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ABDOMINAL IMAGING

ORIGINAL ARTICLE

MRI/US fusion-guided prostate biopsy allows for equivalent cancer detection with significantly fewer needle cores in biopsy-naive men

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PURPOSE
We aimed to investigate the efficiency and cancer detection of magnetic resonance imaging (MRI) / ultrasonography (US) fusion-guided prostate biopsy in a cohort of biopsy-naive men compared with standard-of-care systematic extended sextant transrectal ultrasonography (TRUS)-guided biopsy.

METHODS
From 2014 to 2016, 72 biopsy-naive men referred for initial prostate cancer evaluation who underwent MRI of the prostate were prospectively evaluated. Retrospective review was performed on 69 patients with lesions suspicious for malignancy who underwent MRI/US fusion-guided biopsy in addition to systematic extended sextant biopsy. Biometric, imaging, and pathology data from both the MRI-targeted biopsies and systematic biopsies were analyzed and compared.

RESULTS
There were no significant differences in overall prostate cancer detection when comparing MRI-targeted biopsies to standard systematic biopsies ($P = 0.39$). Furthermore, there were no significant differences in the distribution of severity of cancers based on grade groups in cases with cancer detection ($P = 0.68$). However, significantly fewer needle cores were taken during the MRI/US fusion-guided biopsy compared with systematic biopsy (63% less cores sampled, $P < 0.001$)

CONCLUSION
In biopsy-naive men, MRI/US fusion-guided prostate biopsy offers equal prostate cancer detection compared with systematic TRUS-guided biopsy with significantly fewer tissue cores using the targeted technique. This approach can potentially reduce morbidity in the future if used instead of systematic biopsy without sacrificing the ability to detect prostate cancer, particularly in cases with higher grade disease.

Prostate cancer remains the most common noncutaneous cancer diagnosis in American men. There is an estimated 180 890 patients diagnosed each year in the United States and a corresponding 9% cancer mortality (1). Soon after its discovery, prostate-specific antigen (PSA) became the most common test used in the algorithm of prostate cancer screening (2). Historically, standard practice for diagnosis of prostate cancer has been to perform a systematic 12-core, extended-sextant biopsy using transrectal ultrasonography (TRUS) guidance in patients with an elevated PSA. However, in 2012, the United States Preventive Services Task Force (USPSTF) made a recommendation against the use of widespread PSA screening. This was in part due to the morbidity associated with diagnosing and subsequently definitively treating cases of clinically-insignificant prostate cancer. This has led to a change in the demographics and level of prostate cancer aggressiveness detected in recent years (3).

As widespread PSA screening alone is no longer considered adequate and widely implemented into routine primary care cancer screening, adjunct measures have been studied for improving the screening and diagnosis of prostate cancer. Notable amongst these adjuncts is prostate multiparametric magnetic resonance imaging (MRI). The use of MRI findings in combination with serum PSA assessment has improved sensitivity and specificity

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in detecting clinically-significant prostate cancer (4–6). MRI/US fusion-guided biopsy has been shown to detect more cancer per biopsy core for lesions suspicious on MRI (7, 8). In addition, MRI/US fusion-guided biopsy has been shown to be effective in detecting prostate cancer in patients with clinical suspicion of prostate cancer despite history of prior negative 12-core systematic biopsy (9, 10). As such, the recent American Urological Association (AUA) and Society of Abdominal Radiology (SAR) Consensus Statement recommended the use of MRI-targeted prostate biopsy in men with suspicion of prostate cancer and prior negative systematic biopsy (11).

While there is a growing amount of data supporting the efficacy of MRI/US fusion-guided biopsy, the majority of studies have looked at all patients with suspicion of prostate cancer including its use in patients who are considering active surveillance (12, 13). To date, there have been limited studies comparing biopsy-naive patients who undergo MRI/US fusion-guided biopsy versus those who undergo systematic extended-sextant TRUS biopsy. The utilization of MRI in the earlier stages of prostate cancer screening offer the potential of avoiding unnecessary biopsies and their associated morbidity (14, 15). In this study, we demonstrate the utility of MRI/US fusion-guided prostate biopsy over traditional systematic 12-core, extended-sextant TRUS biopsy in patients who have not had a prior prostate biopsy.

Methods

This study was approved by our institutional review board. We retrospectively reviewed data from a prospectively maintained dataset of all men who underwent multiparametric MRI and MRI/US fusion-guided biopsy between 2014 and 2016 with clinical suspicion of prostate cancer based on elevated PSA (PSA >4 ng/mL) or abnormal finding on digital rectal examination. We excluded all men who had previous prostate biopsy history and those who did not have MRI-targeted biopsy and concurrent systematic TRUS-guided biopsy (Fig. 1).

All patients underwent MRI of the prostate utilizing a 3.0 Tesla MRI and a phased-array surface coil as previously described (16). MRIs were reviewed at a multidisciplinary prostate imaging conference attended by fellowship trained body radiologists and urologic oncologists trained in prostate MRI and MRI/US fusion-guided biopsy procedures, respectively. The two radiologists leading this conference have 10 and 4 years of prostate MRI experience, respectively. This multidisciplinary approach was utilized to achieve a consensus interpretation for each case identifying regions of interest concerning the prostate cancer. Lesions were assigned a PI-RADS v2.0 score at the setting of this multidisciplinary prostate imaging consensus conference (17). For cases predating the implementation of the second version of PI-RADS, all cases were retrospectively reassigned PI-RADS v.2.0 scores by a group of radiologists and urologic oncologists specialized in prostate MRI. Whole gland prostate volumes and lesions suspicious for harboring prostate cancer were segmented in three-dimensions using the DynaCAD post-image processing software (InVivo Corp).

Patients with lesions suspicious for malignancy were offered MRI/US fusion-guided biopsy in addition to standard systematic 12-core, extended-sextant TRUS-guided biopsy after providing informed consent. All lesions with PI-RADS score greater than or equal to 3 were targeted for biopsy. MRI/US fusion-guided biopsy was performed using the UroNav system (Philips/InVivo) in the previously described technique (7). Following targeted biopsy core sampling, a systematic 12-core, extended-sextant TRUS-guided biopsy was performed using freehand TRUS technique. The vast majority underwent 12-core sampling with two cores in each of two sextants defined as the apex, mid, and base regions of each of the right and left lobes of the gland. Due to patient discomfort some patients did not complete full 12-core sampling. As such, all patients who underwent less than 10 systematic cores were excluded from this study for not meeting guideline recommendations. All pathologic specimens were evaluated by a fellowship-trained, genitourinary-specialized surgical pathologist.

Main points

- There were no significant differences in overall prostate cancer detection when comparing MRI-targeted biopsies to standard systematic biopsies in biopsy-naive men.
- Significantly fewer needle cores were required with MRI/US fusion-guided biopsy compared with systematic biopsy in biopsy-naive men.
- In biopsy-naive men, MRI/US fusion-guided prostate biopsy approach can potentially reduce morbidity without sacrificing the ability to detect prostate cancer.

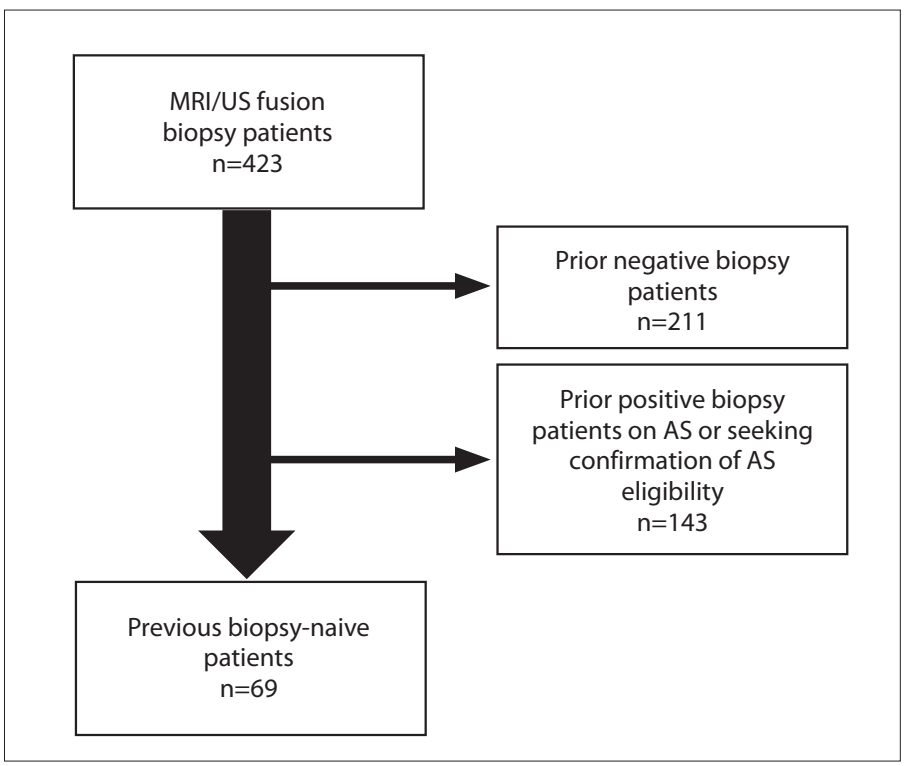

Figure 1. Flowchart for study inclusion. AS, active surveillance.

Statistical analysis

Univariate statistical analysis was performed using the t-test for continuous variables and Fisher's exact tests for categorical variables. A *P* value less 0.05 was considered significant and all tests were 2-tailed.

Results

Of 423 patients who underwent MRI/US fusion-guided biopsy over this time period, 69 biopsy-naive men who underwent both MRI/US fusion-guided biopsy and concurrent systematic 12-core, extended-sextant TRUS-guided biopsy were identified and their records reviewed. Three additional patients who were biopsy naive underwent multiparametric MRI based upon PSA elevation suspicion for prostate cancer, of whom two had MRI studies without areas of significant suspicion for harboring prostate cancer and one had a technically limited study which was non-diagnostic. Biometric and biopsy data are presented in Table 1. The average patient age was 64 years and the average PSA value at the time of biopsy was 7.71 ng/mL. Patients had an average of 1.97 lesions detected on MRI that were suspicious for prostate cancer. The average number of cores taken for MRI-targeted biopsies was 4.42 compared with 11.93 for systematic biopsies (63% less cores taken, $P < 0.001$). The percentage of targeted cores positive for prostate cancer was significantly higher than the random cores (35.1% vs. 21.3%, $P < 0.0001$).

A total of 45 men were diagnosed with prostate cancer; 38 were diagnosed by MRI/US fusion-guided biopsy compared with 40 by systematic extended-sextant TRUS-guided biopsy. Although the number of men found to have prostate cancer on systematic extended-sextant TRUS-guided biopsy was slightly higher, this difference in overall cancer detection was not statistically significant (40 vs. 38, $P = 0.39$). Tumors were graded using prostate cancer Grade Groups, originally described by Epstein et al. and recently adopted by the International Society of Urological Pathology (ISUP) and World Health Organization (WHO) (18, 19). Furthermore, there was no statistically significant difference in the prostate cancer Grade Groups when comparing MRI/US targeted biopsy to systematic 12-core, extended sextant TRUS-guided biopsy (Table 2 and Fig. 2).

Table 1. Patient demographics and biopsy characteristics

Variables	Values	
Total number of patients (n)	69	
Age (years), mean±SD (range)	64.33±8.3 (43–82)	
PSA (ng/mL), mean±SD (range)	7.71±5.66 (1.43–26.88)	
PSA density (ng/mL^2), mean±SD (range)	0.21±0.23 (0.03–1.26)	
Prostate volume (cc), mean±SD (range)	54.26±27.48 (19.86–127)	
Mean number of lesions, mean±SD (range)	1.97±0.80 (1–4)	
1 lesion, n (%)	21 (30.4)	
2 lesions, n (%)	31 (44.9)	
3 lesions, n (%)	15 (21.7)	
4 lesions, n (%)	2 (2.9)	
Highest PI-RADS, n (%)		
3	36 (52.2)	
4	26 (37.7)	
5	7 (10.1)	
Number of cores sampled, mean±SD (range)		$P < 0.0001$
Standard systematic biopsy	11.93±0.31 (10–12)	
MRI-targeted biopsy	4.42±1.65 (1–9)	
Percentage of positive cores, n/N (%)		$P < 0.0001$
Standard systematic biopsy	175/823 (21.3)	
MRI-targeted biopsy	107/305 (35.1)	
Cases with cancer detection, n (%)		$P = 0.39$
Standard systematic biopsy	40 (58.0)	
MRI-targeted biopsy	38 (55.1)	

MRI, magnetic resonance imaging; PI-RADS, prostate imaging reporting and data system; PSA, prostate specific antigen.

Discussion

MRI has been shown to be effective in detecting clinically-significant prostate cancer in patients suspected to harbor prostate cancer with a history of at least one prior negative TRUS biopsy. MRI is also being used in the algorithm for monitoring patients on active surveillance. However, there is sparse data regarding patients who have never had a prior biopsy.

Prior small series have shown the utility of targeted MRI/US fusion-guided prostate biopsy in biopsy-naive patients. Fascelli et al. (20) showed in a small study of 59 biopsy-naive patients that MRI-targeted lesions performed better than PSA and PSA density as markers for detecting prostate cancer. Larger studies have shown conflicting results regarding the equivalency of cancer detection between these two modalities. Quentin et al. (21) showed in a prospective study of 132 biopsy-naive patients that MRI/US fusion-guided biopsy and systematic TRUS-guided biopsy had equal rates of prostate cancer detection (21). Our study produced similar conclusions in terms of equivalent cancer detection rates between the two modalities.

In contrast to this, Delongchamps et al. (22) showed in a prospective multicenter controlled trial looking at 108 biopsy-naive patients that systematic TRUS-guided biopsy detected prostate cancer in more patients compared with MRI/US fusion-guided biopsy. However, there was no significant difference in detection of clinically-significant prostate cancer. Furthermore, the multi-institutional effort published by Delongchamps et al. (22) only investigated patients with a single suspicious lesion on MRI of the prostate, thereby excluding a large number of patients, posing a potential significant bias. In fact, these stringent criteria of patients only harboring a single MRI targeted lesion of suspicion would account for only 30.4% of the total population of patients included in our data analysis.

Table 2. Standard systematic versus MRI-targeted biopsy prostate cancer detection stratified by distribution of grade group

		Standard systematic biopsy						
		No Cancer	GG1	GG2	GG3	GG4	GG5	Total
MRI-targeted biopsy	No Cancer	24	5	2	0	0	0	31
	GG1	3	9	1	0	0	0	13
	GG2	0	1	5	0	2	1	9
	GG3	1	1	1	3	1	0	7
	GG4	0	0	0	1	3	0	4
	GG5	1	0	0	0	1	3	5
	Total	29	16	9	4	7	4	69

MRI, magnetic resonance imaging; GG, grade group.

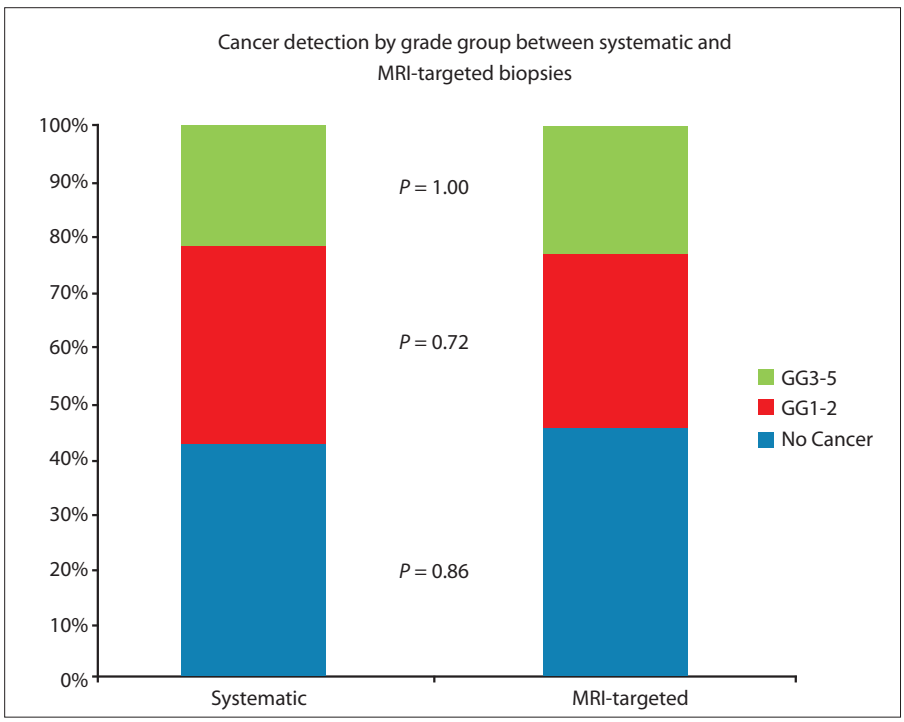

Figure 2. Cancer detection by grade group between standard systematic TRUS-guided and MRI/US fusion-guided biopsy approaches.

In our study, we demonstrated in a biopsy-naive cohort that MRI/US fusion-guided prostate biopsy offers equivalent cancer detection rates compared with systematic extended-sextant TRUS-guided prostate biopsy. A greater differential in detection of clinically-significant prostate cancers on targeted biopsy could have potentially been shown if stratifying the data for patients who had PI-RADS 4 or 5 lesions targeted. However, our limited patient population would not allow adequate statistical power to analyze the biopsy outcomes stratified by PI-RADS values. Expansion of this patient cohort or collaborative multi-institutional efforts could allow for these added investigations which may bear a significant impact in the biopsy-naive population of men undergoing multiparametric MRI. Also, there is a potential bias of optimizing the detection of prostate cancer on the systematic 12-core, extended sextant biopsy cores in our patient series, found to be as high as 58%. This may be a result of the urologic oncologist performing the biopsy sampling the MRI-targeted lesions first and then not purposefully avoiding these targeted regions when conducting a systematic, well-distributed biopsy sampling.

In addition to detecting prostate cancer at an equivalent rate to the standard-of-care approach via systematic extended-sextant TRUS-guided biopsy, MRI/US fusion-guided biopsy is able to do so while requiring significantly fewer cores which has also previously been shown (23). On average, patients in our study underwent only 4.42 targeted biopsies compared with 11.93 random biopsies ($P < 0.0001$). Siddiqui et al. (24) demonstrated similar improved efficiency in a large study of 1003 patients with suspicion of prostate cancer, showing targeted biopsies to be more efficient in detecting all prostate cancer (44.5% vs. 24.0%) and clinically-significant prostate cancer (63.9% vs. 34.1%) (24). However, in this prior study, a majority of patients had a history of prior prostate biopsy. Our study confirms these results in an exclusively biopsy-naive cohort, which represents the majority of patients who undergo prostate biopsy in the United States.

As we continue to search for an improved prostate cancer screening algorithm, our data supports the use of MRI in patients with suspicion of prostate cancer who have never undergone prior biopsy building on prior findings in similar patients (25). While the costs of MRI are an understandable concern, this could be offset by the reduced morbidity associated with systematic biopsy. Cost-effectiveness studies have shown reduced costs when comparing MRI-based screening methods to standard screening protocols (26). This may be a result of multiple benefits rendered by MRI-targeted biopsies. More accurate detection of clinically-significant disease in the initial biopsy setting may expedite necessary definitive treatment with curative intent and also may prompt appropriate staging in patients with higher risk disease (16). Additionally, optimizing proper grading and staging of prostate cancers detected may also more definitively help patients select active surveillance when safe and appropriate, which would be of cost benefit in terms of limiting or postponing radical treatments and subsequent costs from related morbidities associated with those treatments (13). Studies suggest that the overall rate of infection after prostate biopsy is 5%–7% with 1%–3% of patients needing to be hospitalized (27). Further, multiple studies have also suggested that a higher number of cores of tissue taken correlates with increased rates of sepsis (14, 28). A cost-effectiveness model suggests that the average cost of post-biopsy infectious complications based on Medicare reimbursement is around $5 900 (29). Recent studies have also suggested

the number of cores taken can lead to increased perioperative blood loss during subsequent radical prostatectomy (30). Therefore, taking this into consideration, the utilization of MRI to target suspicious lesions instead of randomly sampling the entire prostate could potentially reduce the rates of septic complications following prostate biopsy, improve the patient experience and potentially reduce the overall cost of screening without sacrificing the ability to detect prostate cancer.

Limitations of this study include the relatively small and retrospective sample size used in our data analysis. Given the number of patients in this study and further limited numbers in subset analyses that would be required, we also did not have statistical power to evaluate for a potential correlation of PI-RADS suspicion score to targeted biopsy Gleason score. There are new systems for improving systematic biopsy schemas with image-guidance and robotic assistance; however, these were not investigated in this current study which may alter findings if integrated into standard practice in the future (31). Additionally, we also did not compare the final radical prostatectomy pathology with the biopsy data for confirmation of disease grade as it was not available for the majority of patients in our patient cohort. Also, our study only encompassed patients from our institution, which is a large urban academic referral center. Since our center serves a large region and it was recognized that complications would not be comprehensively captured for all patients undergoing this outpatient office procedure, we did not collect these data in our dataset. Our patient population is likely not a perfect reflection of the population seen in more prevalent community settings. Additionally, the positive and negative predictive value of MRI and subsequent MRI/US fusion-guided biopsy are dependent upon the radiologist's interpretations and urologist performing the targeted biopsies which may vary by institution based upon experience.

In the first three years of implementing MRI into our practice pattern, we have demonstrated an equivalent cancer detection rate between systematic TRUS-guided and MRI-targeted prostate biopsies in a biopsy-naive population. This detection rate was achieved using significantly fewer biopsy cores. Further studies are necessary to investigate the safety of utilizing MRI earlier in prostate cancer detection. However, our results suggest that the MRI/US fusion-guided biopsy technique could lead to fewer biopsies being performed with an associated potential decrease in biopsy-associated morbidity.

In conclusion, we demonstrate that MRI/US fusion-guided prostate biopsy offers equal diagnostic performance to the systematic extended-sextant TRUS-guided biopsy in biopsy-naive men. Further, since the MRI/US fusion-guided biopsy approach acquires less tissue sampling without compromising diagnostic yield, there is a potential in reducing morbidity in the future.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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