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Original article

Impact of prebiopsy magnetic resonance imaging of the prostate on cancer detection and treatment patterns

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Abstract

Purpose: Though superior in clinical trial settings, outcomes following magnetic resonance image (MRI)-guided prostate biopsies have not been reported broadly. We compared prostate cancer detection rates for men who did and did not undergo prebiopsy MRI and evaluated treatment patterns based on biopsy approach, year of biopsy, and proximity to early adopters.

Methods: Using private insurance claims (2009–2015), we identified men who underwent prostate biopsy using appropriate procedure codes. Exposure was receipt of prebiopsy MRI within 3 months prior to biopsy. Outcomes included new prostate cancer diagnosis, treatment with prostatectomy/radiation, and receipt of adjunct procedures typically used for higher-risk disease (i.e., lymphadenectomy with prostatectomy, androgen deprivation therapy with radiation). Hierarchical mixed-effects multivariable logistic regression predicted probabilities of each outcome.

Results: We identified 77,350 men (mean age 57.5 ± 5.4 years) who underwent biopsy with 12% having had a prior negative biopsy. Use of prebiopsy MRI was more common among men biopsied from 2014 to 2015 (4.4% vs. 1.3% 2012–2013), in metropolitan statistical areas (2.6% vs. 1.1% not), residing close to early adopters (5.5% vs. 1.5% far), and with prior negative biopsy (7.3% vs. 1.7% biopsy-naïve; all $P < 0.001$). Compared to patients with a prior negative biopsy and no MRI, men were more likely to be diagnosed with prostate cancer if they had a prior negative biopsy and MRI (24.7% vs. 21.4% prior negative without MRI, odds ratio 1.25, 95% confidence interval 1.04–1.51) or an initial biopsy without prior MRI (40.0% vs. 21.4% prior negative without MRI, odds ratio 2.49, 95% confidence interval 2.36–2.64; $P < 0.001$). Predicted probability of treatment overall and adjunct treatment did not differ based on receipt of pre-biopsy MRI.

Conclusions: Among privately insured men in the United States, use of prostate MRI prior to prostate biopsy was associated with increased cancer detection among those with prior negative biopsies, but we did not observe significant changes with downstream treatment patterns. Published by Elsevier Inc.

Keywords: Prostatic neoplasms; Image-guided biopsy; Magnetic resonance imaging; Prostate biopsy; Radical prostatectomy; Health services research

1. Introduction

Over the past decade, there has been growing consensus that magnetic resonance imaging (MRI) of the prostate can improve detection of clinically significant cancer compared to the traditional transrectal ultrasound

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(TRUS)-guided approach. Though initial reports of the benefits of MRI-guidance were published as early as 2008, 2 large institutional cohort studies published in 2015 to 2016 demonstrated the improved detection of clinically significant cancer with fusion MR-US image-guided biopsies [1,2]. Notably, population-level adoption of MRI before prostate biopsy rose rapidly after 2013 among both Medicare beneficiaries [3] and younger, privately insured men [4].

With any broad dissemination of new technology, there can be gaps in outcomes between experienced centers and those with less familiarity with a new approach. Successful execution of MRI-guided prostate biopsies may have a particularly steep and complex learning curve, as it requires expertise and coordination across 3 specialties: radiology, urology, and pathology. In that context, population-level performance of prostate biopsies relying on preprocedure prostate MRI for guidance remains unexplored.

To that end, we assessed prostate cancer detection and treatment patterns among privately insured men who underwent transrectal US-guided biopsy with or without a prebiopsy prostate MRI. This work has the potential to identify whether MRI-guided biopsy outcomes seen broadly are similar to those borne out from the large cohort studies published previously. Furthermore, we will be able to assess whether proximity to early adopters impacts outcomes, as well as whether cancer detection following MRI-guided biopsies improves over time at a population level.

2. Methods

2.1. Dataset

We identified our analytic cohort within the MarketScan Commercial Claims database (TruvenHealth, Ann Arbor, MI) using administrative claims from 2009 through 2015. Marketscan contains data related to patient demographics, inpatient and outpatient services, and pharmaceutical claims for over 250 million unique individuals covered by selected employer-sponsored health insurance plans since 1999. The dataset allows for longitudinal tracking of care through any patient's coverage window.

2.2. Study cohort

We identified men younger than 65 years of age with 1+ claim associated with prostate biopsy between 2009 and 2015 based on appropriate Common Procedural Terminology procedure codes (Appendix A). Because use of prebiopsy MRI was relatively rare prior to 2012, we restricted our analysis of outcomes to 2012 to 2015. If a patient had more than one biopsy, we considered the latest biopsy as the index biopsy. To capture performance of an MRI before the biopsy and treatment received after a diagnosis, we limited our cohort to men with at least 3 months of continuous insurance coverage prior to, and 6 months following, the biopsy date. We also excluded men with evidence of a prostate cancer diagnosis prior to the biopsy (International Classification of Diseases, ninth Revision, Clinical Modification [ICD-9-CM] 185) or metastasis to the retroperitoneal/pelvic lymph nodes or bone (ICD-9-CM 196.2, 196.6, 198.5).

2.3. Exposures and outcomes

Our primary exposure was receipt of prebiopsy MRI within 3 months of prostate biopsy, defined by appropriate procedure codes for pelvic MRI with and/or without contrast (Appendix A). Other covariates of interest included patient age, health plan (e.g., high-deductible health plan, preferred provider organization, etc.), residence within a metropolitan statistical area (MSA), receipt of prior biopsy (based on claims back to 2009), comorbidity, year of biopsy, and proximity to an early adopter of MRI-biopsy technology. Comorbidity was based on a score of comorbid conditions based on criteria defined by Charlson et al. [5]. Several academic centers were early adopters of MR-US fusion prostate biopsy, including the National Cancer Institute in Bethesda, Maryland, the University of California in Los Angeles, and New York University Langone Medical Center in New York City. We designated whether patients resided in MSAs close to these institutions as "close to early adopters" (Appendix B).

Our primary outcome was new prostate cancer diagnosis, defined by identification of any encounter with ICD-9-CM diagnosis code 185.0 in the 6 months following the biopsy. Among those with a new cancer diagnosis, we also assessed predicted treatment with radical prostatectomy or radiation therapy as an outcome with appropriate procedure codes (Appendix A). Finally, we evaluated predicted receipt of adjunct procedures (i.e., pelvic lymphadenectomy with prostatectomy, androgen deprivation therapy with radiation) typically reserved for more advanced disease as a third outcome among those who underwent treatment.

2.4. Statistical analysis

In a first step, we evaluated associations between our exposure, other covariates, and primary outcome for our entire cohort using appropriate parametric and nonparametric bivariate testing. This was repeated among patients who were newly diagnosed with cancer with treatment as an outcome, as well as receipt of adjunct treatments among patients who were treated. From there, we constructed a series of hierarchical multivariable logistic regression models for each outcome using MSA as a random-effect variable, which would help account for clustering of patients at a metropolitan level. Covariates were selected for the model with a P value threshold of 0.20 on bivariate testing. For our prostate cancer detection model, we tested and identified a significant interaction between biopsy type (MRI- vs. TRUS-guided) and receipt of prior negative

Table 1
Characteristics of analytic cohort ($n = 77,350$).

Covariate	n (%)[a]	Prebiopsy MRI (%)[b] ($n = 1,802$)	No prebiopsy MRI (%)[b] ($n = 75,548$)
Age (y) (mean, SD)	57.2 (5.2)		
<55	20,339 (26)	461 (2)	19,878 (98)
55−59	25,895 (34)	602 (2)	25,293 (98)
60−64	31,116 (40)	739 (2)	30,377 (98)
Year of biopsy*			
2012−2013	51,385 (66)	651 (1)	50,734 (99)
2014−2015	25,965 (34)	1,151 (4)	24,814 (96)
Comorbidity			
0	60,067 (78)	1,397 (2)	58,670 (98)
1−2	15,077 (19)	348 (2)	14,729 (98)
3+	2,206 (3)	57 (3)	2,149 (97)
Residence in metropolitan statistical area*	64,858 (84)	1,664 (3)	63,194 (97)
Residence close to early adopter*	15,478 (20)	856 (6)	14,622 (94)
Health plan[c],*			
Preferred/extended provider organization	48,738 (65)	1,149 (2)	47,589 (98)
Health maintenance organization	8,824 (12)	172 (2)	8,652 (98)
High-deductible/consumer-driven health plan	8,517 (11)	198 (2)	8,319 (98)
Point-of-service ± capitation	6,290 (8)	164 (3)	6,126 (97)
Comprehensive	2,384 (3)	33 (1)	2,351 (99)
Region[d],*			
South	29,545 (38)	504 (2)	29,041 (98)
North Central	17,387 (22)	254 (1)	17,133 (99)
Northeast	15,953 (21)	725 (5)	15,228 (95)
West	12,983 (17)	296 (2)	12,687 (98)
Prior negative biopsy*	9,167 (12)	669 (7)	8,498 (93)

Abbreviations: MRI = magnetic resonance imaging; SD = standard deviation.
[a] Column percentage.
[b] Row percentage.
[c] Missing in 2,597 cases.
[d] Unknown in 1,482 cases.
* $P < 0.01$.

biopsy. The data for the models were also stratified by dichotomous exposures of interest: year of biopsy (2012−2013 vs. 2014−2015), proximity to early adopter, and receipt of prior negative biopsy. Statistical significance was set at $\alpha = 0.05$, and all testing was 2-sided. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). As these data are deidentified, we were granted IRB exemption for this study.

3. Results

The characteristics of our analytic cohort are shown in Table 1. The mean age was 57 ± 5 years, and 12% of men had a prior negative biopsy. One-third of the biopsies occurred after 2013. Overall, 20% of the cohort resided near an early adopter. Nearly two-thirds of men were covered by a health plan with preferred/extended provider organization. Use of prebiopsy MRI was more common among men biopsied from 2014 to 2015 (4.4% vs. 1.3% 2012−2013), in MSAs (2.6% vs. 1.1% not), residing close to early adopters (5.5% vs. 1.5% not), and with prior negative biopsy (7.3% vs. 1.7% biopsy-naïve) (all $P < 0.001$).

Table 2 shows estimates from the hierarchical multivariate regression model assessing cancer detection by biopsy type. Men were more likely to have been diagnosed with prostate cancer if they were biopsied between 2014 and 2015, were more than 55 years of age, had more comorbid disease burden, had health plans other than health maintenance organization coverage, or resided in the North Central or Southern regions (vs. Northeast) of the United States (all $P < 0.001$). Living close to centers that were early adopters of MR-US fusion biopsy was associated with a lower likelihood of being diagnosed with cancer (35.0% vs. 38.4% not close, odds ratio [OR] 0.93, 95% confidence interval [CI] 0.89−0.98). Men were more likely to be diagnosed with prostate cancer if they had a prior negative biopsy and underwent MRI (24.7% vs. 21.4% prior negative without MRI, OR 1.25, 95% CI 1.04−1.51) or an initial biopsy without an MRI (40.0% vs. 21.4% prior negative without MRI, OR 2.49, 95% CI 2.36−2.64) compared to patients with a prior negative biopsy without MRI ($P < 0.001$). In biopsy-naïve patients, diagnosis of prostate cancer was similar with or without prebiopsy MRI (36.5% and 40.0%, respectively; Fig. 2, panel 2).

Table 2
Estimates from multivariable regression model assessing cancer detection by biopsy type.

Covariate	*n* (% cancer)	Odds ratio (95% CI)	
Year of biopsy			0.009
2012–2013	19,276 (37.5)	–	
2014–2015	9,930 (38.2)	1.04 (1.01–1.08)	
Age (y)			<0.001
<55	6,969 (34.3)	–	
55–59	9,857 (38.1)	1.20 (1.16–1.25)	
60–64	12,380 (39.8)	1.29 (1.24–1.34)	
Comorbidity			0.030
0	22,452 (37.4)	–	
1–2	5,878 (39.0)	1.04 (1.01–1.09)	
3+	876 (39.7)	1.07 (0.98–1.18)	
Residence in MSA			0.064
No	4,977 (39.8)	–	
Yes	24,229 (37.4)	0.96 (0.92–1.00)	
Proximity to early adopter			0.003
Not close	23,782 (38.4)	–	
Close	5,424 (35.0)	0.93 (0.89–0.98)	
Health plan			0.024
Health maintenance organization	3,169 (35.9)	–	
Comprehensive	1,003 (42.1)	1.17 (1.06–1.28)	
High-deductible/consumer-driven health plan	3,236 (38.0)	1.03 (0.97–1.10)	
Point-of-service ± capitation	2,334 (37.1)	1.00 (0.94–1.08)	
Preferred/extended provider organization	18,507 (38.0)	1.04 (0.99–1.09)	
Region			<0.001
Northeast	5,710 (35.8)	–	
North Central	6,787 (39.0)	1.09 (1.03–1.15)	
South	11,475 (38.8)	1.10 (1.04–1.15)	
West	4,601 (35.4)	0.96 (0.91–1.02)	
Unknown	633 (42.7)	1.22 (1.09–1.38)	
Prior negative biopsy and MRI			<0.001
Prior negative, no MRI	1,815 (21.4)	–	
Prior negative, MRI	165 (24.7)	1.25 (1.04–1.51)	
Initial biopsy, MRI	414 (36.5)	2.25 (1.97–2.58)	
Initial biopsy, no MRI	26,812 (40.0)	2.49 (2.36–2.64)	

Abbreviations: MRI = magnetic resonance imaging, MSA = metropolitan statistical area.

After adjusting for other factors, predicted prostate cancer detection after TRUS-guided prostate biopsy was higher compared to MRI-guided biopsy overall (37.9% vs. 32.1%, $P < 0.001$). When first stratified by receipt of prior negative biopsy, those who were receiving an initial biopsy had higher predicted cancer detection than those who had prior negative biopsies (36.9%–41.5% vs. 19.3%–22.7%, respectively; Fig. 1). However, within the strata of whether patients had a prior negative biopsy, predicted detection rates did not differ significantly based on proximity to early adopters, year of biopsy, or biopsy approach. Fig. 2 depicts the predicted treatment rates after prostate cancer diagnosis. Here, treatment patterns ranged between 61.9% and 79.3% across strata and did not vary significantly based on proximity to early adopter, year of biopsy, or use of prebiopsy MRI. Among patients who were treated for prostate cancer, predicted rate of adjunct procedures (i.e., lymphadenectomy with prostatectomy or androgen deprivation therapy with radiation treatment) were comparable for MRI-Bx and

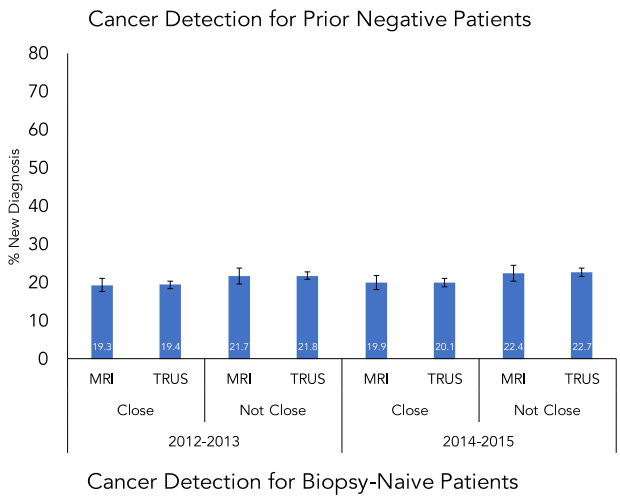

Fig. 1. Predicted prostate cancer detection by year, proximity to early adopter, and use of prebiopsy MRI.

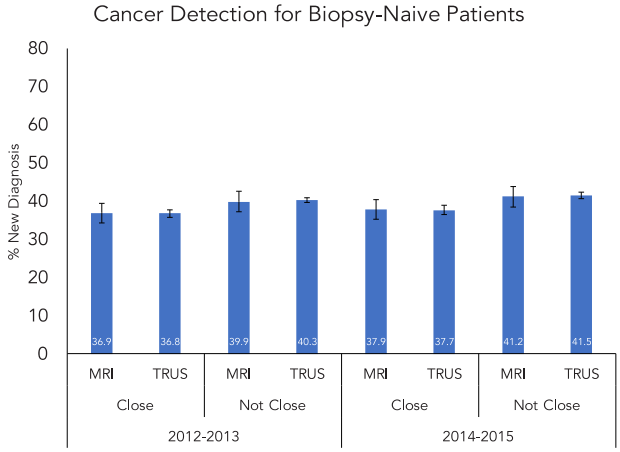

Fig. 2. Predicted prostate cancer treatment by year, proximity to early adopter, and use of prebiopsy MRI.

TRUS-Bx (32.4% and 33.0%). Predicted adjunctive treatment rates ranged from 30.3% to 34.2%, with statistically similar proportions based on year of biopsy, proximity to early adopters, and use of prebiopsy MRI (Fig. 3).

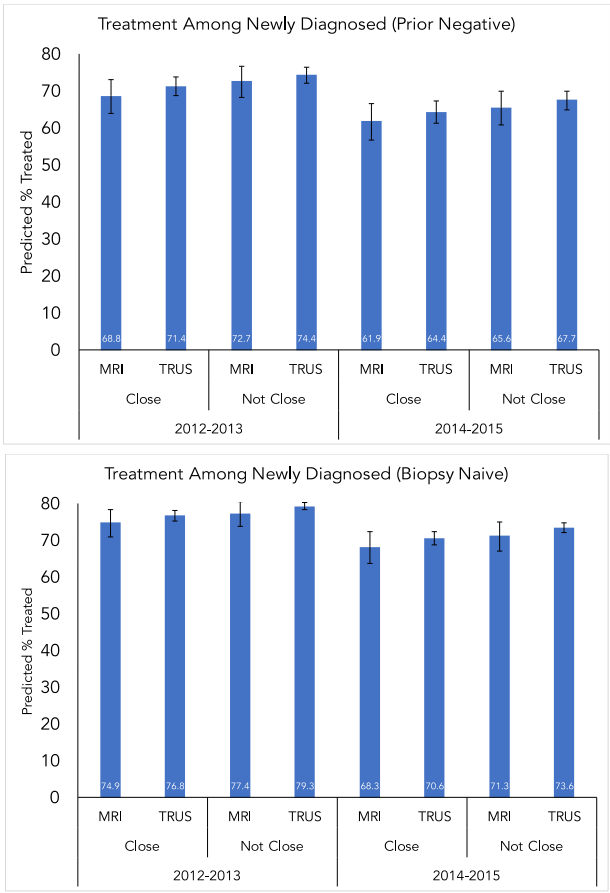

Fig. 3. Predicted receipt of lymphadenectomy with prostatectomy or androgen deprivation therapy with radiation treatment by year, proximity to early adopter, and use of prebiopsy MRI.

4. Discussion

This analysis is the first to examine prostate cancer detection and treatment patterns among men receiving following prebiopsy prostate MRI vs. traditional TRUS-guided biopsy, at the population-level. We report 3 key findings. First, we found that cancer detection improved for men who had a prior negative biopsy and prebiopsy MRI vs. no MRI among the overall cohort. Second, we did not observe improved cancer detection associated with use of a prebiopsy MRI among biopsy-naïve patients. Finally, we found that use of prebiopsy prostate MRI was not associated with marked changes on broad treatment patterns for men with a new prostate cancer diagnosis.

Importantly, we did note increased cancer detection among men with a prior negative biopsy. It is among this group for which early cohort studies of men undergoing MRI-guided prostate biopsies initially demonstrated benefit [6,7]. Furthermore, the first consensus document from the American Urological Association and Society for Abdominal Radiology emphasized that men with prior negative biopsies may derive the most benefit from subsequent MRI-guided prostate biopsies [8]. However, we did not observe improved cancer detection among patients who were biopsy-naïve, which has been demonstrated in a number of large cohort studies [1,9,10] and more recently, randomized clinical trials. The PROMIS trial, which compared prostate MRI-guided biopsies to template prostate mapping biopsy in biopsy-naïve men with elevated PSAs, found that upfront MRIs could potentially avoid 27% of initial prostate biopsies and increase detection of clinically significant prostate cancer by 18% [11]. The multicenter randomized PRECISION trial found superior detection of clinically significant cancer in 38% of the MRI-targeted biopsy group compared to 26% in the standard TRUS-biopsy group [12]. The population-level patterns seen in our results highlight the necessity of performing pragmatic trials to validate the clinical benefit shown by efficacy trials such as PRECISION.

Demonstrating efficacy and effectiveness for new technologies are separate endeavors, with the former being the expected results under ideal circumstances, and the latter being the effect in real-world clinical practice [13]. Though several studies have suggested efficacy of MRI-guided prostate biopsies in select academic settings, there remains significant room for determining its effectiveness across diverse clinical settings. Following a prebiopsy MRI, nearly one-third of men in our cohort were newly diagnosed with prostate cancer, which is at the lower end of the 31% to 51% range reported by institutional cohort studies [1,2,14,15]. The difference between our observed results and those seen in other studies is likely due to the younger study population and exclusion of active surveillance patients with a prior prostate cancer diagnosis, among other reasons.

One key issue that deserves greater clarity is the variation in experience and interpretation of images across—and within—practice settings. The American Urological Association Multiparametric Prostate MRI Consensus Panel supported MRI-based risk stratification for decision-making related to prostate cancer detection but emphasized that this should only occur with high quality mpMRI protocols using experienced readers [16]. Although PI-RADS v2 (Prostate Imaging − Reporting and Data System Version 2) is the current standard for radiologists in interpreting and reporting of prostate MRI, there are still discrepancies and only moderate levels of inter-observer agreement between radiologists [17−19]. One academic center reported considerable variability in cancer detection rate and PIRADS score assignment between radiologists, which was independent of radiologist volume or study time period [20]. Similarly, we did not see any changes in cancer detection over time or with closer proximity to early adopters. With this variation, there may be a role for stronger oversight and quality control to maintain consistency of MRI interpretation.

Even among patients with prior negative biopsies, we did not identify marked population-level changes in treatment patterns for men with a new prostate cancer diagnosis following a prebiopsy MRI. Presumably, results from existing studies suggest that there should be more men diagnosed with clinically significant cancer after prebiopsy MRI. As such, we expected greater rates of treatment and use of lymphadenectomy and androgen deprivation therapy following MRI-guided biopsies. Since this was not seen in this cohort, perhaps provider and facility treatment patterns are overriding the improved cancer detection seen at certain centers. That is, gains made in improved detection of clinically significant cancer broadly may be dampened by continued overtreatment of men with indolent tumors. This issue obviously merits exploration with more detailed cancer-specific data.

This study has a few limitations to consider. The definition of a pre-biopsy MRI is not yet validated, though the steep adoption curve observed in this cohort reported elsewhere [4] is in line with trends reported in the Medicare population [3]. These outcomes are described in a younger population, where outcomes related to cancer detection and treatment patterns may be less generalizable to a geriatric cohort. Also, the study period examined here predates the widespread adoption of prebiopsy MRI following level 1 evidence for improved detection of clinically significant prostate cancer [12]. As prostate cancer care continues to evolve in light of recent trial findings, it is important to continue exploring contemporary trends.

Additionally, we may have misclassified men as biopsy-naïve when they had prior negative biopsies prior to their employer-based coverage. Finally, there is a lack of cancer-specific details, though capture of downstream treatment should be fairly accurate based on billing claims.

Despite those limitations, this work represents an important first look at the outcomes related to adoption of prebiopsy prostate MRI in the United States. Future population-based work will also have to assess the market- and facility-based volume-outcome relationship—if present—for MRI-guided prostate biopsies. Furthermore, finding the "success stories" in settings where MRI-guided biopsy outcomes recapitulate results seen in clinical trials will help identify factors that may be exported to settings that may need improvement. Alternatively, it may be more effective to regionalize prostate cancer detection to highly skilled center of excellence, as has been suggested for bladder and testis cancer care [21−23]. However, such an approach must consider potential disparities in access and care based on race/ethnicity and geographic region, which have been hinted at with preliminary work in the Medicare population [3]. Ultimately, identification of factors in establishing successful and effective MRI-biopsy use, defining requirements for cost-effectiveness of prostate MRI deployment, and understanding referral patterns across regions will be necessary.

Conclusions

During the initial adoption of prebiopsy MRI in the United States, prostate cancer detection improved in men with prior negative biopsies but not in biopsy-naïve men, and there was no observable impact on downstream treatment patterns.

Disclosure

All authors reviewed this manuscript and edited where necessary.

Conflict of interest

The authors otherwise have no conflicts of interest to disclose.

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.urolonc.2018.11.004.

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