3% (26/27)	90.3% (28/31)	100% (13/13)
Pathologic grade of mpMRI-detected index lesions				
⩽ 3+3	3.8% (2/53)	10.0% (2/20)	0 (0/21)	0 (0/12)
3+4	50.9% (27/53)	60.0% (12/20)	61.9% (13/21)	16.7% (2/12)
4+3	18.9% (10/53)	15.0% (3/20)	14.3% (3/21)	33.3% (4/12)
8–9	26.4% (14/53)	15.0% (3/20)	23.8% (5/21)	50.0% (6/12)
Pathologic grade of mpMRI-occult index lesions				
3+3	11.1% (2/18)	14.3% (1/7)	10.0% (1/10)	0 (0/1)
3+4	66.7% (12/18)	71.4% (5/7)	60.0% (6/10)	100% (1/1)
4+3	11.1% (2/18)	14.3% (1/7)	10.0% (1/10)	0 (0/1)
8–9	11.1% (2/18)	0 (0/7)	20.0% (2/10)	0 (0/1)
mpMRI detection of a satellite lesion				
No	49.3% (35/71)	59.3% (16/27)	51.6% (16/31)	23.1% (3/13)
Yes	50.7% (36/71)	40.7% (11/27)	48.4% (15/31)	76.9% (10/13)
Pathologic grade of mpMRI-detected satellite lesions				
⩽ 3+3	46.4% (13/28)	45.5% (5/11)	40.0% (4/10)	57.1% (4/7)
3+4	25.0% (7/28)	36.4% (4/11)	20.0% (2/10)	14.3% (1/7)
4+3	14.3% (4/28)	18.2% (2/11)	10.0% (1/10)	14.3% (1/7)
8	14.3% (4/28)	0 (0/11)	30.0% (3/10)	14.3% (1/7)
Pathologic grade of mpMRI-occult satellite lesions				
⩽ 3+3	42.1% (8/19)	14.3% (1/7)	54.5% (6/11)	100% (1/1)
3+4	52.6% (10/19)	71.4% (5/7)	45.5% (5/11)	0 (0/1)
4+3	5.3% (1/19)	14.3% (1/7)	0 (0/11)	0 (0/1)

Abbreviations: mpMRI, multiparametric magnetic resonance imaging; RP, radical prostatectomy. Please note that the ‘high-risk’ group encompasses both ‘high-risk’ and ‘very high-risk’ patients per National Comprehensive Care Network guidelines.

Table 5.

Univariate logistic regression analysis to predict satellite lesions at RP

Predictor	Odds ratio	95% confidence interval	*P*-value
Age	0.97	0.91–1.04	0.45
PSA	1.03	0.94–1.14	0.47
Clinical T-category (T2 vs T1)	1.10	0.33–3.65	0.88
Biopsy Gleason score			
3+3/3+4 vs 4+3	2.16	0.61–7.73	0.23
3+3/3+4 vs 8–10	0.69	0.18–2.66	0.59
4+3 vs 8–10	0.32	0.06–1.62	0.17
3+3/3+4/4+3 vs 8–10	0.47	0.12–1.81	0.27
Percent positive biopsies	1.15	0.85–1.56	0.35
MRI dominant lesion greatest dimension	0.94	0.86–1.04	0.24
MRI suspicion score of dominant lesion	0.75	0.45–1.26	0.28
ADC of dominant lesion	1.14	0.87–1.5	0.34
K^{trans} of dominant lesion	0.95	0.77–1.19	0.68
Presence of MRI satellite lesions	2.95	1.05–8.25	0.040[a]
MRI T-category			
T2 vs T1	0.60	0.06–6.17	0.67
T3 vs T1	1.00	0.06–16.00	1.00
T3 vs T2	1.66	0.31–8.96	0.56

Abbreviations: ADC, Apparent Diffusion Coefficient; MRI, magnetic resonance imaging; RP, radical prostatectomy.

[a]Statistically significant.

Table 6.

Performance characteristics for detecting RP satellite lesions

A. Performance characteristics of mpMRI in the entire cohort (*N* = 71) for detecting satellite lesions on RP		
	Detection of any satellite lesion	**Detection of clinically significant satellite lesion (GS ⩾ 3+4 and size ⩾ 5 mm, or any GS but size ⩾ 10 mm)**
Sensitivity	59.6%	59.5%
Specificity	66.7%	58.8%
Positive predictive value	77.8%	61.1%
Negative predictive value	45.7%	57.1%
Accuracy	62.0%	59.2%

B. Performance characteristics for mpMRI detecting any RP satellite lesions on RP stratified by risk group			
	Favorable intermediate risk (*N* = 27)	**Unfavorable intermediate risk (*N* = 31)**	**High risk (*N* = 13)**
Sensitivity	61.1%	47.6%	87.5%
Specificity	100%	50.0%	40.0%
Positive predictive value	100%	66.7%	70.0%
Negative predictive value	56.3%	31.3%	66.7%
Accuracy	74.1%	48.4%	69.2%

C. Accuracy of laterality localization with combined biopsy and mpMRI data				
	All risk (*N* = 71)	**Favorable intermediate risk (*N* = 27)**	**Unfavorable intermediate risk (*N* = 31)**	**High risk (*N* = 13)**
Accuracy of laterality for all tumors at RP using combined biopsy +mpMRI	76.1% (54/71)	66.7% (18/27)	83.9% (26/31)	76.9% (10/13)

Abbreviations: GS, Gleason score; mpMRI, multiparametric magnetic resonance imaging; RP, radical prostatectomy. Please note that the ‘high-risk’ group encompasses both ‘high-risk’ and ‘very high-risk’ patients per National Comprehensive Care Network guidelines.