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Jea Young Min Date

Comparing 10-Core versus 16-Core Biopsy Protocols in Repeat Prostate Biopsies: A Retrospective, Multivariable Analysis of 950 Veterans

By

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Master of Public Health

Epidemiology

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A Retrospective, Multivariable Analysis of 950 Veterans

By

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Pharm.D.
University of Iowa
2008

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Abstract

Comparing 10-Core versus 16-Core Biopsy Protocols in Repeat Prostate Biopsies:

A Retrospective, Multivariable Analysis of 950 Veterans

By Jea Young Min

Patients with a high risk for prostate cancer and previously negative prostate biopsies are often referred for repeat biopsy procedures. For initial biopsy, the current literature indicates that extended sampling protocols with optimal peripheral zone targeting can increase the likelihood of detecting cancer. However, there are relatively few studies that examine the optimal number of cores for repeat biopsy procedures. In this retrospective study, we analyzed 967 consecutive repeat biopsy procedures that used either 10-core or 16-core biopsy protocols at the Atlanta Veterans Affairs Medical Center (VAMC). Descriptive statistics were obtained from univariable analyses comparing the two protocols. Multivariable models were built to compare the rates of cancer detection in the two protocols and obtain odds ratios and corresponding 95% confidence intervals (CIs). A separate multivariable analysis was performed only for subjects who had their initial biopsy at the Atlanta VAMC, controlling for additional variables relating to the initial procedure. Among subjects who had cancer, the disease characteristics were compared in the two protocols. Overall, prostate cancer was detected in 418 subjects (43.2%), with 36.8% in the 10-core group and 45.7% in the 16-core group. The 16-core group was more likely to have a positive biopsy compared to the 10-core group (OR=1.67, 95% CI 1.19-2.35) when adjusting for potential confounders. In the analysis restricted to subjects who received their initial biopsy at the VA the difference between the two groups was not statistically significant although the point estimate was larger (OR=2.36, 95% CI 0.90-6.14). Having an 8-core initial biopsy and having a high-grade prostatic intraepithelial neoplasia (HGPIN) on initial biopsy were positively associated with cancer detection on repeat biopsy. The proportion of patients with high grade or high volume cancer was not significantly different in the two groups. In summary, we found that 16-core protocol was more likely to detect cancer compared to the 10-core protocol. Patient-specific factors such as previous biopsy and clinical characteristics should be considered when deciding the optimal number of cores for repeat prostate biopsies.

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Comparing 10-Core versus 16-Core Biopsy Protocols in Repeat Prostate Biopsies: A Retrospective, Multivariable Analysis of 950 Veterans

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ABSTRACT

Patients with a high risk for prostate cancer and previously negative prostate biopsies are often referred for repeat biopsy procedures. For initial biopsy procedures, the current literature supports that extended biopsy protocols with optimal peripheral zone targeting can increase the likelihood of detecting cancer. However, there are a relatively small number of studies that examine the optimal number of cores for repeat biopsy procedures. In this retrospective study, we analyzed 967 consecutive repeat biopsy procedures that used either 10-core or 16-core biopsy protocols at the Atlanta VA Medical Center. Descriptive statistics were obtained from univariable analyses comparing the two protocols. Multivariable models were built to compare the rates of cancer detection in the two protocols and obtain odds ratios and corresponding 95% confidence intervals. A separate multivariable analysis was performed only for subjects who had their initial biopsy at the Atlanta VAMC, controlling for additional variables relating to the initial procedure. Among subjects who had cancer, the characteristics of cancer were compared in the two protocols. Overall, prostate cancer was detected in 418 subjects (43.2%), with 36.8% in the 10-core group and 45.7% in the 16-core group. The 16-core group was more likely to have a positive biopsy compared to the 10-core group (OR=1.67, 95% CI 1.19-2.35) when adjusting for potential confounders. However, the analysis restricted to subjects who received their initial biopsy at the VA did not demonstrate a significant difference in the proportion of positive biopsy in the two groups (OR=2.36, 95% CI 0.90-6.14). Having an 8-core initial biopsy and having a high-grade prostatic intraepithelial neoplasia (HGPIN) on initial biopsy were positively associated with cancer detection on repeat biopsy. The proportion of patients with high grade or high volume cancer was not significantly different in the two groups. In summary, we found that 16-core protocol was more likely to detect cancer compared to the 10-core protocol. However, this difference may be attenuated when the initial biopsy is considered adequate. Patient-specific factors such as previous biopsy and clinical characteristics should be considered when deciding the optimal number of cores for repeat prostate biopsies.

INTRODUCTION

Prostate cancer is the most common type of cancer among men in the US with an estimate of 240,890 new cases in 2011 (1). The accuracy of the prostate cancer diagnosis depends on the adequacy of the prostate gland tissue sampling, which in turn may be determined by the number and location of the biopsy cores. The overall rate of positive biopsy for cancer is approximately 25% with significant variability that can approach 40% (2), and a repeat biopsy among subjects with a negative initial result can yield an additional 13-41% (3).

Recent studies have shown that there can be a significant improvement in cancer detection when additional cores are obtained from lateral zones of the prostate, recommending that at least 8 cores be obtained for each biopsy procedure (2, 4). However it has been unclear whether obtaining cores in addition to this 8-core minimum is necessary for better cancer detection. In a recent study of a large series of initial prostate biopsy procedures, there was no difference in the rate of prostate cancer diagnosis between 12-core and 8-core biopsy protocols (2). These findings seem to indicate that when the prostate is properly targeted and adequately sampled, additional cores do not impact the diagnosis.

The question regarding the optimal number of cores has also been raised for repeat biopsies among patients who did not have a positive biopsy initially but continued to have worsening clinical signs or symptoms. While some studies in the past have recommended 8 to 12 cores in the repeat biopsy population, many recent studies have even recommended saturation biopsies with up to 20 or more cores (3-7).

In the current communication we build on our previous research conducted by Abd et al (2) by assessing the relation between the number of cores and the biopsy result among patients who undergo a repeat procedure. At the Atlanta VA Medical Center, a 10-core

biopsy protocol was adopted in January 2001 for the repeat biopsy populations, and in April 2004, the number of biopsy cores was increased to 16 cores. Similar to the initial biopsy procedure, the primary target for both protocols was the peripheral zone at the apex and lateral regions. During this 10-year period, nearly 1000 patients have undergone first-time repeat biopsy using one of the two protocols described above. In this study, we retrospectively analyze and compare the two repeat biopsy protocols in this veteran population during the two time periods. The primary objective of the study is to determine whether additional biopsy cores improve cancer detection for patients who did not have cancer detected at their initial biopsy. In addition, we will examine whether the two protocols differ in their rate of high grade and high volume cancer detection, and also identify demographic, clinical, and laboratory factors that may be related to the rate of prostate cancer detection, including characteristics of the initial biopsy such as previous high-grade prostatic intraepithelial neoplasia (HGPIN), the number of cores obtained in the initial biopsy, and the time interval between the first and second biopsies.

METHODS

This study was approved by the Institutional Review Boards of the Emory University and the Atlanta VA Medical Center. The study population included 967 patients who underwent second biopsy procedures at the Atlanta VA Medical Center over a period of 10 years (January 2001 to December 2011). All patients received digital rectal examination (DRE) and measurement of prostate-specific antigen (PSA). Patients were referred for a repeat prostate biopsy based on continued or worsening clinical signs and/or symptoms such as high PSA levels, high PSA velocity, and abnormal DRE. No age cutoffs were used in the inclusion or exclusion criteria for the study.

Only first-time repeat (i.e., second-ever) biopsy procedures using the 10-core or 16-core biopsy protocols were included in the analysis. The dependent variable of interest in these analyses was positive biopsy for cancer (versus normal result); the biopsies that revealed high-grade prostatic intraepithelial neoplasia (HGPIN) and atypical small acinar proliferation (ASAP) were not considered. Demographic, clinical and laboratory data included age, race, height, weight, body mass index (BMI), pre-biopsy serum PSA, prostate volume, family history of prostate cancer, medication profile, and whether the first biopsy was performed at the Atlanta VA Medical Center. Among the patients who received their first biopsy at the Atlanta VA Medical Center, more information about the first procedure included the number of cores obtained from the initial biopsy and the pathology results, specifically the presence of HGPIN.

All prostate biopsy procedures were performed transrectally using an ultrasound-guided 18-guage biopsy needle loaded on a spring-loaded biopsy device (Pro-Mag I 2.2; Med-Tech, Oxford, CT) (2). Prostate volume was calculated using the standard ellipsoid formula (2). The same device was used for the procedures over the entire study period, and all biopsies were performed by the same group of urology providers.

The two main repeat biopsy protocols included in the analysis were used over different time periods. The 10-core protocol was used during the first 3 years of the study period (January 2001 to March 2004) and the 16-core protocol was used during the later 7 years of the study period (April 2004 to December 2011). The 10-core protocol consisted of sextant cores plus 4 cores taken from the peripheral zone which is lateral and apical in location. The 16-core protocol consisted of sextant cores plus 6 cores from the peripheral zone and 4 cores from the transition zone.

The data analysis followed the methodology described in the earlier study of initial biopsy results that was based on the same VA population (2). Descriptive analyses of the data were performed to compare the distributions of demographic and clinical characteristics of patients in the two biopsy protocols. For the main multivariable analysis, logistic regression models were used to obtain the adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI) which show the association between positive biopsy and the number of cores obtained, while controlling for potential confounders such as age, race, PSA, PSA velocity, prostate volume, DRE findings, family history, BMI, 5-α reductase inhibitor (5ARI) use, and location of first biopsy procedure (Atlanta VAMC or an outside hospital).

The multivariable models were tested for interaction using two-way interaction terms that involved the number of cores and other variables of interest. Interaction terms that were not significant at the 5% level were removed from the model. Previous study results from the same source of data showed that there was a strong interaction between DRE and PSA, so an interaction term was created and included for better model fit. Collinearity between variables was assessed using SAS macro for Eigenvalues, condition indices, and variance decomposition proportions.

For biopsy results that showed evidence of prostate cancer, tumor characteristics such as biopsy Gleason score and cancer volume were analyzed and compared between the two protocols. A second multivariable logistic regression model that included only those with positive biopsy was used to identify predictors of high-grade cancer (Gleason scores 8 and 9) compared with low-grade cancer (Gleason scores 6 and 7) controlling for the same confounders as in the first model that included all patients. A similar logistic regression

model was used to identify predictors of high cancer volume (>50%) compared with low cancer volume (≤ 50%).

In addition, a sub-analysis of only those patients who underwent first biopsy at the Atlanta VA Medical Center was conducted to restrict the adequacy of the initial biopsy. This analysis included the number of biopsy cores obtained at first biopsy, time interval between the first and second biopsies, and previous pathology result of HGPIN as additional variables of interest in the multivariable model to evaluate whether these factors impact the results of the repeat biopsy, in addition to the confounders that were controlled for in the first model. PSA and DRE variables were included in the model separately and not as interaction terms.

All data management and statistical analyses were carried out using SAS 9.3 for Windows (SAS Institute, Cary, NC) statistical software package.

RESULTS

A total of 967 consecutive biopsy procedures were included in the analysis. Overall, the proportion of the study population that had a positive repeat biopsy result (excluding those who had HGPIN and ASAP) was 43.2%. Among all study participants 48.3% were African American (AA), and 49.8% were between age 60 and 69. PSA values varied widely, with 33.5% of patients having PSA values greater than 10 ng/mL. Descriptive analyses comparing demographic and clinical characteristics between patients who received 10-core versus 16-core biopsies are shown in Table 1. Approximately 27.5% of the study population received the 10-core biopsy. The unadjusted results in Table 1 show that there was a statistically significant difference in the proportion of positive biopsy results among those who received 10 versus 16 cores (p=0.01). The differences in the distribution of age, PSA,

first biopsy at outside hospital, and abnormal DRE between the 10-core and 16-core protocols also appeared to be statistically significant. The multivariable logistic regression model controlling for first biopsy at outside hospital, age, race, family history, BMI, PSA and DRE, prostate volume, and Proscar use showed that the 16-core protocol was associated with increased likelihood of a positive biopsy compared to the 10-core protocol (OR=1.67, 95% CI 1.19-2.35). The frequency of cancer detection was found to be higher among those in the 70+ age group compared to those younger than 60 (OR=2.47, 95% CI 1.59-3.86), and in African Americans (AA) compared to persons of other racial groups (OR=1.68, 95% CI 1.25-2.25). Obese subjects were more likely to have positive biopsy compared to normal weight subjects (OR=1.51, 95% CI 1.01-2.24). Men with prostate volume greater than 40 cc were less likely to have positive biopsy, as were those who were taking Proscar [Table 2].

The multivariable analysis restricted to subjects who received their first biopsy at the VA [Table 3] showed that the proportion of positive biopsy for 10-core and 16-core protocols did not differ significantly, however the point estimate for the VA-only group was further away from the null (OR=2.36, 95% CI 0.90-6.14). Having an 8-core initial biopsy (compared to a 12-core biopsy) was associated with positive repeat result (OR=2.74, 95% CI 1.29-5.82), and having a HGPIN on initial biopsy was also associated with positive repeat biopsy (OR=2.68, 95% CI 1.36-5.27).

Table 4 shows that the distribution of cancer characteristics for positive biopsy patients was not significantly different among those with 10-core versus 16-core protocols when the cancer grade and volume variables were dichotomized. The multivariable analyses evaluating the association between the number of cores and tumor characteristics among patients with a positive biopsy revealed that the proportion of subjects with high grade cancer was not significantly different for those who had the 16-core biopsy compared to the

10-core biopsy (OR=1.59, 95% CI 0.65-3.90) [Table 5]. Similarly, the proportion of subjects with high cancer volume was also not different across the two protocols (OR=0.75, 95% CI 0.38-1.46) [Table 6].

DISCUSSION

The impact of the number and location of biopsy cores on prostate cancer detection continues to be a topic of debate. Optimizing the yield of biopsy protocol remains an important clinical and public health issue. It not only affects the morbidity and psychological stress of individual patients and family but can also contribute significantly to health care cost. The overall goal is to diagnose clinically significant, yet curable, cancer through the utilization of the lowest number of biopsy cores in order to minimize adverse effects and avoid unnecessary cost.

In our study evaluating repeat prostate biopsies, the 16-core protocol was more likely to detect cancer than the 10-core protocol. We also found that after adjusting for other factors (including the number of cores) HGPIN on the first biopsy was associated with increased frequency of a positive repeat procedure, and the greater (≥12 versus <12) number of cores on the initial biopsy was associated with a decreased likelihood of a cancer diagnosis following the second biopsy. When the data were limited to subjects who had a positive repeat biopsy, there was no evidence that the 16-core protocol was more likely to identify more aggressive (i.e. high grade or high volume) disease. Abnormal DRE was the only risk factor that was a significant predictor of high grade and high volume prostate cancer.

Multiple previous studies have explored the optimal number of cores for initial prostate biopsies. Most of these studies demonstrated that adding lateral cores to the traditional sextant biopsy can improve detection of cancer. Studies comparing the sextant

prostate biopsy to extended protocols consisting of 10-18 cores found that the sextant biopsy approach could miss up to 20% of cancers (11). However, when other investigators examined whether increasing the number of cores increased the biopsy yield accordingly, they found that beyond 18 cores there was no significant benefit (11). In our previous study, we found no evidence that the 12-core biopsy was more likely to detect cancer compared to the 8-core biopsy when the peripheral zone was well-targeted (2). In summary, the optimal number of cores for initial biopsy appears to range from 8 to 18 cores with appropriate peripheral zone targeting, and the exact number requires consideration of the additional clinical characteristics such as prostate size (11).

In contrast to relatively numerous studies evaluating initial biopsy results in relation to the number of cores the corresponding literature pertaining to repeat biopsies is sparse. In a recent study of 1,056 subjects with initially negative biopsies, Zaytoun et al compared the prostate cancer detection rate for an extended biopsy protocol (12 to 14 cores) and a saturation biopsy protocol (20 to 24 cores), and found that the saturation biopsy led to a significantly higher cancer detection rate compared to the extended biopsy (32.7% vs 24.9%) (6). Other studies have examined the effectiveness of saturation biopsies following initially negative sextant biopsies, and reported that they can lead to a diagnostic yield of up to 34% (3, 7-9), although they did not specifically compare it to a different protocol. Lee et al observed that among men who had a previous HGPIN, a saturation biopsy scheme with 20 or more cores had a greater proportion of positive results than an extended biopsy scheme of 14 or less cores (12). In comparison, a smaller study of 185 patients conducted by Chon et al reported that increasing the number of repeat biopsy cores beyond 8 cores did not appear to increase the cancer detection rate, although they did find that 8 cores was still significantly more likely to detect cancer compared to 6 cores(4). It is important to note that most of

these studies did not adjust for potential confounders, but rather compared crude rates of cancer detection. Therefore stronger evidence may be needed to justify the use of saturation biopsies. One of the strengths of our study is that we adjusted for potential confounders such as age, race, PSA, PSA volume, and BMI in a multivariable model, and also included a large sample of patients. The sample size of the previous studies of repeat biopsies discussed above ranged from 57 to 408, with the exception of the Zaytoun et al study which included more than 1,000 subjects and was comparable in sample size to our study.

An important result from our study that requires further discussion is that among patients who received their initial biopsy at the Atlanta VAMC there was no difference in cancer detection for the two protocols. This finding suggests that the adequacy of the initial biopsy can potentially have a significant impact on the result of the second biopsy and may be used to help determine the number of cores that should be obtained in subsequent biopsies. The adequacy of the initial biopsy procedure and its impact on the second biopsy results is addressed in many studies. The current literature indicates that the probability of a positive repeat biopsy is significantly higher after an initial sextant biopsy compared to an initial extended biopsy with 10 or more cores (13-16). In our study, the subjects who had their initial biopsy at the Atlanta VAMC underwent either an 8-core or 12-core biopsy. Unfortunately, for the subjects who had their initial biopsy at an outside hospital, we have no information on the number of cores that were obtained on the first biopsy, what the results were, or how adequate the techniques and methods used to carry out the biopsy procedures were. For this reason our overall results may have been affected by the fact that 64.8% of the study population had their initial biopsy at an outside hospital and the initial biopsy schemes are unknown.

We also found that patients who had HGPIN on their initial biopsy were more likely to have cancer detected on their second biopsy, which is consistent with some of the earlier reports (17). Singh et al demonstrated that subjects who had a positive 12-core repeat biopsy were 5 times more likely to have had a HGPIN result on their previous 12-core biopsy (OR=5.07, 95% CI 1.54-16.74) (18). However another study found that when an extended biopsy with 8 or more cores is performed initially, the repeat biopsy within 1 year following a diagnosis of HGPIN did not lead to a significant increase in cancer detection (19), suggesting that an immediate re-biopsy may not be indicated for those with HGPIN given that they had an adequate initial biopsy (11).

Although our findings suggest that additional cores may lead to better detection of prostate cancer overall, we also found that it did not lead to identification of more high grade or high volume cancer. Based on this finding additional cores may not improve the diagnosis of more clinically significant cancer.

The findings from our previous study based on the same Atlanta VAMC patient population showed that cancer detection was not significantly different for 8-core versus 12-core protocols in initial biopsy procedures (2). Although these earlier findings appear to contradict our current results, it is important to keep in mind that repeat biopsy subjects are inherently different from the initial biopsy patients in that they were referred for a second biopsy due to clinical suspicion of cancer with worsening clinical signs and symptoms or worsening laboratory markers despite the past history of a negative biopsy result. Another important reason that our results may be different from the previous study of initial biopsies is the large proportion of men whose initial biopsy was performed at an outside hospital. As discussed previously, we cannot assume that these patients received initial biopsies with adequate sampling and targeting. An important limitation of our study is that it may be only

applicable to the VA population and is limited to the 10-core versus 16-core biopsy comparison. For this reason the applicability of our findings to non-VA settings and to other biopsy schemes may be questionable. Another limitation of our data is lack of information on the morbidity outcomes from the two different protocols. Although this information may have been useful it is unlikely that the number of cores plays an important role in post-biopsy side effects because previous research showed that even saturation biopsy schemes are well tolerated by most patients (20).

Recently some investigators have proposed nomograms for predicting the probability of prostate cancer detection on repeat biopsy. Benecchi and colleagues developed a nomogram based on a multivariable model evaluating factors such as age, DRE, PSA, free-to-total PSA ratio, PSA density, and previous HGPIN (21). They found that all factors except for age and PSA led to an increased accuracy of the model in predicting the outcome of repeat biopsies. In a different study, Moussa et al developed a predictive model which included even more patient specific risk factors such as family history, months from previous or initial biopsy, and history of ASAP (22). The Vienna Nomogram is another example, however this tool is intended to identify the optimal number of repeat biopsy cores based on the patient's age and total prostate volume rather than predict biopsy results (23). While further studies are needed to evaluate these nomograms in depth, recent studies seem to underscore the importance of considering many different factors when deciding on the number of cores for repeat biopsy procedures.

CONCLUSION

This large study of repeat prostate biopsy procedures in the VA population provided some evidence that a 16-core biopsy may lead to greater probability of detecting prostate

cancer compared to a 10-core biopsy. However, this difference was attenuated and was no longer significant in cases where the initial biopsy was considered adequate. While these results are only applicable to the 10-core versus 16-core comparison, the findings of our study suggest that the initial biopsy scheme, previous HGPIN, and potentially other clinical factors such as prostate volume may need to be considered to determine the optimal number of cores for repeat biopsies. Further studies which evaluate the use of different protocols or nomograms that account for these factors in a large and more diverse population are warranted to establish clear patient-specific guidelines.

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TABLES

Table 1. Descriptive characteristics of the study population (n=967)*

Patient Characteristics		Total Patients (n=967)		10 Biopsy Cores (n=266)		16 Biopsy Cores (n=701)		p-value
		N	%	N	Col %	N	Col %	
Biopsy Result	Negative	**549**	*56.8*	**168**	*63.2*	**381**	*54.4*	**0.01**
	Positive	**418**	*43.2*	**98**	*36.8*	**320**	*45.7*	
First Bx at OSH	No	**340**	*35.2*	**45**	*16.9*	**295**	*42.1*	**<0.0001**
	Yes	**627**	*64.8*	**221**	*83.1*	**406**	*57.9*	
Age	<60	**219**	*22.7*	**51**	*19.2*	**168**	*24.0*	**0.0003**
	60-69	**481**	*49.8*	**117**	*44.0*	**364**	*52.0*	
	70+	**266**	*27.5*	**98**	*36.8*	**168**	*24.0*	
Race	Non-AA	**500**	*51.7*	**147**	*55.3*	**353**	*50.4*	0.17
	AA	**467**	*48.3*	**119**	*44.7*	**348**	*49.6*	
Family History	No	**767**	*79.3*	**213**	*80.1*	**554**	*79.0*	0.72
	Yes	**200**	*20.7*	**53**	*19.9*	**147**	*21.0*	
BMI (kg/m^2)	<25	**229**	*23.9*	**61**	*23.5*	**168**	*24.0*	0.45
	25-29.9	**417**	*43.4*	**121**	*46.5*	**296**	*42.3*	
	>30	**314**	*32.7*	**78**	*30.0*	**236**	*33.7*	
Prostate Vol (cc)	<=30	**205**	*21.2*	**59**	*22.2*	**146**	*20.9*	0.82
	30 to 40	**177**	*18.3*	**44**	*16.5*	**133**	*19.0*	
	40 to 50	**152**	*15.7*	**41**	*15.4*	**111**	*15.9*	
	>50	**432**	*44.7*	**122**	*45.9*	**310**	*44.3*	
PSA (ng/mL)	<4.1	**138**	*14.3*	**47**	*17.7*	**91**	*13.0*	**0.04**
	4.1-10	**505**	*52.2*	**123**	*46.2*	**382**	*54.5*	
	>10	**324**	*33.5*	**96**	*36.1*	**228**	*32.5*	
PSA Density	<0.15	**466**	*48.2*	**121**	*45.5*	**345**	*49.3*	0.29
	>=0.15	**500**	*51.8*	**145**	*54.5*	**355**	*50.7*	
Abnormal DRE	Yes	**390**	*40.3*	**124**	*46.6*	**266**	*38.0*	**0.01**
	No	**577**	*59.7*	**142**	*53.4*	**435**	*62.1*	
Proscar Use	No	**771**	*79.7*	**214**	*80.5*	**557**	*79.5*	0.73
	Yes	**196**	*20.3*	**52**	*19.6*	**144**	*20.5*	

* This population excludes those with a pathology result of HGPIN. It also excludes those who did not have either 10 or 16 biopsy cores.

Table 2. Multivariate analysis of the association between positive biopsy result and variables relating to patient characteristics, clinical profile, and biopsy protocol (n=967)

Patient Characteristics		Positive Biopsy (n=418)	Negative Biopsy (n=549)	Crude OR (95% CI)	Adjusted OR (95% CI)
		N	N		
Planned Cores	10 Cores	**108**	**182**	1	1
	16 Cores	**342**	**443**	1.44 (1.08-1.92)	**1.67 (1.19-2.35)**
First biopsy at OSH	No	**176**	**272**	1	1
	Yes	**274**	**353**	1.06 (0.81-1.38)	1.26 (0.92-1.72)
Age	<60	**98**	**140**	1	1
	60-69	**214**	**326**	0.95 (0.69-1.31)	1.39 (0.95-2.03)
	70+	**138**	**158**	1.27 (0.88-1.82)	**2.47 (1.59-3.86)**
Race	Non-AA	**196**	**349**	1	1
	AA	**254**	**276**	1.64 (1.27-2.12)	**1.68 (1.25-2.25)**
Family History	No	**342**	**500**	1	1
	Yes	**108**	**125**	1.31 (0.96-1.79)	1.34 (0.94-1.90)
BMI (kg/m^2)	<25	**116**	**130**	1	1
	25-29.9	**176**	**302**	0.66 (0.48-0.91)	0.87 (0.61-1.26)
	>30	**156**	**188**	0.92 (0.66-1.29)	**1.51 (1.01-2.24)**
Prostate Vol (cc)	<=30	**131**	**88**	1	1
	30 to 40	**110**	**79**	0.92 (0.61-1.39)	0.70 (0.44-1.11)
	40 to 50	**76**	**96**	0.55 (0.36-0.84)	**0.33 (0.21-0.55)**
	>50	**133**	**361**	0.26 (0.18-0.37)	**0.14 (0.09-0.21)**
PSA level and DRE	PSA<4.1 and DRE(-)	**18**	**25**	1	1
	PSA 4-10 and DRE(-)	**143**	**217**	0.88 (0.45-1.71)	1.43 (0.68-3.01)
	PSA>10 and DRE(-)	**96**	**148**	0.93 (0.47-1.85)	**2.21 (1.01-4.83)**
	PSA<4.1 and DRE(+)	**29**	**78**	0.46 (0.21-1.00)	**0.36 (0.15-0.84)**
	PSA 4-10 and DRE(+)	**89**	**105**	1.21 (0.60-2.43)	1.95 (0.89-4.26)
	PSA>10 and DRE(+)	**75**	**52**	2.03 (0.97-4.24)	**3.73 (1.62-8.61)**
Proscar Use	No	**387**	**451**	1	1
	Yes	**63**	**174**	0.44 (0.31-0.62)	**0.44 (0.30-0.65)**

Table 3. Multivariate analysis of the association between positive biopsy result and variables relating to patient characteristics, clinical profile, and biopsy protocol only in patients who received initial biopsy at the VA (n=340)

Patient Characteristics		Positive Biopsy (n=144)	Negative Biopsy (n=196)	Crude OR (95% CI)	Adjusted OR (95% CI)
		N	N		
Planned Cores	10 Cores	**17**	**28**	1	1
	16 Cores	**127**	**168**	1.25 (0.65-2.37)	2.36 (0.90-6.14)
First biopsy cores	12+ Cores	**94**	**139**	1	1
	8 Cores	**50**	**57**	1.30 (0.82-2.06)	**2.74 (1.29-5.82)**
HGPIN on first biopsy	No	**48**	**51**	1	1
	Yes	**96**	**145**	1.42 (0.89-2.28)	**2.68 (1.36-5.27)**
Time between biopsies	<= 1 year	**68**	**109**	1	1
	> 1 year	**76**	**87**	1.40 (0.91-2.16)	1.84 (0.98-3.47)
Age	<60	**43**	**62**	1	1
	60-69	**63**	**100**	0.91 (0.55-1.50)	1.27 (0.69-2.35)
	70+	**38**	**34**	1.61 (0.88-2.95)	**4.03 (1.83-8.90)**
Race	Non-AA	**64**	**104**	1	1
	AA	**80**	**92**	1.41 (0.92-2.18)	**1.76 (1.03-3.02)**
Family History	No	**109**	**160**	1	1
	Yes	**35**	**36**	1.43 (0.84-2.41)	1.59 (0.86-2.95)
BMI (kg/m^2)	<25	**41**	**45**	1	1
	25-29.9	**55**	**87**	0.71 (0.41-1.22)	0.89 (0.46-1.70)
	>30	**48**	**63**	0.86 (0.49-1.50)	1.62 (0.79-3.33)
Prostate Vol (cc)	<=30	**45**	**32**	1	1
	30 to 40	**42**	**39**	0.77 (0.41-1.44)	0.47 (0.22-1.02)
	40 to 50	**24**	**32**	0.53 (0.27-1.07)	**0.24 (0.10-0.57)**
	>50	**33**	**93**	0.25 (0.14-0.46)	**0.07 (0.03-0.17)**
PSA level and DRE	PSA<4.1 and DRE(-)	**5**	**13**	1	1
	PSA 4-10 and DRE(-)	**59**	**68**	2.26 (0.76-6.70)	3.15 (0.88-11.26)
	PSA>10 and DRE(-)	**27**	**45**	1.56 (0.50-4.86)	2.77 (0.70-10.86)
	PSA<4.1 and DRE(+)	**9**	**27**	0.87 (0.24-3.11)	0.39 (0.09-1.76)
	PSA 4-10 and DRE(+)	**29**	**28**	2.69 (0.85-8.55)	**5.54 (1.39-22.13)**
	PSA>10 and DRE(+)	**15**	**15**	2.60 (0.74-9.12)	0.42 (0.22-16.64)
Proscar Use	No	**125**	**143**	1	1
	Yes	**19**	**53**	0.41 (0.23-0.73)	**0.42 (0.22-0.84)**

Table 4. Prostate cancer characteristics by biopsy protocol among patients with positive biopsy result (n=418)

Patient Characteristics		10 Biopsy Cores (n=98)		16 Biopsy Cores (n=320)		p-value
		N	Col %	N	Col %	
Gleason Score	5	0	0.0	1	0.3	0.03[a]
	6	64	65.3	145	46.0	
	7	26	26.5	138	43.8	
	8	3	3.1	17	5.4	
	9	5	5.1	13	4.1	
	10	0	0.0	1	0.3	
Gleason Score (dichotomized)	< 8	90	91.8	284	90.2	0.62
	>= 8	8	8.2	31	9.8	
Cancer volume	0-25%	57	58.2	220	70.1	0.08
	25-50%	19	19.4	48	15.3	
	50-75%	12	12.2	18	5.7	
	75-100%	10	10.2	28	8.9	
Cancer volume (dichotomized)	< 50%	76	77.6	268	85.4	0.07
	>= 50%	22	22.5	46	14.7	

[a] 50% of the cells have expected counts less than 5. Chi-Square may not be a valid test.

Table 5. Multivariate analysis of the association between high grade tumor result (Gleason score 8 or greater) and variables relating to patient characteristics, clinical profile, and biopsy protocol only in patients who had positive biopsy (n=413)*

Patient Characteristics		High Grade Tumor (n=39)	Low Grade Tumor (n=374)	Adjusted OR (95% CI)
		N	N	
Planned Cores	10 Cores	**8**	**90**	1
	16 Cores	**31**	**284**	1.59 (0.65-3.90)
First biopsy at OSH	No	**10**	**133**	1
	Yes	**29**	**241**	1.35 (0.60-3.05)
Age	<60	**5**	**85**	1
	60-69	**15**	**182**	1.07 (0.34-3.32)
	70+	**19**	**107**	2.23 (0.71-7.01)
Race	Non-AA	**64**	**104**	1
	AA	**24**	**206**	1.81 (0.83-3.93)
Family History	No	**33**	**284**	1
	Yes	**6**	**90**	0.60 (0.23-1.54)
BMI (kg/m^2)	<25	**10**	**102**	1
	25-29.9	**17**	**141**	1.34 (0.55-3.27)
	>30	**12**	**131**	1.47 (0.57-3.81)
Prostate Vol (cc)	<=30	**10**	**112**	1
	30 to 40	**10**	**91**	1.19 (0.43-3.31)
	40 to 50	**8**	**61**	1.53 (0.51-4.61)
	>50	**11**	**110**	0.75 (0.27-2.09)
Abnormal DRE	No	**11**	**225**	1
	Yes	**28**	**149**	**4.75 (2.12-10.63)**
PSA (ng/mL)	<4.1	**2**	**40**	1
	4.1-10	**14**	**201**	2.24 (0.45-11.24)
	>10	**23**	**133**	4.25 (0.87-20.87)
Proscar Use	No	**30**	**328**	1
	Yes	**9**	**46**	2.15 (0.92-5.04)

* 5 patients had missing gleason score and were excluded from the analysis

Table 6. Multivariate analysis of the association between high cancer volume (greater than 50%) and variables relating to patient characteristics, clinical profile, and biopsy protocol only in patients who had positive biopsy (n=412)*

Patient Characteristics		High Vol Cancer (n=68)	Low Vol Cancer (n=344)	Adjusted OR (95% CI)
		N	N	
Planned Cores	10 Cores	**22**	**76**	1
	16 Cores	**46**	**268**	0.75 (0.38-1.46)
First biopsy at OSH	No	**13**	**130**	1
	Yes	**55**	**214**	1.89 (0.91-3.93)
Age	<60	**12**	**77**	1
	60-69	**27**	**170**	1.03 (0.43-2.48)
	70+	**29**	**97**	1.83 (0.73-4.57)
Race	Non-AA	**29**	**153**	1
	AA	**39**	**191**	0.84 (0.45-1.58)
Family History	No	**52**	**264**	1
	Yes	**16**	**80**	1.10 (0.54-2.22)
BMI (kg/m^2)	<25	**17**	**94**	1
	25-29.9	**28**	**130**	1.56 (0.72-3.39)
	>30	**23**	**120**	1.68 (0.75-3.78)
Prostate Vol (cc)	<=30	**26**	**96**	1
	30 to 40	**14**	**86**	0.57 (0.25-1.32)
	40 to 50	**10**	**59**	0.41 (0.16-1.08)
	>50	**18**	**103**	0.42 (0.18-0.97)
Abnormal DRE	No	**22**	**213**	1
	Yes	**46**	**131**	**3.52 (1.87-6.64)**
PSA (ng/mL)	<4.1	**4**	**38**	1
	4.1-10	**13**	**201**	1.09 (0.32-3.78)
	>10	**51**	**105**	**9.70 (2.94-32.08)**
Proscar Use	No	**61**	**296**	1
	Yes	**7**	**48**	0.72 (0.30-1.72)

* 5 patients had missing gleason score and were excluded from the analysis