In-Bore MRI-guided Prostate Biopsies in Patients with Prior Positive Transrectal US–guided Biopsy Results: Pathologic Outcomes and Predictors of Missed Cancers

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Conflicts of interest are listed at the end of this article.

See also the commentary by Weiss and Solomon in this issue.

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Purpose: To evaluate the role of confirmatory in-bore MRI-guided biopsy in patients with low- or intermediate-risk disease diagnosed at prior transrectal US-guided biopsy and to evaluate the rate and predictors for missed cancers.

Materials and Methods: A retrospective evaluation of 50 consecutive men who had previously undergone transrectal US-guided biopsy with positive results and who underwent subsequent in-bore MRI-guided biopsy at our university hospital (average time interval, 11 months) between 2012 and 2016 was performed. Ten men were excluded because of a history of treatment after transrectal US-guided biopsy. A total of 40 men (mean age, 63 years; range, 47–84 years) were included in this study. Multiparametric 3-T MRI (T2-weighted, diffusion-weighted, and dynamic contrast material–enhanced) and transrectal in-bore MRI-guided biopsy were performed. Cancer detection, disease-grade changes, and cancers missed at in-bore MRI-guided biopsy were evaluated. Descriptive statistics were used to report different rates. The Fisher exact test was used for categoric variables. The Mann-Whitney U test and independent Student t test were used for nonparametric and parametric data, respectively. The McNemar test was used for paired data.

Results: The overall cancer detection rate when using in-bore MRI-guided biopsy was 65% (26 of 40). In-bore MRI-guided biopsy detected 14 previously undiscovered cancerous lesions (clinically significant cancers [CSCs], 57.1% [eight of 14]). An overall disease upgrade by in-bore MRI-guided biopsy occurred in 40% (16 of 40) of cases (61.5% [16 of 26] of cases with positive results from in-bore MRI-guided biopsy). One case was downgraded from a Gleason score (GS) of 3 + 4 = 7 to a GS of 3 + 3 = 6. Out of 71 sextant biopsies with positive results detected by transrectal US–guided biopsy (from all 40 patients), 80% (57 of 71) were visible on MR images (in-bore MRI-guided biopsy results were positive in 52.6% [30 of 57]), and 20% (14 of 71) had no image correlates on MR images. In-bore MRI-guided biopsy upgraded 60% (18 of 30) and downgraded 3.3% (one of 30) of detected lesions. The false-negative rate was 35% (14.2% [two of 14] of patients had CSCs; GS ≥ 7), was higher in prostate volumes of greater than 40 mL, and was lower in the anterior gland location (P = .04 and .01, respectively).

Conclusion: Performing confirmatory in-bore MRI-guided biopsy following positive transrectal US–guided biopsy resulted in a high disease-upgrade incidence with subsequently improved disease-risk stratification, particularly when considering patients for active surveillance or focal therapy.

Supplemental material is available for this article.

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Patients with low-risk prostate cancer and select patients with intermediate-risk disease are candidates for active surveillance (1, 2). The recent introduction of focal therapy has expanded the management options for these patients, offering a potential cure with reduced morbidity (3, 4). Accurate disease grading, ascertainment of focality, and determination of organ confinement should be established before considering focal treatment.

Currently, systematic transrectal US–guided biopsy is the standard of care for prostate-cancer diagnosis and risk stratification (5). Transrectal US–guided biopsies are associated with low cancer detection rates (CDRs; 27%–40%), underestimation of Gleason scores (GSs; 34%–46%), and poor sampling to anterior gland lesions (6–9). A complete dependence on transrectal US–guided biopsy results can lead to improper disease-risk stratification and may jeopardize the opportunity for active treatment, with increased risk of disease progression and likelihood of metastasis (10, 11). Multiparametric MRI– and MRI-targeted biopsy are being increasingly utilized for the diagnosis of prostate cancer. They facilitate direct visualization and targeting of suspicious foci, rendering focal therapy a viable treatment option. MRI-targeted biopsies have been shown to enable higher detection of clinically significant cancers (CSCs), enable more accurate tumor grading, and have complication
In-Bore MRI-guided Prostate Biopsy following Positive Transrectal US-guided Biopsy Results

Key Points
- In patients with prior positive transrectal US-guided biopsy results, a confirmatory in-bore MRI-guided biopsy led to upgrading disease in 40% (16 of 40) of patients (61.5% [16 of 26] of patients with positive MRI-guided biopsy results).
- In-bore MRI-guided biopsy detected new cancer foci that were not detected when using transrectal US–guided biopsy; 57.1% (eight of 14) were clinically significant cancers.
- In patients with prior positive transrectal US–guided biopsy results, in-bore MRI-guided biopsy had a false-negative rate of 35% (14 of 40), with most missed cancers being clinically insignificant.

Abbreviations
CDR = cancer detection rate, CSC = clinically significant cancer, GG = grade group, GS = Gleason score

Summary
A confirmatory in-bore MRI-guided biopsy after a positive transrectal US–guided biopsy result yielded an upgrade rate of 40% and resulted in missing mostly clinically insignificant cancers and in subsequently improved disease-risk stratification.

Materials and Methods

Study Design
Institutional review board approval and written informed consent were obtained. We retrospectively reviewed our database, which contained 227 patients who had undergone in-bore MRI-guided biopsy between 2012 and 2016. We identified 50 consecutive patients with one or more positive transrectal US–guided biopsy results with low- or intermediate-risk disease and who underwent subsequent in-bore MRI-guided biopsy during the same period. We excluded patients who received treatment after transrectal US–guided biopsy (n = 10) (Fig 1). The final cohort included 40 patients (mean age, 63 years; range, 47–84 years) with a total of 71 sextants with positive transrectal US–guided biopsy results. Six patients were included in a prior study that addressed nontargeted sampling of normal MRI areas (23). Our sampling population was divided into patients (n = 40) and lesions (n = 71). Patients were either referred by urologists for in-bore MRI-guided biopsy to rule out the possibility of higher-risk disease because of a mismatch between prostate-specific antigen trends and diagnosed low- or intermediate-risk disease or were self-referred and seeking focal therapy. Transrectal US–guided biopsies were performed by urologists prior to referral for in-bore MRI-guided biopsy. At least 12 systematic transrectal US–guided biopsy cores were obtained (range, 12–16) per patient.

Multiparametric MRI Protocol
A 3-T MR scanner (Magnetom Trio; Siemens, Erlangen, Germany) with a 32-channel phased-array surface coil was used. Dynamic contrast-enhanced images were obtained after intravenous administration of 20 mL of gadobenate dimeglumine (MultiHance; Bracco Imaging, Milan, Italy) at a rate of 3 mL/sec. Postprocessing was performed by using DynaCAD (Invivo, Gainesville, Fla) software. Detailed multiparametric MRI parameters are listed in Table E1 (supplement).

In-Bore MRI-guided Biopsy
In-bore MRI-guided biopsies were performed with the same 3-T scanner used previously for diagnostic multiparametric MRI by a single experienced interventional radiologist (S.G.N., 19 years of experience) who was aware of clinical data, as the procedures were performed in the routine clinical setting. Patients received moderate sedation under continuous monitoring. Patients were placed in the prone position. After lubrication with lidocaine gel, a DynaTRIM (Invivo) rectal needle sleeve was inserted. Preprocedure images were obtained using axial and sagittal T2-weighted turbo spin-echo imaging and axial diffusion-weighted imaging (repetition time = 6000 msec, echo time = 89 msec, number of signals averaged = 7, and field of view = 300; b values = 0, 1000, 1500, and 2000 sec/mm²). The needle-sleeve position was calibrated on a DynaCAD workstation, target lesions were identified, and trajectory angles were calculated. We targeted focal prostate lesions for biopsy, regardless of their level of suspicion as demonstrated on MR images. Additional cores were obtained from areas with no visible MRI targets to assure a representative sample of the prostate gland (23).

An 18-gauge MRI-compatible fully automatic core-biopsy needle (Invivo) was introduced through the sleeve after adjusting the coordinates to the target. Two to four cores were obtained from each lesion. All tissue biopsy specimens obtained during in-bore MRI-guided biopsy were analyzed at our institution. Transrectal US–guided biopsy specimens were obtained and analyzed either inside or outside our institution.

Image Interpretation
All patients underwent multiparametric MRI prior to in-bore MRI-guided biopsy. Lesion locations on multiparametric MR images were identified by their level (apex, mid-gland, and base),
zone (peripheral zone or central gland), and clock-face position. Anterior gland lesions were defined as lesions located at the 10:00- to 2:00-o’clock position. Transrectal US–guided biopsy sextants were cognitively correlated with multiparametric MR images by a single radiologist who also performed the in-bore MRI-guided biopsy (S.G.N.). Lesions identified only on multiparametric MR images with no corresponding sextants with positive transrectal US–guided biopsy results were designated as “newly detected lesions.” Lesions were assigned various cancer suspicion levels by using our in-house grading system (24).

Data Analysis
Patient data were obtained from electronic medical records. Lesion sizes were categorized as less than or equal to 10 mm, 11–20 mm, or greater than 20 mm. The presence of inflammation indicated by histopathologic results was documented. To determine factors associated with false-negative results, we compared positive and negative in-bore MRI-guided biopsy results at both the patient and individual lesion level. Prostate volumes were categorized into less than or equal to 40 and greater than 40 mL. The GS of each patient was determined on the basis of the highest-grade lesion. We determined the GS change at both the patient (overall disease upgrade or downgrade) and lesion levels. At least one grade group (GG) change was considered a disease change. CSC was defined as any tumor with a GS greater than or equal to 7 (≥GG 2). We assessed the overall CDR and false-negative rate of in-bore MRI-guided biopsy at a patient level.

Statistical Analysis
Categorical variables were interpreted as frequencies and percentages. Quantitative variables were summarized as medians and ranges. Associations between false-negative in-bore MRI-guided biopsy results and possible factors (lesion size, location, prostate-specific antigen level, prostate volumes, presence of inflammation, number of cores, and interval between transrectal US–guided biopsy and in-bore MRI-guided biopsy) were tested using the Fisher exact test for categorical variables, Mann-Whitney U test for nonparametric variables, and Student t test for parametric variables (independent groups). The McNemar test was used to compare disease bilaterally between transrectal US–guided biopsy and in-bore MRI-guided biopsy results. Statistical significance was defined as a P value less than .05. The data were analyzed by using SPSS statistical software (version 23; IBM, Armonk, NY) for Microsoft Windows (Redmond, Wash).

Results

Patient Characteristics
The median age was 63 years (range, 47–84 years), the median prostate-specific antigen level was 5.5 ng/mL (range, 1–15 ng/mL), and the median prostate volume was 43.5 mL (range, 16–79 mL). On in-bore MRI-guided biopsy, 65% (26 of 40) of patients had positive biopsies and 35% (14 of 40) of patients had negative biopsies. A total of 82.5% (33 of 40) of patients had a GS of 3 + 3 = 6 (GG 1), 15% (six of 40) had a GS of 3 + 4 = 7 (GG 2), and 2.5% (one of 40) had a GS of 4 + 3 = 7 (GG 3), as demonstrated by the results of prior transrectal US–guided biopsies. Inflammation was found in 32.5% of the total number of patients (13 of 40). Of these, 53.9% (seven of 13) were positive for cancer on in-bore MRI-guided biopsy, with 28.6% (two of seven) having a GS of 3 + 3 = 6 (GG 1), 57.1% (four of seven) having a GS of 3 + 4 = 7, and 14.3% (one of seven) having a GS of 4 + 4 = 8 (GG 3). Table 1 shows detailed patient characteristics.

Lesion Characteristics
Eighty percent (57 of 71) of the sextants detected by using transrectal US–guided biopsy had corresponding visible targets on MR images (Table 1); 52.6% (30 of 57) of sextants showed positive in-bore MRI-guided biopsy results. The median lesion size was 13 mm (range, 6–29 mm). Most lesions were in the peripheral zone (59.6% [34 of 57]), and 21% (12 of 57) were in anterior gland locations. The GSs for sextants obtained using transrectal US–guided biopsy with corresponding visible MRI targets were 3 + 3 = 6 (87.7% [50 of 57]), 3 + 4 = 7 (8.8% [five of 57]), and 4 + 3 = 7 (3.5% [two of 57]). Table 1 shows detailed lesion characteristics. Multiparametric MRI and/or in-bore MRI-guided biopsy detected additional lesions (n = 14) without having corresponding positive transrectal US–guided biopsy sextants.

Cancer Detection Rate
The overall CDR was 65% (26 of 40; 95% confidence interval: 50.2%, 79.8%), and 65.3% (17 of 26; 95% confidence interval: 47%, 83.6%) were CSCs. In men with unilateral disease diagnosed by transrectal US–guided biopsy, in-bore MRI-guided biopsy detected bilateral disease in 30% (six of 20; P = .7).
In-Bore MRI-guided Prostate Biopsy following Positive Transrectal US-guided Biopsy Results

**Table 1: Patient and Lesion Characteristics**

| Characteristic                                      | Positive In-Bore MRI-guided Biopsy Results | Negative In-Bore MRI-guided Biopsy Results | P Value |
|----------------------------------------------------|--------------------------------------------|--------------------------------------------|---------|
| Patients (n = 40)                                   | 26                                        | 14                                        |         |
| Age (y)                                             | 62.5 (50–78)                               | 65 (47–84)                                 | .7*     |
| Prostate volume                                     |                                            |                                            |         |
| ≤40 mL                                              | 14 (53.8)                                  | 3 (21.4)                                  | .04†    |
| >40 mL                                              | 12 (46.2)                                  | 11 (78.6)                                 |         |
| PSA (ng/mL)                                         | 5 (2.7–11)                                 | 5 (2–15)                                  | .1      |
| Presence of inflammation                           | 7 (26.9)                                   | 6 (42.9)                                  | .45†    |
| Gleason score                                       |                                            |                                            |         |
| 3 + 3 = 6                                          | 9 (34.6)                                   |                                            |         |
| 3 + 4 = 7                                          | 13 (50.0)                                  |                                            |         |
| 4 + 3 = 7                                          | 2 (7.7)                                    |                                            |         |
| 4 + 4 = 8                                          | 1 (3.8)                                    |                                            |         |
| 4 + 5 = 9                                          | 1 (3.8)                                    |                                            |         |
| Interval between transrectal US and MRI-guided biopsy‡ | 11 (4–16)                                  | 8.5 (6.2–18.7)                            | .7§     |
| No. of targets per patient                         | 3.5 (1–7)                                  | 5.5 (1–9)                                 | .1§     |
| Lesions visible at MRI (n = 57)                    | 30                                        | 27                                        |         |
| Lesion size (mm)                                    |                                            |                                            |         |
| ≤10                                                 | 7 (23)                                     | 7 (25.9)                                  | .5†     |
| 11–20                                               | 17 (56.7)                                  | 16 (59)                                   |         |
| >20                                                 | 6 (27.3)                                   | 4 (14.8)                                  |         |
| Lesion location                                     |                                            |                                            |         |
| Right lobe                                          | 16 (53.3)                                  | 12 (44.4)                                 | .5†     |
| Left lobe                                           | 14 (46.7)                                  | 15 (55.6)                                 |         |
| Peripheral                                          | 18 (60)                                    | 16 (59.3)                                 | .5†     |
| Central                                             | 12 (40)                                    | 11 (40.7)                                 |         |
| Apex                                                | 7 (23.3)                                   | 1 (3.7)                                   | .06†    |
| Mid                                                 | 16 (53.3)                                  | 14 (51.9)                                 |         |
| Base                                                | 7 (23.3)                                   | 12 (44.4)                                 |         |
| Anterior gland                                      | 10 (33.3)                                  | 2 (7.4)                                   | .01†    |
| Level of suspicion on the basis of multiparametric MRI |                                            |                                            |         |
| Low                                                 | 10 (45.5)                                  | 10 (40)                                   | .3†     |
| Intermediate                                        | 3 (13.6)                                   | 6 (20)                                    |         |
| High                                                | 17 (40.9)                                  | 11 (40)                                   |         |
| No. of cores                                        | 3 (2–4)                                    | 3 (1–6)                                   | .9§     |

Note.—All values are median with range in parentheses or number with percentage in parentheses unless otherwise specified. PSA = prostate-specific antigen.
* Fisher exact test performed.
† Mann-Whitney U test performed.
‡ The median (interquartile range) is shown for the interval between transrectal US and in-bore MRI-guided biopsy.
§ Independent t test performed.

**GS Change by In-Bore MRI-guided Biopsy**

**Overall disease.**—In-bore MRI-guided biopsy upgraded whole disease (overall disease upgrade) in 40% of all patients (16 of 40; 95% confidence interval: 24.8%, 55%; 61.5% [16 of 26] of patients with positive in-bore MRI-guided biopsy results) (Table 2). These upgrades resulted from the upgrade of individual lesions previously detected at transrectal US-guided biopsy (62.5% [10 of 16]), the detection of new lesions at in-bore MRI-guided biopsy that were not detected at transrectal US-guided biopsy (12.5% [two of 16]), or both (25% [four of 16]). Out of patients with GG 1 disease at transrectal US-guided biopsy, in-bore MRI-guided biopsy upgraded the disease in 39.3% (13 of 33; 95% confidence interval: 22.7%, 56%) to greater than or equal to GG 2.
Matching disease grades from both transrectal US–guided biopsy and in-bore MRI-guided biopsy results were found in 22.5% (nine of 40) of patients. Eight patients had a GS of 6 (GG 1), and one patient had a GS of 3 + 4 = 7 (GG 2). One patient’s disease was downgraded on the basis of the in-bore MRI-guided biopsy results and lesion size, other lesion locations, suspicion of PCa on TRUS images, and histopathologic assessment had no association with false-negative in-bore MRI-guided biopsy results (P = .05). No association was detected between false-negative in-bore MRI-guided biopsy results and lesion size, other lesion locations, suspicion level as demonstrated at multiparametric MRI, number of cores obtained, or interval between transrectal US–guided biopsy and in-bore MRI-guided biopsy (P > .05).

**Individual lesions.**—In-bore MRI-guided biopsy upgraded 60% (18 of 30) of individual lesions (Table 3): 36.7% (11 of 30) of lesions had matching GGS with transrectal US–guided biopsy results. There were no differences between the upgraded and matching lesions regarding lesion location or the time interval between transrectal US–guided biopsy and in-bore MRI-guided biopsy (P > .05). In-bore MRI-guided biopsy downgraded one lesion (3.3% [one of 30]) from a GS of 3 + 4 = 7 (GG 2) to a GS of 3 + 3 = 6 (GG 1). Most of the upgraded lesions had a GS of 3 + 3 = 6 (83.4% [15 of 18]), with a majority of them (93.3% [14 of 15]) upgraded to a GS of 3 + 4 = 7 (median cancer-core percentage length, 45%; range, 59%–90%). Two lesions with a GS of 3 + 4 = 7 on transrectal US–guided biopsy were upgraded to a GS of 4 + 3 = 7 (median cancer-core percentage lengths of 60% and 70%), and one lesion with a GS of 4 + 3 = 7 on transrectal US–guided biopsy was upgraded to a GS of 4 + 4 = 8 (median cancer-core percentage length, 5%).

### False-Negative In-Bore MRI-guided Biopsy Results

The false-negative rate for in-bore MRI-guided biopsy was 35% (14 of 40; 95% confidence interval: 20.2%, 49.8%). Lesions missed when using in-bore MRI-guided biopsy were predominantly low-risk disease. Of patients with false-negative results, 85.7% (12 of 14) had a GS of 3 + 3 = 6 (GG 1) and 14.3% (two of 14) had a GS of 3 + 4 = 7 (GG 2). For transrectal US–guided biopsy sextants with corresponding targets depicted on MR images, the use of in-bore MRI-guided biopsy resulted in missing 47.4% (27 of 57) of lesions in total, with

### Predictors of False-Negative In-Bore MRI-guided Biopsy Results

Regarding the factors that may be associated with false-negative in-bore MRI-guided biopsy results, 20% (14 of 71) of sextants detected by using transrectal US–guided biopsy were not depicted on multiparametric MR images. Of these, 92.9% (13 of 14) of lesions had a GS of 3 + 3 = 6 (GG 1) and 7.1% (one of 14) had a GS of 3 + 4 = 7 (GG 2). Patients with prostate volumes greater than 40 mL had more false-negative in-bore MRI-guided biopsy results (P = .04). The false-negative rate was lower for lesions in anterior gland locations (16.7% [two of 12]; P = .01). Anterior gland lesions showed a higher CDR (83.3% [10 of 12]). The presence of prostate inflammation at histopathologic assessment had no association with false-negative in-bore MRI-guided biopsy results (P > .05). No association was detected between false-negative in-bore MRI-guided biopsy results and lesion size, other lesion locations, suspicion level as demonstrated at multiparametric MRI, number of cores obtained, or interval between transrectal US–guided biopsy and in-bore MRI-guided biopsy (P > .05).

### Table 2: Overall Disease Upgrade after In-Bore MRI-guided Biopsy

| GS from In-Bore MRI-guided Biopsy Results | GS from Transrectal US–guided Biopsy Results |
|------------------------------------------|---------------------------------------------|
| 3 + 3 = 6 (GG 1)                         | 3 + 3 = 6 (GG 1)                            |
| 3 + 4 = 7 (GG 2)                         | 3 + 4 = 7 (GG 2)                            |
| 4 + 3 = 7 (GG 3)                         | 4 + 3 = 7 (GG 3)                            |

Note.—A total of 16 patients had disease upgrade after undergoing in-bore MRI-guided biopsy. Data are numbers of patients with an upgrade, with percentages in parentheses. The data include results from actual lesion upgrades and newly discovered lesions at MRI-guided biopsy. GG = grade group, GS = Gleason score.

### Table 3: Gleason Scores and Locations of Lesions Upgraded after In-Bore MRI-guided Biopsy

| GS from In-Bore MRI-guided Biopsy Results | GS from Transrectal US–guided Biopsy Results |
|------------------------------------------|---------------------------------------------|
| 3 + 3 = 6 (GG 1)                         | 3 + 3 = 6 (GG 1)                            |
| 3 + 4 = 7 (GG 2)                         | 3 + 4 = 7 (GG 2)                            |
| 4 + 3 = 7 (GG 3)                         | 4 + 3 = 7 (GG 3)                            |

Note.—A total of 18 lesions were upgraded. Data are numbers of lesions with an upgrade, with percentages in parentheses. The locations of lesions with upgraded scores were as follows: 50% (nine of 18) in the peripheral zone and 50% (nine of 18) in the central gland; 61.6% (11 of 18) in the right lobe and 38.9% (seven of 18) in the left lobe; and 22.2% (four of 18) in the apex, 44.4% (nine of 18) in the peripheral zone and 50% (nine of 18) in the central gland; 61.6% (11 of 18) in the anterior gland. GG = grade group, GS = Gleason score.
Newly Detected Lesions at In-Bore MRI-guided Biopsy

In-bore MRI-guided biopsy detected 14 previously undiscovered cancers that were not detected using transrectal US-guided biopsy, with 42.9% (six of 14) having a GS of 3 + 3 = 6 (GG 1), 42.9% (six of 14) having a GS of 3 + 4 = 7 (GG 2), 7.1% (one of 14) having a GS of 4 + 3 = 7 (GG 3), and 7.1% (one of 14) having a GS of 4 + 5 = 9 (GG 5). The GG 5 lesion was seen in the seminal vesicle in a patient who has been previously diagnosed with GG 2 disease using transrectal US-guided biopsy. The newly detected lesion locations are illustrated in Table E2 (supplement).

Discussion

In this study, we sought to evaluate the impact of complementary in-bore MRI-guided biopsy in patients diagnosed with low- or intermediate-risk disease by transrectal US-guided biopsy results on disease-risk stratification and the optimal management decision, while also evaluating the rate of missing cancers and predictors for missing cancers. The overall CDR when using in-bore MRI-guided biopsy in our study was 69%, in accordance with findings of other studies (18,25,26). Hu et al (18) reported a 66.4% CDR from using confirmatory MRI/US–fusion biopsy in patients with low-risk disease at transrectal US-guided biopsy. In a similar population, using in-bore biopsy, Hoeks et al (26) detected cancers in 52.7% of patients 3 months after the initial transrectal US-guided biopsy.

Patients with limited low- or intermediate-risk disease may elect to undergo active surveillance or choose focal therapy as a treatment option. It is crucial for these decisions to be based on reliable disease-risk assessment. We report an overall disease-upgrade rate of 40% (16 of 40) when using in-bore MRI-guided biopsy (61.5% [16 of 26] of patients with positive in-bore MRI-guided biopsy results; Table 3), prompting substantial changes in transrectal US-guided biopsy–based management plans by disqualifying this cohort of patients from continued active surveillance or from candidacy for focal therapy. Most of the upgrades were due to a GS upgrade of previously detected cancers. These results suggest the clearly added benefit of performing confirmatory in-bore MRI-guided biopsy over repeat transrectal US-guided biopsy. Berglund et al (27) reported a 27% upgrade rate as a result of repeat transrectal US-guided biopsy results for patients undergoing active surveillance. Similarly, King et al (28) reported an even lower upgrade rate of 17% as a result of repeat transrectal US–guided biopsy results. More importantly, the implementation of MRI-guided biopsy of regions suspected of being cancerous has resulted in detection of predominantly (87–93%) clinically significant prostate cancer (12,29), whereas the use of repeat transrectal US biopsy resulted in an estimated detection of 56% of CSCs (30).

Our results are consistent with those of other studies including similar populations (31,32). Tan et al (31) reported an upgrade rate using 3-T in-bore biopsy of 36.7%. Similarly, Felker et al (32) reported a patient upgrade rate of 33.7% (27 of 80). On the contrary, Hu et al (18) showed a rate of 23% (26 of 113) for upgrading GS 6 disease to GS greater than or equal to 7 when using confirmatory MRI/US–fusion biopsy. It is possible that in-bore MRI-guided biopsy might eliminate the potential error due to misregistration of targets at MRI/US–fusion biopsy. However, this notion needs to be evaluated in a controlled setting, probably using a randomized controlled clinical trial.

In this cohort, multiparametric MRI– and in-bore MRI-guided biopsy enabled detection of additional disease foci not previously detected using transrectal US–guided biopsy (Fig 2). A total of approximately 57% (eight of 14) of the cancers newly detected using in-bore MRI-guided biopsy were CSCs. Felker et al (32) reported a higher incidence of CSCs (81%) detected using in-bore MRI-guided biopsy that were not detected at a prior transrectal US–guided biopsy. This difference is likely because they targeted lesions with at least moderate suspicion, whereas we included low-suspicion targets as well.

An important strength of in-bore MRI-guided biopsy over transrectal US–guided biopsy is its ability to detect targets extending outside the prostate gland confines. One patient in our cohort was diagnosed with prostate cancer with a GS of 3 + 4 = 7 on transrectal US–guided biopsy. In-bore MRI-guided biopsy

Table E2: Table E2: A 78-year-old man with prostate cancer undergoing active surveillance had a Gleason score (GS) of 3 + 3 = 6 (grade group 1) based on the results of a prior transrectal US–guided biopsy. Multiparametric MR images (left to right: axial T2-weighted, diffusion-weighted, and ADC) depict a lesion (arrows) in the anterior gland at 12:00–1:00 o’clock that was not detected at the prior transrectal US–guided biopsy (arrows). In-bore MRI-guided biopsy was performed, resulting in a GS of 3 + 4 = 7.

Figure 2: Figure 2: A 78-year-old man with prostate cancer undergoing active surveillance had a Gleason score (GS) of 3 + 3 = 6 (grade group 1) based on the results of a prior transrectal US–guided biopsy. Multiparametric MR images (left to right: axial T2-weighted, diffusion-weighted, and ADC) depict a lesion (arrows) in the anterior gland at 12:00–1:00 o’clock that was not detected at the prior transrectal US–guided biopsy (arrows). In-bore MRI-guided biopsy was performed, resulting in a GS of 3 + 4 = 7.
Elfatairy et al detected additional infiltrative disease into the seminal vesicle, and the GS was upgraded to 4 + 5 = 9 (Fig 3).

Although the use of in-bore MRI-guided biopsy resulted in missing cancer in a large proportion of patients (false-negative rate, 35%), most of these patients had clinically insignificant cancers (GS of 3 + 3 = 6 [GG 1]; 85.7%). The reasons for missing cancers when using in-bore MRI-guided biopsy in this study can be summarized as either nondepiction of lesions on multiparametric MR images altogether, patient and/or lesion factors, or an inherent targeting error of the in-bore MRI-guided biopsy itself. A total of 20% of cancerous foci diagnosed by transrectal US–guided biopsy in this study had no corresponding visible targets on multiparametric MR images. Most of them had a GS of 3 + 3 = 6 (GG 1) (92.9%; 13 of 14). This corroborates earlier reports of a relatively high negative predictive value for using multiparametric MRI and in-bore MRI-guided biopsy to detect CSCs with GSs greater than or equal to 7 (32–34). The Prostate MRI Imaging Study (PROMIS) trial results showed that use of multiparametric MRI has a higher negative predictive value compared to using transrectal US–guided biopsy (for any GS $\geq 3 + 4 = 7$, 76% vs 63%; $P < .0001$) (33). Wysock et al (34) reported a negative predictive value of 81.3% for using multiparametric MRI to detect all cancers and a negative predicted value of 98.7% for using multiparametric MRI to detect disease with a GS greater than or equal to 7. Felker et al (32) showed that only 5% of lesions missed by using in-bore MRI-guided biopsy and detected by using transrectal US–guided biopsy were CSCs.

For factors related to patients, prostate volumes of more than 40 mL were associated with a lower CDR and yielded more false-negative results than did prostate volumes less than or equal to 40 mL ($P = .007$). Schimmöller et al (35) reported similarly high CDRs in prostate volumes of less than 30 mL. We did not find an association between the presence of inflammation and false-negative in-bore MRI-guided biopsy results. This contradicts an earlier report by Itatani et al (36) which suggested missing cancer when using multiparametric MRI could be due to the presence of prostatitis. They, however, used a lower-field scanner (1.5 T) for multiparametric MRI and used transrectal US–guided biopsy for tissue sampling.

For factors related to lesions, anterior lesion location was associated with a higher CDR (83.3%) and a lower false-negative rate (16.7%; $P = .01$). This is consistent with a prior report illustrating the preferential detection of anterior gland lesions using in-bore MRI-guided biopsy (37). Otherwise, we did not find an association between false-negative in-bore MRI-guided biopsy results and lesion sizes (largest diameter), other lesion locations, suspicion level at MRI, or number of biopsy cores obtained. Schimmöller et al (35), however, found that larger tumor sizes were associated with a higher detection rate when using in-bore MRI-guided biopsy.

An important issue to be addressed is the inherent targeting error of in-bore MRI-guided biopsy. Cash et al (20) reported that sources of error during MRI/US–fusion biopsy were due to prostate displacement or deformation with probe placement, patient movement, image misregistration, sampling error, discrepancy between imaged lesion size and true size (using MRI causes underestimation of the lesion size), and multiparametric MRI interpretation errors (20,38). We think that some of the aforementioned factors may apply to in-bore MRI-guided biopsy. For instance, during in-bore MRI-guided biopsy, we noticed...
that needle-sleeve placement causes deformation and displacement of the prostate and can cause tissue compression, distorting diffusion-weighted images and potentially masking targets at the posterior aspect of the gland. Needle-placement errors were previously tested on phantoms in both 3-T and 1.5-T systems with estimated placement errors of 2.5–3 mm (39,40) and in clinical settings with an average placement error of 5.4 mm. In our study, needle-placement errors were largely circumvented by acquiring confirmation images of needle locations relative to targets prior to sampling and by obtaining two to four cores from each lesion at 1- to 3-mm intervals to ensure adequate representation of sampled targets.

Our study limitations included inevitable potential selection bias owing to the retrospective nature of this analysis with a subset of patients in whom urologists were already concerned about the possibility of higher-risk disease. The limitations also included the lack of correlation with surgical pathologic findings and with the more widely available MRI/US–fusi...
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