Prostate cancer detection with magnetic resonance imaging (MRI)/cognitive fusion biopsy: Comparing standard and targeted prostate biopsy with final prostatectomy histology

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Abstract

Introduction: The use of multiparametric magnetic resonance imaging (MRI) with targeted biopsies of the prostate improves the diagnosis of clinically significant prostate cancer. Recent studies have shown that targeted prostate biopsies also more accurately predict final histopathology after radical prostatectomy (RP). There are three broad techniques for performing MRI-targeted prostate biopsy: cognitive MRI/ultrasound (US) fusion, software MRI/US fusion, and in-bore MRI-guided. Current practices recommend that a standard systematic 12-core prostate biopsy be performed, as well as targeted biopsies in patients with positive MRI findings. This study aimed to evaluate the accuracy of histological grading of cognitive MRI/US fusion prostate biopsy by comparing the histology from the targeted biopsy specimens (TB), standard systematic specimens (SB), and the combination of both (CB) specimens with the final histological grade from subsequent prostatectomy.

Methods: A retrospective, single-center review of 115 patients who underwent standard systematic and cognitive MRI/US-targeted biopsy of the prostate before undergoing a RP between 2016 and 2019 was performed. MRI findings, biopsy, final histology International Society of Urological Pathology (ISUP) grades, and patient demographics were collected. Cochran's Q test and McNemar test were used to compare the differences in upgrading, downgrading, and concordance between each biopsy group.

Results: The concordance between SB, TB, and CB biopsy were 28.7%, 49.6%, and 50.4%, respectively. There was no significant difference in concordance between TB and CB. Patients were more likely to be downgraded on the final histology when comparing CB with TB alone (26.1% vs. 16.5%, $p<0.05$). In cases where an ISUP grade 1 cancer was diagnosed on TB (n=24), there was a 62.5% chance that the final histology would be upgraded. In the same sample, when combined with a SB, the risk of upgrading on final histology was reduced to 37.5%.

Conclusions: Although grading concordance between TB and CB were similar, the concomitant use of a SB significantly reduced the rate of upgrading in the final RP histopathology. CB may result in better decision-making regarding treatment options and also have implications for intraoperative planning.

Introduction

Prostate cancer is the most common malignancy diagnosed in men;[1] it is estimated that one in seven men will be diagnosed with the disease during their lifetime.[2] Men with a clinical suspicion of prostate cancer based on a high prostate-specific antigen (PSA) or abnormal digital rectal examination (DRE) would traditionally be offered a standard transrectal ultrasound-guided biopsy of the prostate. This approach has led to the under-detection of clinically significant prostate cancer and the overdiagnosis of clinically insignificant cancer, resulting in either over-treatment or repeated investigations under active surveillance.[3]

Studies have shown that multiparametric magnetic resonance imaging (mpMRI) combined with MRI-targeted biopsy improves the detection of clinically significant prostate cancer and reduces the likelihood of detecting a clinically insignificant cancer.[4,5] There are three broad techniques for performing MRI-targeted prostate biopsy: cognitive MRI/ultrasound (US) fusion, software MRI/US fusion, and in-bore MRI-guided. The cognitive fusion approach requires the physician to review the MRI and cognitively register the location of the suspected lesion on US and guide the biopsy gun towards the target. The software MRI/US fusion technology fuses the MRI picture with the images in real time on the US probe. The in-bore MRI-guided technique uses MRI compatible biopsy tools, however, this is imilted by availability and cost. All of these techniques seem to yield similar results in the detection of clinically significant cancer.[6-8]

Concomitant standard biopsies are still recommended to reduce the risk of missing targeted areas of interest and the significant risk of false-negatives on mpMRI.[9] There is strong evidence to suggest the improvement in the detec-

tion of clinically significant prostate cancer when combining standard and MRI-targeted biopsy.[10-13]Gleason score (GS) remains one of the most valuable prognostic factors and a vital part in determining the best choice of treatment. If the patient chooses to proceed with surgery, GS also plays an important role in determining the need for a lymph node dissection and also suitability for a nerve-sparing procedure, which is a key factor in maintaining potency postoperatively.[14] Therefore, improving the concordance of prostate biopsies with final radical prostatectomy (RP) specimens will likely improve the functional and oncological outcomes for patients. A large meta-analysis highlighted the limited concordance between standard prostate biopsies and final histological grade, approximately 60%, with histology upgraded in 30% of cases and downgraded in 10% of cases.[15] The concordance of MRI-targeted biopsies and final histology has been shown to be anywhere from 60–90%;[10,16-18] no study to date has evaluated the correlation of cognitive MRI/US fusion targeted biopsy and standard biopsy with the final RP specimen.

Therefore, the aim of this study was to evaluate the accuracy of histological grading of cognitive MRI/US fusion targeted biopsy and standard biopsy with the final histological grade obtained from subsequent RP.

Methods

A retrospective, single-center study was carried out. A review of 362 patients who underwent a cognitive MRI/US fusion targeted prostate biopsy between 2016 and 2019 was performed. Patients who subsequently proceeded to RP (115 of the 362) were included in the study. Patient demographics, radiological and histological data were collected on all patients.

Patients were referred to the rapid access prostate cancer clinic as per the National Cancer Control Program guideline.[19] After consultation with a consultant urologist, patients were either referred directly for a standard prostate biopsy, mpMRI, or close PSA surveillance. All patients who underwent pre-biopsy mpMRI were performed on a 1.5 T MRI scanner (Siemens Magnetom Avanto). During this study period, there was also a large scale international change in approach to prostate cancer diagnostics. Previously mpMRI was only performed in the setting of a negative prostate biopsy or prior to commencing active surveillance. However, since 2018 all men with a clinical suspicion of localized prostate cancer underwent pre-biopsy mpMRI in keeping with the latest guidelines.[9,20] The mpMRI protocol followed Prostate Imaging Reporting & Data System (PI-RADS) guidelines with T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences. The mpMRI images were reported by senior radiologists with subspecialist experience in prostate MRI and assigned a PI-RADS score.[21] Patients with a PI-RADS score of 3 or greater subsequently proceeded to transrectal ultrasound (TRUS)-guided prostate biopsy, with a combination of standard systematic 12-core biopsy and cognitive MRI/US fusion targeted biopsy being performed in all patients. The biopsies were performed exclusively by four radiologists who reviewed the MRI prior to performing the biopsies. A minimum of two cores were taken for each targeted lesion, followed by a standard 12-core biopsy. The indication for RP was taken in line with European Association of Urology (EAU) guidelines. All RPs were performed either with an open approach or robotic-assisted laparoscopic approach by experienced urologists.

Biopsy and RP specimens were assessed by two highly experienced uro-pathologists and all specimens were discussed at a multidisciplinary team meeting. Where there was discrepancy, the specimen was reviewed at a pathologists' departmental meeting. For the targeted biopsy specimens (TB), standard systematic specimens (SB), and the combination of both (CB) specimens, the overall grade was based on the highest GS achieved in each biopsy. The results of these biopsies were compared to the GS of the RP specimen. Gleason scores were reported in concordance with the International Society of Urological Pathology (ISUP) guidelines.[22] Gleason scores were reported as groups 1–5 and significant prostate cancer was defined by an ISUP grade ≥2.

Data was exported to Minitab for analysis and statistical significance was considered at $p < 0.05$. Cochran's Q test was used to test for the difference in concordance, upgrading, and downgrading with final histology between SB, TB, and CB. McNemar test was used to compare difference in concordance between each biopsy group head-to-head. Qualitative data was tested with the Fischer exact test and continuous data was tested with the Student t-test.

Results

Patient demographics, radiological findings, and number of biopsies performed are shown in Table 1. The mean prostate volume was 39.4 cc. mpMRI identified a single index lesion with a PI-RADS score of 3 in 13.9% (n=16) of cases, 4 in 52.1% (n=60) of cases, and 5 in 23.5% (n=27) of cases. Of note, a PI-RADS score was not assigned for 12 patients (10.5%) — these MRIs were performed prior to PI-RADS becoming a standard reporting requirement.

The overall ISUP grade for SB, TB, and CB, as well as the ISUP grade of the final RP specimen are shown in Table 2. This table highlights the significant number of ISUP grade 1 cancers diagnosed in the SB group compared to the TB or CB groups (41.7% [n=48]) vs. 20.8% [n=24] vs. 14.8% [(n=17], respectively, $p<0.05$). The final pathological stage from the radical prostatectomy specimen is shown in Fig. 1.

Figs. 2 and 3 show the grading concordance rates between TB, SB, CB, and RP grades in all specimens, as well as in specimens with ISUP >1 on final RP histology, respectively.

Table 1. Patient demographics	
Age, mean, years	62.7 (51–74)
PSA, mean, ng/ml	7.43 (1.5–19.7)
Prostate volume, mean, cc	39.4 (14–147)
Number of target lesions	
1	91 (79.1%)
2	17 (14.8%)
3	4 (3.5%)
4	1 (0.8%)
PI-RADS score	
3	16 (13.9%)
4	60 (52.2%)
5	27 (23.5%)
Unknown	12 (10.4%)
Mean target lesion size, mm	12.13 (5–30)
Mean number of target cores	4.6 (2–7)
Mean number of standard cores	12 (12)

PI-RADS: Prostate Imaging Reporting & Data System; PSA: prostate-specific antigen.

The concordance rate was significantly lower with SB (26%) compared to the TB (46.1%) and CB (48.1%). Cochran's Q test was used to test the difference between the three groups. This test highlighted a statistically significant difference in all categories whether it was for concordance ($p<0.001$), upgrading ($p<0.001$), or downgrading ($p<0.001$). McNemar test was performed to compare each group head-to-head. Again, the difference was statistically significant between all groups in terms of upgrading and downgrading with final histology specimen. The TB and CB groups were concordant ($p=0.32$) due to the fact that the TB grade is often the highest-grade lesion and therefore will determine the CB grade. The upgrading rate in RP specimens decreased by 9.6% when SB was combined with TB. in the CB group, 33.1% of cases were downgraded on final RP specimens.

PI-RADS 4 and 5 lesions had a similar level of concordance between target biopsy and final RP histology compared to PIRADs 3 lesions (53.3% vs. 55.6% vs. 37.5%, $p<0.05$). There were similar levels of upgrading and downgrading of targeted biopsies with final RP specimen histology in PIRADS 4 and 5 lesions, respectively, 28.3% vs. 26% and 18.3% vs. 18.5%.

A subgroup analysis of TB specimens including only ISUP grade 1 (n=24) showed that there was a significant increase in upgrading on final RP histology in this group (62.5%, n=15). However, the addition of standard systematic 12-core biopsy resulted in a significant decrease in the rate of upgrading in the final RP specimen in this group (37.5%, n=9 vs. 62.5%, n=15). If all ISUP grade 1 specimens are excluded from the targeted biopsy cohort, concordance remained similar (52.7%, n=48), while there was a significant decrease in the rate of upgrading in final RP histology (13.6%, n=15).

Table 2. ISUP grades of SB, TB, SB + TB biopsies and final RP specimen				
ISUP grade	Standard	Target	Combined	RP specimen
Negative	5 (4.3%)	2 (1.7%)	–	–
1	48 (41.7%)	24 (20.9%)	18 (15.6%)	11 (9.6%)
2	20 (17.4%)	37 (32.2%)	35 (30.4%)	55 (47.8%)
3	17 (14.8%)	29 (25.2%)	29 (25.2%)	36 (31.3%)
4	19 (16.6%)	18 (15.6%)	22 (19.2%)	6 (5.2%)
5	6 (5.2%)	5 (4.4%)	11 (9.6%)	7 (6.1%)

ISUP: International Society of Urological Pathology; RP: radical prostatectomy; SB: standard systematic specimens; TB: targeted biopsy specimens.

Discussion

The literature has demonstrated the benefit of MRI to detect clinically significant prostate cancer compared to traditional TRUS-guided, standard, 12-core prostate biopsy. The PRECISION trial showed that pre-biopsy MRI, with or without target biopsy, led to fewer men undergoing biopsy, more clinically significant cancers being diagnosed and less over-detection of clinically insignificant cancers.[5] Many studies have shown that MRI-targeted biopsy has an improved detection rate for clinically significant prostate cancer and better concordance with prostatectomy compared to standard TRUS biopsy.[17,18,23] Current EAU guidelines recommend mpMRI prior to biopsy in men with a clinical suspicion of prostate cancer either based off an elevated PSA or abnormal DRE.[24] The findings in this study further support the benefit of pre-biopsy MRI in the diagnostic pathway of men with a clinical suspicion of prostate cancer.In our study, TB identified clinically significant cancer in 77.4% (n=89) of cases. SB diagnosed ISUP grade 1 cancers far more frequently compared to TB. In this sample, we found

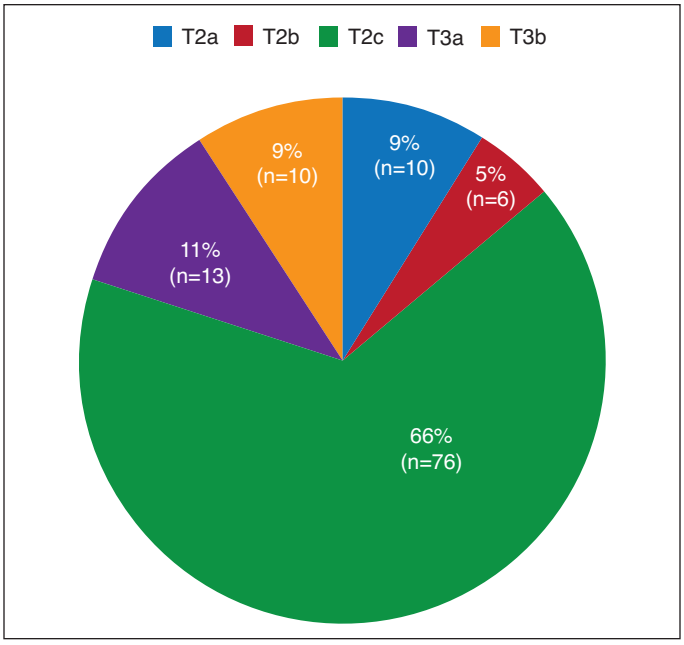

Fig. 1. Final pathological stage in the radical prostatectomy specimen.

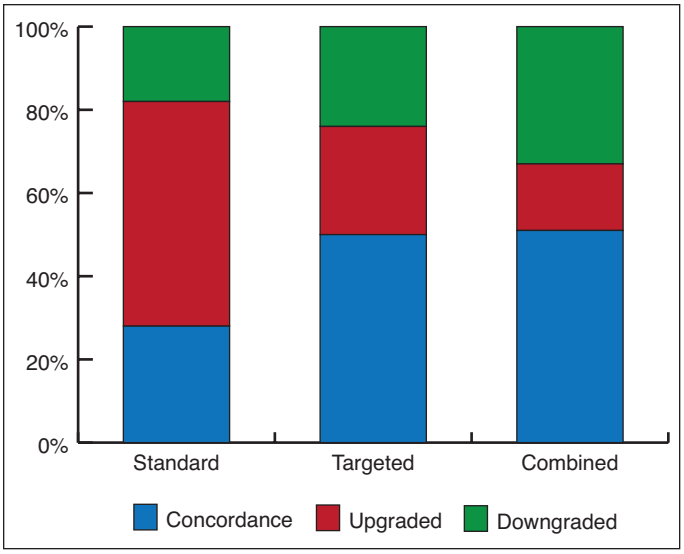

Fig. 2. Rates of concordance, upgrading and downgrading with final radical prostatectomy specimen by standard systematic specimens (SB), targeted biopsy specimens (TB), and combined biopsy specimens (CB).

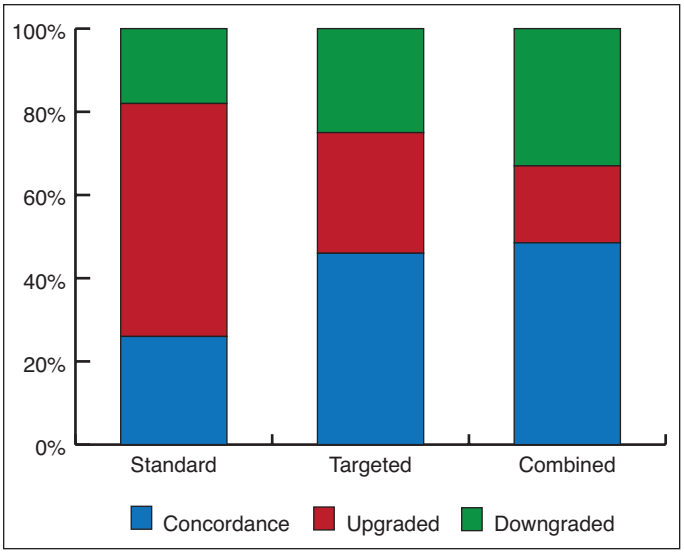

Fig. 3. Rates of concordance, upgrading, and downgrading with final radical prostatectomy (RP) specimen by standard systematic specimens (SB), targeted biopsy specimens (TB), and combined biopsy specimens (CB) in patients with final RP histology International Society of Urological Pathology (ISUP) grade >1 (n=104).

a significant difference in concordance with the final histology at prostatectomy between TB and SB. This finding is in contrast to a study by Diamand et al that suggested that concordance between standard and target biopsy with final RP histology was similar (49.4% vs. 51.2%).[16] Diamand et al performed a large retrospective study reviewing 443 patients who had positive MRI findings who underwent MRI/fusion target biopsy and RP to compare SB, TB, and CB with final RP histology. Concordance in ISUP grade between SB, TB, and CB was 49.4%, 51.2%, and 63.2%, respectively. This paper also found that the addition of SB combined with TB significantly increased concordance with final RP histology.[16] Our results further confirm that the MRI-guided pathway with targeted biopsy outperforms standard biopsy alone in the investigation of men with a clinical suspicion of prostate cancer.

The level of concordance with cognitive fusion targeted biopsy in this study is similar to other studies examining MRI/US fusion technology or in-bore MRI-targeted biopsy techniques.[10,16] Puech et al compared cognitive fusion vs. MRI/US fusion targeted biopsy and found no difference in cancer detection rate.[25] Wysock et al also demonstrated that overall cancer detection rate was similar between the above biopsy techniques.[26] However both studies were limited, as they did not include RP specimens as a standard. This suggests that the cognitive fusion technique used in TB is comparable to other techniques in predicting grade group concordance with final RP histology. TB also resulted in fewer ISUP grade 1 cancers being diagnosed compared to standard biopsy.

There are also questions regarding the benefit of concomitant SB, given that TB should accurately biopsy the index lesion, leading to a prediction of the final RP histology. The use of SB may result in the diagnosis of clinically insignificant prostate cancer, leading to over-treatment or costly/invasive active surveillance programs. Recent large, multicenter studies have examined the benefit of concomitant standard biopsy in patients with positive MRI findings to predict final RP histology and found there was a significant improvement in grading concordance by adding SB.[10,11,16] Ploussard et al compared grade group concordance of software MRI/US fusion target biopsy, systematic 10-core biopsy, and RP histology in 478 consecutive patients who had positive MRI imaging. Concordance between TB and CB histology and final RP histology was 45.2% and 51.7%, respectively. They found that grade group concordance between biopsy and final RP histology improved with the addition of a systematic biopsy. SB also reclassified a small number of cases towards a higher-risk category and, therefore, concluded that systematic biopsy could alter treatment decision-making. In our study, in ISUP grade 1 cancers (n=24) that were diagnosed on targeted biopsy, the concomitant use of a SB upgraded the histology in 29.1% (n=7) of cases. In this subgroup, 62.5% (n=15) of TB were upgraded on final RP histology, compared to 37.5% (n=9) when combined with a SB.

In our study, we found a similar level of concordance between TB and CB biopsy with final RP histology. However, with the concomitant use of a standard biopsy, the level of upgrading in final RP specimen histology reduced significantly compared to TB alone.

These findings suggest that TB and CB concordance with final RP histology are very similar, however, there is a higher chance that final RP histology will be upgraded when compared with TB alone vs. CB. Ploussard et al revealed similar results, with upgrading on final histo-pathology decreasing

by 22% when combining both target and standard biopsy histology.[10]

To our knowledge, this is the largest study comparing cognitive MRI/US fusion targeted biopsy and final RP specimen histology. However, several limitations should be highlighted. This was a single-center, retrospective review that only included patients with abnormal MRI findings who went on to have a RP. Patients who went on to an active surveillance regimen or radiotherapy were not included in the study. There was also some heterogeneity in the MRI data, especially in cases where the MRI was performed in an outside center. Finally, some of the MRIs (n=12) performed earlier in the study cohort did not have an assigned PI-RADS score, as these were performed prior to PI-RADS scoring becoming standard practice.

Conclusions

This study further supports the image-guided pathway with MRI ± targeted biopsy in men with a clinical suspicion of prostate cancer. Although grading concordance between TB and CB were similar, the concomitant use of a SB significantly reduced the rate of upgrading in final RP histopathology. CB may result in better decision-making regarding treatment options and also have implications for intraoperative planning. Prospective, multicenter trials will need to explore this topic further before SB is excluded in patients with positive MRI findings.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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