Yield of second-round MRI targeted ultrasound-guided fusion prostate biopsy after initial first-round targeted biopsy

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**ABSTRACT**

**Introduction:** We aimed to determine the yield of second-round magnetic resonance imaging-ultrasound (MRI-US) fusion biopsy and factors that may predict eventual clinically significant (CS) prostate cancer (PCa) diagnosis.

**Methods:** From 2013 to 2021, 85 men underwent second-round MRI-US fusion biopsy of 92 lesions (47.8% [44/92] peripheral zone and 52.2% [48/92] transition zone). Patient age, prostate-specific antigen (PSA), PSA density (PSAD), size/location of lesions, ADC value, Prostate Imaging–Reporting and Data System (PI-RADS), and PRECISE scores were recorded and compared to histopathological diagnosis (International Society of Urological Pathology [ISUP] grade-group 1 PCa, CS PCa=ISUP grade group ≥2 PCa) using logistic regression.

**Results:** Mean patient age, PSA, and PSAD were 64±7 years, 8.5±7.0 ng/ml, and 0.17±0.11, respectively. Results from first-round targeted biopsy were 63% (58/92) negative and 37% (34/92) clinically insignificant (grade group 1) PCa. Overall, second-round targeted biopsy identified 25% (23/92) CS PCa (grade group 2, n=19; grade group 3, n=4). Considering only

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**KEY MESSAGES**

- Overall, 2nd-round targeted biopsy identified 25% more clinically significant (ISUP grade group ≥2) cancer in PI-RADS 3 or higher lesions with initially negative or ISUP grade group 1 diagnosis.
- In men with initially negative targeted biopsy, 2nd-round targeted biopsy identified 21% (12/58) clinically significant PCa.
- Precise score had significant association (p<0.01) with eventual clinically significant PCa diagnosis and high negative predictive value.
lesions with initial negative targeted-biopsy results (n=58), 21% (12/58; grade group 2, n=8; grade group 3, n=4) CS PCa and 13 grade group 1 PCa were diagnosed at second-round biopsy. There was no difference in PSA (p=0.564), size (p=0.595), location (p=0.293), or PI-RADS score (p=0.342) of lesions by eventual CS PCa diagnosis. PSAD (0.2±1.4 vs. 0.16±0.10, p=0.167), ADC (0.748±0.199 vs. 0.833±0.257, p=0.151), and PRECISE score (p<0.01) showed a trend towards association or association with eventual CS PCa diagnosis.  

**Conclusions:** Repeat second-round targeted MRI-US fusion biopsy yielded CS PCa diagnosis in the targeted biopsy specimen in approximately 20% of patients in our study. PRECISE score may be a useful marker to help predict which patients require second-round biopsy.

**INTRODUCTION**

Targeted biopsy of abnormalities detected on prostate MRI has been shown to be an effective method to diagnose clinically significant prostate cancer (CS-pca, International Society of Urogenital Pathology [ISUP] grade-group ≥2) [1; 2]. Accurate results from targeted biopsy require precise placement of the biopsy needle into the region of interest. Currently, the most common method of obtaining targeted prostate biopsy is by using Ultrasound (US) guidance with manual (cognitive) or software fusion of US and MRI images [3]. In-bore (in-gantry) MRI guided biopsy is also possible; however, this approach is time consuming and studies have failed to demonstrate superiority compared to fusion biopsy [4]. Irrespective of the imaging guidance used (US or MRI) and fusion method employed (cognitive or software), negative biopsy results pose a common clinical scenario.

Management of patients with negative targeted biopsy is controversial. Options include immediate rebiopsy or PSA surveillance (with or without a repeat MRI or biopsy) [5-7]. Studies reviewing repeat (i.e. Second-round) MRI targeted biopsy has reported a wide range in CS-pca detection. A previous mini-systematic review on the topic conducted in 2022 including 9 studies and 485 patients reported any pca and CS-pca detection percentages of 0-80% and 0-20% for PI-RADS 3 lesions and 15-86% and 8-57% for PI-RADS 4 or 5 lesions [8]. Clinical or imaging markers to identify which lesions harbor undiagnosed pca and which do not and thus, which patients should undergo repeat biopsy are lacking. In one study, growth of a lesion on MRI was the only significant predictor of subsequent pca detection at second-round biopsy [5] and in another study, persistence of pirads 4/5 at repeat MRI was a predictor of cancer on repeat biopsy [9].

The purpose of the present study was to report the percentage of CS-pca diagnosed at second-round targeted biopsy in a tertiary care referral center for pca and to determine if there are clinical or imaging features which are associated with eventual CS-pca diagnosis and that may help to predict which men should undergo immediate repeat targeted biopsy.
METHODS

Patients
This research ethics board (REB) approved retrospective study was conducted by using a database search of our institutional picture archiving and data reporting system (PACS; Change Healthcare) to identify all patients who underwent US guided biopsy of the prostate between January 1 2013 and December 30 2021 after a prostate MRI. We identified 940 patients and excluded 185 men because MRI was negative. 106 other men were excluded because targeted biopsy was performed due to suspicion of locally recurrent tumor after radical prostatectomy or radiotherapy or after rectal or bladder cancer staging. Of the remaining 649 patients, we identified 85 men with 92 lesions who underwent a second-round of targeted biopsy. A summary of patient inclusion and exclusion criteria is provided in (Figure 1).

MRI
All MRI examinations were performed on a clinical 3 Tesla MRI system (Discovery 750W, general electric medical, Milwaukee WI) using integrated body array coils (endorectal coil was not used) and with sequence parameters compliant with PI-RADS version 2 [10; 11]. A summary of the MRI protocol used at our institution is provided in (Appendix 1).

MRI TRUS-guided targeted fusion biopsy and histopathology results
Targeted biopsies were performed using transrectal US (TRUS) guidance with cognitive or software fusion of MRI data onto real time 2-Dimensional TRUS images. All ultrasound examinations were performed using modern ultrasound equipment (Aloka Prosound Alpha 10, Aloka Hitahi medical, general electric logiq E9, general electric healthcare, Philips Epic 7 or Canon Aplio 600, Canon Medical) using endoluminal 4-8 mhz end-fire probes. Software fusion at our institution consists of electromagnetic guidance (Philips medical, Canon medical). All biopsies were performed by fellowship trained abdominal radiologists. The decision to use cognitive or software fusion was operator dependent and at the discretion of the operator performing the biopsy. Typically, at our institution, when an US correlate for the MRI lesion is well seen, then software fusion may be omitted.

The TRUS-guided biopsy system used for all biopsies employed an 18-gauge side-cutting needle. The majority of men are provided with anesthesia using a 1% Lidocaine nerve block, whereas, 1% Lidocaine nerve block in addition to conscious sedation was reserved for patients who could not tolerate TRUS, had anal stricture, had rectal tumor or otherwise had a strong preference for sedation. A fleet enema was prescribed prior to the procedure and antibiotic prophylaxis to prevent infection as described previously [12]. At our institution, at time of targeted biopsy a simultaneous extended sextant template biopsy of the peripheral zone was also performed including 12 biopsies (two each from the bilateral base, middle and apical portions of the PZ) in accordance with provincial standards for pca diagnosis [13]. Core-needle biopsy
specimens were submitted for laboratory processing and interpretation in separate pathology
case containers according the site of sampling. Tissue from biopsy specimens were fixed
overnight in 10% neutral buffered formalin. Three histological slides were prepared from each
block, each with three serial sections cut at 3μm in thickness and stained with haematoxylin and
eosin (H&E). Biopsy results were reported for each core specimen individually.

The MRI fusion TRUS-guided biopsy reports used at our institution employ a mandatory
standardized reporting template which specifies: the operator and the number of core biopsies
per target. In general, a minimum of 2-3 core biopsies are performed per target.

Historical data collection
All clinical and imaging variables were recorded by a fellowship trained abdominal radiologist
with 1 year of experience in prostate MRI (blinded). The radiologist retrieved the biopsy results
from the patient electronic medical record. The presence of cancer at a biopsy site (targeted or
template) was recorded and the individual gleason score from core-needle biopsy specimens at
each biopsy site was documented. ISUP grade group ≥ 2 was considered clinically significant
in this study. In this way, a biopsy result for each targeted lesion, as well as, the remainder of
the peripheral zone after template biopsy was recorded.

The radiologist extracted the PSA and PSA density (PSAD) from the electronic medical
record. The location (peripheral or transition zone, apex, middle or base), size and PI-RADS v2
category for each lesion was extracted from the MRI report. At our institution, prostate MRI is
reported by a group of approximately 12 Fellowship trained abdominal radiologists, each having
reported over 200 prostate MRI.

Apparent diffusion coefficient (ADC) and PRECISE
Two fellowship-trained abdominal radiologists, each with 1 year of experience in prostate MRI
(blinded) independently reviewed the MRI images for each patient provided only with the
location of the lesion described in the original MRI report (so as to confirm the lesion evaluated
on MRI corresponded to the lesion which underwent targeted biopsy). The first radiologist
measured the ADC value for each lesion by placing a circular region of interest within the lesion
on ADC map images and recording the mean value in mm2/sec, (Figure 2). For homogeneous
lesions, a circular ROI was placed on the axial image where the lesion appeared the largest
encompassing 2/3 of the area of the lesion. For heterogeneous lesions, a circular ROI was placed
on the darkest portion of the lesion, where the ROI was required to measure at least 5 mm in
diameter. A repeat MRI before second-round targeted biopsy was available in 47% (43/92)
lesions and the time interval between MRI was 5 ± 47 months. The radiologist evaluated the first
and second MRI in these patients and assigned a precise score (Likert scale 1-5, a predictor of
disease progression for AS) to each individual lesion, see Supplementary (Table 2). The second
radiologist also evaluated the first and second MRI in these patients and recorded the ADC value
of the lesion from the first MRI (which was used to determine inter-observer agreement of
measurements) and the precise score (also to determine inter-observer agreement). A precise
score was applied to each lesion so that precise data are reported on a per-lesion and not per-patient level.

**Statistical analysis**

The primary outcome of this study was to determine the rate of clinically significant and ISUP grade group 1 pca diagnosed after second-round targeted biopsy in targeted biopsy specimens. Clinical and imaging variables extracted were compared to histological diagnosis of CS-pca after second-round targeted biopsy in targeted biopsy specimens only using multi-variable logistic regression testing. Inter-group comparisons, by clinical indication, were performed using independent t-tests of Chi square. Statistical analyses were performed using stata version 13.0 (Statacorp, College station TX).

**RESULTS**

Mean patient age was 64±7 years and mean PSA and PSAD were 8.5±6.9 ng/ml and 0.17±0.11. Clinical indications for MRI were: previously negative template biopsy with persisting clinical suspicion of pca (64% [54/85]) and biopsy naïve with elevated PSA, abnormal digital rectal exam or positive family of pca (36% [31/85]). A summary of patient demographics is provided in (Table 1).

Pathology results for the 92 lesions at first-round targeted biopsy were: 63.0% (58/92) negative and 37% (34/92) clinically insignificant (Grade group 1) pca. There were 60% (51/85) men who had grade group 1 pca diagnosed in off-target template biopsy during their first-round template biopsy session, of which, 33% (28/85) had grade group 1 pca diagnosed only on template biopsy. A summary of results from first-round targeted biopsy session, by clinical indication, is provided in (Table 2).

The median time interval between initial and second-round biopsy was 13 months (interquartile range 8-23 months). Overall, second-round targeted biopsy identified 25.0% (23/92) CS-pca (Grade group 2 N=19, grade group 3 N=4) and an additional eight grade group 1 pca in the targeted biopsy specimen. On a per patient basis, there were 26% (22/85) patients with cspca diagnosed on second-round targeted biopsy. Considering only the 58 lesions with negative first-round targeted biopsy, CS-pca was diagnosed in 21% (12/58; Grade group 2 N=8, grade group 3 N=4) and grade group 1 pca was diagnosed in 22% (13/58) lesions. A summary of second-round targeted biopsy results, by clinical indication, is provided in (Table 3). Concurrent template biopsy performed during second-round targeted biopsy session identified an an additional ten men with grade group 1 pca diagnosed in second round template biopsy specimens, (Table 3).

Comparing lesions which had CS-pca diagnosed at second-round targeted biopsy to those lesions which had either no cancer or Gleason score 3+3=6 pca, there was no difference in: PSA (7.8±4.5 versus 8.8±7.6 ng/ml, p=0.564), size of lesion (15±6 versus 14±6 mm, p=0.595), location of lesion (27.3% [12/44] CS-pca in peripheral zone versus 22.9% [11/48] CS-pca in transition zone, p=0.293; and 22.4% [17/76] CS-pca in the prostate base/middle gland versus
37.5% [6/16] CS-pca in the apex, \( p=0.204 \) and, PI-RADS v2 score (29.4%[5/17] CS-pca for score 3, 17.5% [7/40] CS-pca for score 4 and 31.4% [11/35] CS-pca for score 5, \( p=0.342 \)).
PSAD (0.2±1.4 versus 0.16±0.10, \( p=0.167 \)), mean ADC (0.748±0.199 versus 0.833±0.257, \( p=0.151 \)) and precise score (\( p<0.01 \)) showed a trend or significant difference between groups. A precise score of \( \geq 3 \) had high sensitivity (100% radiologist 1, 93.3% radiologist 2) for diagnosis of CS-pca in the targeted biopsy specimen and a score of \( \leq 2 \) had a high negative predictive value (100% radiologist 1, 85.7% radiologist 2), (Table 4). In patients with negative first-round targeted biopsy, a repeat MRI was available in 32 lesions. A precise score of \( \geq 3 \) had high sensitivity (100% radiologist 1, 87.5% radiologist 2) for diagnosis of CS-pca in the targeted biopsy specimen and a score of \( \leq 2 \) had a high negative predictive value (100% radiologist 1, 83.3% radiologist 2), (Table 4) and (Figures 3 and 4). Precise scoring showed substantial agreement (Kappa 0.719) and there was a low mean ADC difference in measurements (0.021 [95%CI -0.065-0.021) between radiologists.

**DISCUSSION**

This study evaluated 92 prostate lesions which underwent second-round MRI targeted US guided fusion biopsy. Approximately 2/3 of lesions had initially negative targeted biopsy and 1/3 had ISUP grade group 1 (Gleason 3+3=6 pca) diagnosis. At repeat second-round targeted biopsy, 25% clinically significant pca were detected overall and 21% clinically significant pca were detected when considering only the lesions which had negative first-round biopsy. This study is limited by a relatively small sample size and heterogeneous patient population.

Available data evaluating the management of patients with initially negative MRI guided targeted US prostate biopsy and yield of second round biopsy is limited. In studies evaluating the diagnostic yield of second-round targeted biopsy, variable rates of detection of pca have been reported. A previous mini-systematic review on the topic conducted in 2022 including 9 studies and 485 patients reported any pca and CS-pca detection percentages of 0-80% and 0-20% for PI-RADS 3 lesions and 15-86% and 8-57% for PI-RADS 4 or 5 lesions [8]. In a 2022 abstract by Futterer et al., repeat biopsies in men with prior negative MRI-guided targeted biopsy showed clinically significant pca and any pca in 14% (7/50) and 32% (16/50) [14].

A challenge of deciding which patients require repeat second-round biopsy versus surveillance is the inability to predict who would benefit most from a repeat biopsy. Chelluri et al. Previously showed that growth of a lesion on MRI was the only significant predictor of subsequent pca detection at second-round biopsy [5]. In the study by Meng et al. Which focused on lesions with negative first-round targeted biopsy, repeat MRI and second-round biopsy persistence of PI-RADS score 4/5 at repeat MRI predicted a higher risk of missed cancer at second-round biopsy [9]. In 45 men with PI-RADS score 4/5 who underwent repeat MRI after negative first-round biopsy, 35% (16/45) lesions regressed completely to PI-RADS score 1. In 38% (17/45) PI-RADS score regressed to PI-RADS score 2/3 and in this cohort of men, only 2/13 patients had pca diagnosed at second-round targeted biopsy [9]. These features (lesion
growth, change in PI-RADS score) assessed over time on MRI are to some extent components of
the precise scoring system which aims to risk stratify lesions on serial MRI in men treated with
AS [15]. To our knowledge, this is the first study to formally study the precise MRI scoring
system in the patient population of men with initial negative targeted prostate biopsy. Our
results, using precise on a per-lesion level, are similar to the results reported by Chelluri et al.
And Meng et al., namely, a low (score 1 or 2) precise score had high negative predictive value to
exclude clinically significant cancer and a precise score of ≥3 had high sensitivity for detection
of clinically significant cancer at second-round targeted biopsy of a pre-existing lesion with
initial biopsy negative for significant cancer. A challenge of using precise; however, is a low
specificity due to a large number of patients with precise score ≥3 that did not have clinically
significant cancer on second-round targeted biopsy.

Our study has limitations. Our sample size is relatively small; however, is the second
largest cohort evaluating first-round negative biopsy results with repeat biopsy published in the
literature to date. Our population is not consecutive, that is, men with a negative first-round
targeted biopsy who did not have a second-round targeted biopsy were excluded. This includes
men who may have sought management (including biopsy) elsewhere or were lost to follow-up.
Not all men in our cohort with second-round targeted biopsy had intervening MRI, which further
reduces our sample size to evaluate the efficacy of MRI for predicting which men may benefit
most from second-round biopsy. We applied precise on a per-lesion level for those men who had
intervening MRI before repeat second-round biopsy and focused on the second-round targeted
biopsy results for initial lesions detected at first-round biopsy. Thus, we did not include
additional lesions detected on the second MRI which would increase the precise score on a per-
patient level due to concern of potential bias towards inflating the performance of precise for
predicting cspca. Including additional new lesions, which influence precise on a per patient level,
likely further emphasizes the potential importance of serial MRI and precise in men with prior
negative targeted biopsy. This study used both cognitive and software fusion biopsy
 interchangeably, at the discretion of the biopsy operator. It is possible that different results could
be observed in centers using exclusively cognitive or software fusion biopsy methods. At our
institution, PI-RADS score 3 lesions are typically not biopsied unless there are other clinical
factors (e.g. PSAD >0.15, patient desire) which may prompt biopsy and this may influence the
cancer detection rate among PI-RADS score 3 lesions in our study.

In conclusion, a second-round targeted biopsy of prostate lesions with negative or
Gleason score 3+3=6 prostate cancer diagnosis yielded a clinically significant cancer diagnosis
in 25% of lesions. When considering lesions with only negative first-round biopsy results,
clinically significant cancer was diagnosed in 21% of lesions at second-round biopsy. The use of
the precise scoring system in men with negative or ISUP 1 diagnosis after first-round targeted
biopsy at intervening MRI might better risk stratify which men should undergo second-round
biopsy versus surveillance. In particular, a precise score of ≤2 had a high negative predictive
value and a score of $\geq 3$ was sensitive for eventual prediction of clinically significant prostate cancer diagnosis at second-round targeted biopsy.

REFERENCES

6 Costa DN, Kay FU, Pedrosa I et al (2017) An initial negative round of targeted biopsies in men with highly suspicious multiparametric magnetic resonance findings does not exclude clinically significant prostate cancer-Preliminary experience. Urol Oncol 35:149 e115-149 e121
FIGURES AND TABLES

Figure 1. Flow diagram indicating patient inclusion and exclusion criteria for the study.
Figure 2. 57-year-old man with elevated PSA. (a) Axial T2-weighted; (b) axial b 1500 mm²/sec diffusion-weighted image; (c) axial apparent diffusion coefficient (ADC) map image. Images depict an 11 mm lesion in the left transition zone (arrows). The lesion was categorized as PI-RADS score 4. Methodology for measurement of ADC value is depicted in (c), where a circular region of interest (ROI) was placed within the center of homogeneous lesions encompassing 2/3 of the surface area and in the area with most restricted diffusion for heterogeneous lesions. Targeted biopsy yielded benign tissue, concurrent template biopsy diagnosed ISUP grade-group 1 (Gleason score 3+3=6) prostate cancer. Second-round targeted biopsy yielded ISUP grade-group 2 (Gleason score 3+4=7) prostate cancer.
Figure 3. 62-year-old man with elevated PSA. Initial MRI (a) axial T2W; (b) axial b 1500 mm²/sec; (c) axial ADC map demonstrated a 5 mm lesion in the left of midline peripheral zone lesion with marked restricted diffusion (arrows). The lesion is categorized as PI-RADS 3. Initial targeted and template biopsy were negative. PSA remained stable on followup MRI: (d) axial T2W, (e) axial 1500 mm²/sec; (f) axial ADC map performed 1 year after initial MRI demonstrates that the lesion has become less conspicuous on T2W and now shows only mild to moderate restricted diffusion and is given a PI-RADS score of 3 and PRECISE score of 2. Repeat targeted and template biopsy were negative.
Figure 4. 74-year-old man with elevated PSA and negative initial template biopsy. MRI: (a) axial T2W; (b) axial b 1500 mm²/sec; (c) axial ADC map show an ill-defined 12 mm lenticular lesion in the left anterior transition zone at the base with marked restricted diffusion (arrows). The lesion is categorized as PI-RADS 4. Initial targeted biopsy yielded ISUP grade group 1 (Gleason score 3+3 =6) prostate cancer. During active surveillance, PSA continued to rise and follow up MRI after 1 year: (d) axial T2W; (e) axial b 1500 mm²/sec; (f) axial ADC map demonstrate that the lesion has increased in size now measuring 18 mm and is more conspicuous (arrows). The lesion is now categorized as PI-RADS score 5 and precise score 4. Targeted biopsy yielded ISUP grade group 2 (Gleason score 3+4=7) prostate cancer.
### Table 1. Summary of patient distribution and demographics by clinical indication for initial first-round MRI targeted ultrasound-guided biopsy

<table>
<thead>
<tr>
<th>Indication</th>
<th>Age (years)</th>
<th>PSA (ng/ml)</th>
<th>Volume of prostate (ml)</th>
<th>PSAD</th>
<th>Results from initial template biopsy (if performed)</th>
<th>PI-RADS score of lesions (n=92)</th>
<th>Lesion size (mm)</th>
<th>Lesion location for all lesions (n=92)</th>
<th>Change in PSA between 1st and 2nd-round biopsy</th>
<th>Change in PSAD between 1st and 2nd-round biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative template biopsy, rule out underlying lesion</td>
<td>64±7</td>
<td>9.4±8.5</td>
<td>54±27 (range 22–159)</td>
<td>0.18±0.11</td>
<td>Negative</td>
<td>PI-RADS 5 55% (23/60)  PI-RADS 4 40% (24/60)  PI-RADS 3 22% (13/60)</td>
<td>15±5 (range 4–29)</td>
<td>Peripheral zone 45% (27/60) Transition zone 55% (33/60)</td>
<td>2.0±6.4 (range -2.2–15.1)</td>
<td>0.04±0.17 (range -0.34 –0.34)</td>
</tr>
<tr>
<td>Biopsy-naive, risk factor for prostate cancer</td>
<td>65±7</td>
<td>7.2±2.8</td>
<td>60±31 (range 27–196)</td>
<td>0.17±0.10</td>
<td>Not applicable</td>
<td>PI-RADS 5 38% (12/32)</td>
<td></td>
<td>Peripheral zone 53% (17/32)</td>
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<td></td>
</tr>
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</table>
(36% [31/85] with 35% [32/92] lesions)

<table>
<thead>
<tr>
<th></th>
<th>PI-RADS 4 50% (16/32)</th>
<th>PI-RADS 3 13% (4/32)</th>
<th>14±8 (range 3–32)</th>
<th>Transition zone 47% (15/32)</th>
<th>0.6±2.9 (range 6.8–5.5)</th>
<th>0.04±0.12 (range -0.15–0.41)</th>
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<tbody>
<tr>
<td></td>
<td>0.23</td>
<td>0.17</td>
<td>0.21</td>
<td>0.49</td>
<td>0.61</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Prostate volume derived from formula for an ellipse (length x width x height /2) applied to measurements obtained from MRI. **Comparisons performed between groups using independent t-tests or the rank sum test. PSA: prostate-specific antigen; PSAD: prostate-specific antigen density.
Table 2. Results of first-round targeted and template biopsy (performed with first-round targeted biopsy) stratified by clinical indication

<table>
<thead>
<tr>
<th>Patient group</th>
<th>First-round targeted biopsy, negative</th>
<th>First-round targeted biopsy: ISUP grade group 1 prostate cancer</th>
<th>Concurrent template biopsy: Negative</th>
<th>Concurrent template biopsy: ISUP grade group 1 prostate cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative template biopsy, rule out underlying lesion</td>
<td>65% (35/54)</td>
<td>35% (19/54)</td>
<td>50% (27/54)</td>
<td>50% (27/54)</td>
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<tr>
<td>(64% [54/85])</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biopsy-naive, risk factor for prostate cancer</td>
<td>58% (18/31)</td>
<td>42% (13/31)</td>
<td>23% (7/31)</td>
<td>77% (24/31)</td>
</tr>
<tr>
<td>(36% [31/85])</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>p*</td>
<td>0.54</td>
<td></td>
<td>0.01</td>
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</table>

*Comparisons performed using the Chi-squared test. ISUP: International Society of Urogenital Pathology.

Table 3. Results of second-round targeted and template (performed during targeted biopsy) biopsy stratified by clinical indication and results from first-round targeted and concurrent template biopsy session

<table>
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</thead>
<tbody>
<tr>
<td>Negative template biopsy, rule out underlying lesion</td>
<td>59% (23/39)</td>
<td>18% (7/39)</td>
<td>23% (9/39) [7 ISUP 2 PCa, 2 ISUP 3 PCa]</td>
<td>51% (20/39)</td>
<td>31% (12/39)</td>
<td>18% (7/39) [6 ISUP 2 PCa, 1 ISUP 4 PCa]</td>
</tr>
<tr>
<td>1st-round targeted biopsy negative (N=39 lesions)</td>
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In 21 lesions with ISUP grade-group 1 prostate cancer diagnosed at first-round target biopsy, template biopsy was also positive for ISUP grade-group 1 prostate cancer in 71% (15/21) patients.** In 13 lesions with ISUP grade-group 1 prostate cancer diagnosed at first-round target biopsy, template biopsy was also positive for ISUP grade-group 1 prostate cancer in 85% (11/13) patients. ISUP: International Society of Urogenital Pathology; PCa: prostate cancer.
Table 4. Summary of precise scores for overall dataset (43 patients with negative or ISUP grade group 1 PCa) and patients with negative (32 patients) first-round biopsy results with repeat MRI prior to second-round targeted biopsy

<table>
<thead>
<tr>
<th>Overall (N=43)</th>
<th>Radiologist 1</th>
<th>p*</th>
<th>Radiologist 2</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CS PCa (n=15)</td>
<td>Negative or ISUP grade group 1 PCa (n=28)</td>
<td>CS PCa (n=15)</td>
<td>Negative or ISUP grade group 1 PCa (n=28)</td>
</tr>
<tr>
<td>PRECISE score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0% (0/15)</td>
<td>11% (3/28)</td>
<td>0% (0/15)</td>
<td>7.1% (2/28)</td>
</tr>
<tr>
<td>2</td>
<td>0% (0/15)</td>
<td>7% (2/28)</td>
<td>7% (1/15)</td>
<td>14% (4/28)</td>
</tr>
<tr>
<td>3</td>
<td>40% (6/15)</td>
<td>61% (17/28)</td>
<td>33% (5/15)</td>
<td>50% (14/28)</td>
</tr>
<tr>
<td>4</td>
<td>53% (8/15)</td>
<td>21% (6/28)</td>
<td>53% (8/15)</td>
<td>21% (6/28)</td>
</tr>
<tr>
<td>5</td>
<td>7% (1/15)</td>
<td>0% (0/28)</td>
<td>7% (1/15)</td>
<td>7.1% (2/28)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Initial diagnosis benign (N=32)</th>
<th>Radiologist 1</th>
<th>p*</th>
<th>Radiologist 2</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CS PCa (n=8)</td>
<td>Negative or ISUP grade group 1 PCa (n=24)</td>
<td>CS PCa (n=8)</td>
<td>Negative or ISUP grade group 1 PCa (n=24)</td>
</tr>
<tr>
<td>PRECISE score</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1</td>
<td>0% (0/8)</td>
<td>13% (3/24)</td>
<td>0% (0/8)</td>
<td>8.3% (2/24)</td>
</tr>
<tr>
<td>2</td>
<td>0% (0/8)</td>
<td>8.3% (2/24)</td>
<td>13% (1/8)</td>
<td>13% (3/24)</td>
</tr>
<tr>
<td>3</td>
<td>25% (2/8)</td>
<td>63% (15/24)</td>
<td>13% (1/8)</td>
<td>54% (13/24)</td>
</tr>
<tr>
<td>4</td>
<td>63% (5/8)</td>
<td>17% (4/24)</td>
<td>63% (5/8)</td>
<td>21% (5/24)</td>
</tr>
<tr>
<td>5</td>
<td>13% (1/8)</td>
<td>0% (0/24)</td>
<td>13% (1/8)</td>
<td>4.2% (1/24)</td>
</tr>
</tbody>
</table>

*Comparisons performed using Wilcoxon sign-rank test. CS: clinically significant (ISUP grade group ≥2); ISUP: International Society of Urogenital Pathology; MRI: magnetic resonance imaging.