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Increasing Use of Dose-escalated External Beam Radiation Therapy for Men with Non-Metastatic Prostate Cancer

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Abstract

Background—Dose-escalated external beam radiotherapy (EBRT) is associated with improved tumor control rates for men with prostate cancer. In this study, we examine recent practice patterns using a large national cancer registry to understand the extent to which dose-escalated EBRT has been incorporated into routine clinical practice.

Methods—We conducted a retrospective observational cohort study using the National Cancer Database (NCDB), a nationwide oncology outcomes database in the United States. We identified 98,755 men diagnosed with non-metastatic prostate cancer between 2006 and 2011 who received definitive EBRT and classified patients into NCCN risk groups. We defined dose-escalated EBRT as total prescribed dose of ≥ 75.6 Gy. Using multivariable logistic regression, we examined the

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association of patient, clinical, and demographic characteristics with the use of dose-escalated EBRT.

Results—Overall, 81.6% of men received dose-escalated EBRT during the study period. The use of dose-escalated EBRT did not vary substantially by NCCN risk group. Use of dose-escalated EBRT increased from 70.7% of patients receiving treatment in 2006 to 89.8% of patients receiving treatment in 2011. On multivariable analysis, year of diagnosis and use of intensity modulated radiation therapy (IMRT) were significantly associated with receipt of dose-escalated EBRT.

Conclusions—Our study results indicate that dose-escalated EBRT has been widely adopted by radiation oncologists treating prostate cancer in the United States. The proportion of patients receiving dose-escalated EBRT increased nearly 20% between 2006 and 2011. We observed high utilization rates of dose-escalated EBRT within all disease risk groups. Adoption of IMRT was strongly associated with use of dose-escalated treatment.

INTRODUCTION

Dose-escalated external beam radiation therapy (EBRT) for prostate cancer is associated with improved tumor control rates in all disease risk groups.^{1–7} Randomized controlled trials (RCTs) conducted in the United States demonstrated improved PSA control following treatment of localized prostate cancer with EBRT doses of 78 Gy and 79.2 Gy compared to 70 Gy.^{8,9} Clinical guidelines of the National Comprehensive Cancer Network (NCCN) have evolved over the last decade but have generally suggested doses between 70–79 Gy for men with low risk disease and 75–80+ Gy for men with intermediate and high risk disease.^{10,11} Thus, in 2007 the use of higher dose EBRT (> 75 Gy) was established as a clinical performance measure in assessing the quality of prostate cancer radiotherapy.¹²

Despite these observed benefits, selection of patients most likely to benefit from dose-escalated EBRT is complicated by several factors. Notably, higher doses of radiation therapy may be associated with greater treatment related toxicities, and improvements in overall survival (OS) following dose-escalated EBRT have not been observed.¹ Furthermore, growing evidence suggests that men with indolent prostate cancer derive little or no benefit from radical treatment.^{13,14}

Patterns of care associated with the use of dose-escalated EBRT are important to understand, given the potential for increased toxicities and the ongoing debate regarding the absolute benefits associated with its use. Prior studies have been limited by self reported outcomes and small sample size.^{15,16} Therefore, we examined the extent to which dose escalation has been incorporated into routine clinical practice using a large national cancer registry.

MATERIAL AND METHODS

Data Source

This retrospective, observational cohort study used data from the National Cancer Database (NCDB) and was approved by our institutional review board. The NCDB is a national cancer registry sponsored by the American College of Surgeons Commission on Cancer

(ACS-COC) and the American Cancer Society. An estimated 70% of incident cancer cases diagnosed annually in the United States are reported to NCDB.¹⁷

Cohort

Figure 1 (Available online) illustrates the definition of the study cohort. We identified 123,471 men with pathologically confirmed non-metastatic invasive prostate cancer diagnosed between January 1, 2006 and December 31, 2011 who received EBRT with MV photons. Patients undergoing surgery, brachytherapy, stereotactic body radiation therapy or other alternative forms of treatment were excluded. In order to be consistent with NCDB guidelines for confidentiality, we excluded patients receiving proton therapy because of concerns that the small number of COC affiliated proton therapy centers would be readily identifiable in the data. Furthermore, NCDB does not offer its registrars guidance on recording proton therapy dose prescriptions or handling differences in relative biological effectiveness (RBE) between treatment modalities. EBRT dose was available in 119,132 (96.5%) of these patients. We excluded 9,904 patients with EBRT dose < 59.4 Gy because such patients may have either not completed a definitive course of radiotherapy or may have received hypofractionated EBRT. We also excluded 1,988 patients with EBRT dose > 90 Gy as outliers due to concerns of potential recording errors in such cases. Finally, we excluded 8,485 patients who could not be classified by disease risk group because of missing data. Our final cohort included 24,991 low, 40,835 intermediate, and 32,929 high risk patients with non-metastatic prostate cancer.

Primary Outcome

The primary study outcome was the total EBRT dose received. NCDB tumor registrars extract EBRT dose data from review of the radiation treatment summary records.¹⁷ For the purposes of this analysis, we classified patients as receiving dose-escalated or standard dose EBRT within risk groups. We considered a total dose ≥ 75.6 Gy to be dose-escalated EBRT and a total dose < 75.6 Gy as standard dose EBRT. We selected these dose thresholds because EBRT doses > 75.6 Gy have been published by the Quality Research in Radiation Oncology Genitourinary Committee as a clinical performance measure and indicator of care quality for prostate cancer.¹²

Independent Variables

Patient characteristics included age at diagnosis, and race. Clinical characteristics included clinical tumor stage (American Joint Committee on Cancer, 6th edition), Gleason sum, pre-treatment PSA, estimated comorbidity, receipt of androgen deprivation therapy (ADT), EBRT treatment technique, and treatment facility type. We classified EBRT treatment technique as intensity modulated radiation therapy (IMRT) or non-IMRT. Patient comorbidities are reported as a truncated Charlson/Deyo Score of 0, 1, or 2 because of the small number of cases with a score > 2.¹⁸

We classified treatment facilities as high-volume academic, low-volume academic, high-volume comprehensive, low-volume comprehensive, or community based on their ACS-COC accreditation status and the average annual volume of prostate cancer patients receiving EBRT at each facility. Consistent with prior studies, treatment facilities were

classified into quartiles of case volume according to the number of patients within the cohort receiving treatment at the facility.^{19–23} Facilities within the highest quartile were classified as high-volume, while those with case volume in the lower three quartiles were classified as low-volume.²⁴ Very few community facilities were within the upper quartile of case volume, and therefore were not classified with respect to case volume.

Demographic characteristics included year of diagnosis, median household income, insurance status, and county or metropolitan area population. Because individual-level socioeconomic data are not available, the NCDB records median household income for a patient's area of residence by matching their ZIP code with files from the 2000 U.S. Census data. Insurance status is recorded as the patient's primary insurance carrier at the time of initial diagnosis and/or treatment.

Disease Risk Grouping

We examined EBRT dose by disease risk group because recommendations and evidence for EBRT dose vary between low, intermediate and high risk patients. We classified patients according to NCCN criteria with minor modification as follows: low risk (PSA $\leq$ 10 ng/ml, Gleason sum $\leq$ 7, T1-2a), intermediate risk (PSA 10.1–20 ng/ml, or Gleason sum 7, or T2b-2c), and high risk (PSA $>$ 20 ng/ml, or Gleason sum $>$ 7, or T3-4). We did not classify patients as “very low risk” as per NCCN criteria because data regarding PSA density and number of involved biopsy cores are not available in NCDB. In addition, we categorized patients with T3b-T4 disease as high risk rather than “very high risk” as in the NCCN guidelines.

Statistical Analysis

We report the proportion of patients receiving dose-escalated EBRT, and provide frequencies and proportions of patient, clinical, and demographic factors within each disease risk group. We performed univariate and multivariate logistic regression to evaluate factors associated with the use of dose-escalated EBRT. To account for clustering within institution, we used generalized estimating equations (GEE) methods to obtain correct robust sandwich variance estimates. Corresponding odds ratios and 95% confidence intervals are reported for these associations. In sensitivity analysis, we examined the 8,485 patients who could not be classified by disease risk group and observed patterns consistent with our overall findings (data not shown). Statistical analysis was performed using SAS version 9.2 (Cary, North Carolina). Associations were considered to be statistically significant when $p < 0.05$; all tests were 2-tailed.

RESULTS

Temporal Trends in the Use of Dose-escalated EBRT

Overall, 81.6% of men received dose-escalated EBRT during the study period. Use of dose-escalated EBRT increased from 70.7% of patients receiving treatment in 2006 to 89.8% of patients receiving treatment in 2011. Temporal trends in the use of dose-escalated EBRT by disease risk group, and radiation treatment modality are shown in Figure 3.

Total EBRT Dose by Disease Risk Group

EBRT doses in low, intermediate, and high risk disease groups were similar [Median (Interquartile Range, IQR): 76 Gy (2.4 Gy), 77.4 Gy (2.4 Gy), 77.4 Gy (3.3 Gy), respectively]. The median total EBRT dose for all disease risk groups increased from 75.6 Gy in 2006, to 77.4 Gy in 2011. A histogram of the distribution of EBRT dose by disease risk group is shown in Figure 2 (Available Online).

Dose-escalated EBRT in Men with Low Risk Disease

In the low risk disease group, 79.8% of men received dose-escalated EBRT 75.6 Gy (Table 1). The use of dose-escalated EBRT increased during the study period from 68.1% in 2006 to 91.0% in 2011. After adjusting for patient, clinical, and demographic factors, patients diagnosed in 2011 were statistically significantly more likely to receive dose-escalated EBRT than those diagnosed in 2006 [odds ratio (OR) 4.43, 95% confidence interval (CI) 3.55–5.53, $p < 0.0001$]. In addition, patients receiving treatment with IMRT were more likely to receive dose-escalated EBRT than those receiving non-IMRT (82.9% vs. 72.3%, OR 1.42, 95% CI 1.25–1.62, $p < 0.0001$). Clinical and patient characteristics such as clinical T-stage, receipt of ADT, facility type, patient age were not statistically significantly associated with receipt of dose-escalated EBRT.

Dose-escalated EBRT in Men with Intermediate Risk Disease

Among men with intermediate risk disease, 83.2% of these men received dose-escalated EBRT 75.6 Gy. The use of dose-escalated EBRT increased over time from 72.8% in 2006 to 90.2% in 2011. After adjusting for patient, clinical, and demographic characteristics, patients diagnosed in 2011 were statistically significantly more likely to receive dose-escalated EBRT compared to those diagnosed in 2006 (OR 2.95, 95% CI 2.51–3.46, $p < 0.0001$). Use of IMRT technique was again significantly associated with receipt of dose-escalated treatment (86.5% vs. 75.2%, OR 1.54, 95% CI 1.40–1.69, $p < 0.0001$). Patients with Gleason sum 7 were more likely to receive dose-escalated EBRT than those with Gleason sum 2–6 (29.9% vs. 25.3%, OR 1.03, 95% CI 1.02–1.04, $p < 0.0001$).

Dose-escalated EBRT in Men with High Risk Disease

Among men with high risk disease, 81.1% received dose-escalated EBRT 75.6 Gy. The use of dose-escalated EBRT in the high risk disease group increased over time from 70.6% in 2006 to 88.5% in 2010. After adjusting for patient, clinical, and demographic factors, patients diagnosed in 2011 were statistically significantly more likely to receive dose-escalated EBRT compared to those diagnosed in 2006 (OR 2.86, 95% CI 2.46–3.31, $p < 0.0001$). The use of IMRT was significantly associated with receipt of dose-escalated EBRT (85.5% vs. 73.1%, OR 1.62, 95% CI 1.48–1.77, $p < 0.0001$). Patients with advanced T-stage (T3–T4) were significantly less likely to receive dose-escalated EBRT (Table 3).

DISCUSSION

We conducted this study to understand the patterns of care associated with the use of dose-escalated EBRT in routine clinical practice for men with non-metastatic prostate cancer. Our results indicate that the large majority of prostate cancer patients in the NCDB undergoing

definitive radiotherapy receive appropriate and acceptable EBRT doses, supported by level I evidence and consensus practice guidelines. The proportion of patients receiving dose-escalated EBRT increased nearly 20% during the study period and as of 2011, approximately 90% of patients received dose-escalated EBRT 75.6 Gy. The adoption of IMRT appears to have been an important factor in facilitating higher EBRT dose prescriptions and was strongly associated with receipt of dose-escalated treatment.

Given societal pressures to establish national care standards and interest in pay-for-performance programs, processes of care for prostate cancer including EBRT dose are a natural focal point for health services research. In contrast to previous studies reporting use of dose-escalated EBRT from physician surveys, our study makes use of a large national cancer registry and documents actual EBRT doses delivered to 98,755 individual patients.^{15,16} Our study findings suggest growing and widespread use of dose-escalated treatment for men with localized prostate cancer receiving EBRT.

Multiple RCTs have found that EBRT dose escalation is associated with significantly improved tumor control rates among patients with localized prostate cancer.²⁻⁵ An RCT conducted by Kuban et al. compared clinical outcomes of 301 patients with localized prostate cancer receiving doses of 70 Gy or 78 Gy. Long term results indicate significant improvements in clinical and biochemical control for those patients with high risk disease or a pre-treatment PSA > 10 ng/ml.²⁵ A similar RCT, conducted by Zietman et al. compared outcomes of 393 men with early stage prostate cancer (T1b-T2b, PSA ≤ 15 ng/ml) receiving EBRT doses of 70.2 GyE or 79.2 GyE delivered with combined photons and protons. Zietman et al. reported significant improvements in long term biochemical control with higher dose EBRT, suggesting that even men with low risk disease are likely to benefit from dose escalation.² However, even with long term follow-up dose escalation has not been associated with improvements in overall survival. An RCT comparing dose-escalated EBRT to standard dose EBRT in prostate cancer with a primary endpoint of overall survival was completed by the RTOG, and final results from this trial will further inform clinicians regarding the absolute benefits of dose-escalated EBRT.²⁶

While dose-escalated EBRT has been recommended in NCCN guidelines since at least 2004, some debate persists regarding the optimal EBRT dose for any given patient, as well as selection of patients most likely to benefit from dose-escalated treatment. RCTs of dose escalation have used a range of doses 74–80+ Gy and therefore there is uncertainty regarding the optimal dose within that range. Although clinical guidelines often recommend specific EBRT doses, defining a single dose threshold to serve as an indicator of care quality may be more challenging, particularly in light of the myriad ways to prescribe and record dose to target volumes.

The lack of an observed overall survival benefit, as well as the potential risk of increased treatment related toxicity could serve as deterrents to dose escalation, particularly for men with competing mortality risks, or favorable risk disease. However, we found that similarly high proportions of men received dose-escalated EBRT regardless of disease risk group. Furthermore, patient factors such as advanced age or comorbidity did not significantly influence the use of dose-escalated treatment even among patients with low risk disease. Our

study results also suggest that EBRT dose escalation is being applied with relative uniformity across a range of patient subgroups, and treatment facility types. Clinical factors such as stage, Gleason sum, PSA, or receipt of ADT were not consistently associated with use of dose-escalated EBRT; nor were treatment facility characteristics such as case volume or academic affiliation. While widespread diffusion of IMRT and imaged guided radiotherapy (IGRT) may facilitate dose escalation across risk groups, our findings also raise the question of whether research focused on more tailored dosing strategies might increase the therapeutic index, especially in this era of personalized medicine.

Our study has limitations. First, there may be factors influencing decisions regarding EBRT dose for prostate cancer patients not identified within NCDB such as performance status, previous RT or urologic procedures, or history of connective tissue disease. However, contraindications to dose-escalated EBRT are anticipated to be uncommon. Second, the availability and use of IGRT may influence the use of dose-escalated EBRT. Unfortunately, NCDB does not capture IGRT; thus we cannot examine this potential relationship further due to inherent limitations of the data source. Third, different methods in prescribing and reporting radiation dose in treatment summaries may be associated with variability in the total dose reported. However, we do not expect this variability to cause bias because it is likely non-differential among risk groups. Moreover, we adjust for year of diagnosis and use of IMRT which are likely to be key factors driving the methods of prescribing and reporting radiation dose. Fourth, NCDB records total radiation dose but does not record dose per fraction. Thus patients receiving hypofractionated radiation therapy in our study may have a lower total dose recorded but in reality have received a comparable dose in terms of relative biological effectiveness (RBE). We excluded patients receiving SBRT, and those receiving total doses < 59.4 Gy in an effort to address this issue; however, this remains a limitation of our analysis. Finally, it should be noted that while the NCDB captures data regarding 70% of incident cancer cases in the U.S., these data are only collected from patients treated at COC accredited institutions. Compared to non-COC accredited institutions, COC-accredited institutions tend to be larger, more frequently urban in location, and more likely to have cancer related services available.²⁷ Although we did not observe significant differences in dose-escalated EBRT use by facility case volume, or urban/rural geography, the selected nature of the data source may limit generalizability of our study findings.

In conclusion, our study describes recent practice patterns of EBRT dose in a large cohort of men with non-metastatic prostate cancer grouped by disease risk category. We found a substantial increase in the use of dose-escalated EBRT between 2006 and 2011. As of 2011, approximately 90% of patients with non-metastatic prostate cancer in the NCDB received dose-escalated EBRT 75.6 Gy. The use of dose-escalated EBRT has been strongly associated with the adoption of IMRT. While best clinical judgment is necessary to select the optimal EBRT dose for individual patients, our results suggest that the vast majority of patients undergoing EBRT in the U.S. receive doses that are consistent with the available evidence and consensus practice guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator. We thank Robert Sunderland, MS for his programming assistance.

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SUMMARY

We examined the dose of external beam radiation therapy (EBRT) received by men with non-metastatic prostate cancer treated in the United States between 2006–2011. We found that the use of dose-escalated EBRT (≥ 75.6 Gy) increased by almost 20% during the study period. As of 2011, approximately 90% of patients with non-metastatic prostate cancer undergoing EBRT receive dose-escalated treatment

Figure 3.

Temporal Trends in the Use of Dose-escalated EBRT by Disease Risk Group

Table 1

Receipt of EBRT Dose 75.6 Gy for Low Risk Disease

Characteristic	n	% Receiving EBRT Dose 75.6 Gy	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Men with Low Risk Disease	24,991	79.8%		
Clinical Stage				
T1	21,237	79.9%		
T2	3,754	79.3%	0.97 (0.90–1.05)	1.01 (0.94–1.09)
Gleason Score				
2–5	741	75.6%		
6	24,250	80.0%	1.29 (1.09–1.53)*	1.14 (0.95–1.36)
Comorbidity Index				
None	22,135	79.8%		
Moderate (1)	2,431	80.5%	1.08 (0.99–1.18)	1.01 (0.93–1.11)
High (2)	425	76.5%	0.90 (0.73, 1.11)	0.81 (0.66–1.00)
EBRT Treatment Technique				
Non-IMRT Photon Therapy	7,144	72.3%		
IMRT	17,847	82.9%	1.56(1.36–1.78)**	1.42(1.25–1.62)**
Androgen Deprivation (ADT)				
ADT not administered	20,423	80.0%		
ADT administered	3,723	77.7%	0.90 (0.83–0.97)*	1.06 (0.98–1.16)
Unknown	845	85.0%	0.89 (0.77–1.04)	1.03 (0.87–1.21)
Treatment Facility				
High-Volume Academic	5,004	81.8%		
Low-Volume Academic	1,542	75.2%	0.89 (0.61–1.32)	0.95 (0.53–1.69)
High-Volume Comprehensive	10,346	80.6%	1.18 (0.82–1.71)	1.12 (0.60–2.10)
Low-Volume Comprehensive	4,866	80.8%	1.13 (0.80–1.58)	1.22 (0.72–2.08)
Community/Other	3,190	76.1%	1.07 (0.75–1.52)	1.10 (0.66–1.86)
Patient Characteristics				
Age at Diagnosis				
30–49	274	83.2%		
50–64	8,073	82.1%	0.94 (0.74–1.19)	0.95 (0.75–1.19)
65–79	15,858	78.8%	0.82 (0.65–1.05)	0.90 (0.70–1.16)
80	786	75.4%	0.70 (0.53, 0.93)*	0.81 (0.62–1.08)
Race				
White	19,932	79.9%		
Black	3,974	79.6%	1.04 (0.96–1.12)	0.98 (0.91–1.06)
Other	710	76.6%	1.18 (0.99–1.40)	1.14 (0.97–1.35)
Unknown	375	84.5%	1.06 (0.88–1.29)	1.15 (0.93–1.42)
Year of Diagnosis				
2006	5,099	68.1%		
2007	5,201	76.9%	1.44 (1.29–1.61)**	1.42 (1.28–1.58)**

Characteristic	<i>n</i>	% Receiving EBRT Dose 75.6 Gy	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
2008	4,669	79.4%	1.76 (1.53–2.03) **	1.72 (1.50–1.97) **
2009	3,636	83.2%	2.12 (1.79–2.50) **	2.08 (1.77–2.45) **
2010	3,242	89.0%	3.35 (2.76–4.06) **	3.28 (2.72–3.95) **
2011	3,144	91.0%	4.44 (3.52–5.61) **	4.43 (3.55–5.53) **
Demographic Characteristics				
Median Income (\$)				
< 30,000	3,288	78.3%		
30,000–34,999	4,254	79.9%	0.99 (0.91–1.09)	1.02 (0.93–1.12)
35,000–45,999	6,715	80.2%	1.02 (0.93–1.12)	1.05 (0.95–1.15)
46,000	9,831	79.8%	0.99 (0.91–1.09)	1.01 (0.92–1.12)
Unknown	903	83.1%	1.06 (0.88–1.29)	1.14 (0.95–1.37)
Insurance Status				
Medicaid	607	80.4%		
Not Insured	353	81.3%	0.95(0.71–1.28)	0.87 (0.63–1.20)
Medicare	13,946	78.9%	0.80 (0.64–0.996) *	0.85 (0.67–1.08)
Commercial Insurance	9,644	80.9%	0.91 (0.72–1.14)	0.90 (0.71–1.15)
Unknown	441	83.4%	1.01 (0.73–1.40)	1.05 (0.76–1.43)
Size of County (Thousands)				
< 250	7,155	79.0%		
250	16,909	80.2%	1.06 (0.96–1.17)	1.12 (1.001–1.26) *
Unknown	927	79.9%	1.10 (0.94–1.28)	1.03 (0.87–1.21)

*
p-value < 0.05

**
p-value < 0.001

Table 2

Receipt of EBRT Dose 75.6 Gy for Intermediate Risk Disease

Characteristic	n	% Receiving EBRT Dose 75.6 Gy	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Clinical Characteristics				
Men with Intermediate Risk Disease	40,835	83.2%		
Clinical Stage				
T1	25,877	84.1%		
T2	14,958	81.8%	0.91 (0.87–0.95)	0.96 (0.91–1.01)
PSA				
< 10.0 ng/ml	28,724	84.1%		
10.0 – 20.0 ng/ml	12,111	81.3%	0.88 (0.84–0.92)**	0.99 (0.94–1.04)
Gleason Score				
2–6	6,975	79.5%		
7	33,860	84.0%	1.32 (1.25–1.40)**	1.21 (1.13–1.30)**
Comorbidity Index				
None	35,497	83.1%		
Moderate (1)	4,407	84.0%	1.05 (0.98–1.12)	0.98 (0.92–1.06)
High (2)	931	83.5%	1.02 (0.89–1.17)	0.94 (0.81–1.09)
EBRT Treatment Technique				
Non-IMRT Photon Therapy	11,754	75.2%		
IMRT	29,081	86.5%	1.70 (1.54–1.87)**	1.54 (1.40–1.69)**
Androgen Deprivation (ADT)				
ADT not administered	22,425	83.5%		
ADT administered	17,458	82.7%	0.95 (0.90–1.01)	1.02 (0.96–1.08)
Unknown	952	88.3%	0.97 (0.85–1.11)	1.12 (0.96–1.31)
Treatment Facility				
High-Volume Academic	8,128	85.2%		
Low-Volume Academic	2,954	81.6%	0.91 (0.60–1.38)	0.87 (0.46–1.63)
High-Volume Comprehensive	16,206	85.3%	1.11 (0.76–1.65)	0.92 (0.48–1.76)
Low-Volume Comprehensive	8,134	81.3%	0.91 (0.63–1.30)	0.94 (0.52–1.69)
Community/Other	5,368	78.5%	0.75 (0.52–1.08)	0.64 (0.35–1.15)
Patient Characteristics				
Age at Diagnosis				
30–49	252	84.1%		
50–64	9,673	84.7%	1.19 (0.93–1.53)	1.24 (0.95–1.62)
65–79	27,626	83.3%	1.09 (0.85–1.40)	1.18 (0.90–1.56)
80	3,284	78.7%	0.88 (0.68–1.14)	0.98 (0.74–1.31)
Race				
White	32,200	83.4%		
Black	6,803	83.9%	1.01 (0.95–1.07)	0.96 (0.90–1.03)
Other	1,250	75.8%	0.94 (0.83–1.06)	0.91 (0.79–1.04)

Characteristic	<i>n</i>	% Receiving EBRT Dose Gy	75.6	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Unknown	582	84.4%		0.94 (0.77–1.15)	1.00(0.82–1.22)
Year of Diagnosis					
2006	6,994	72.8%			
2007	7,684	79.4%		1.36 (1.25–1.47) **	1.32 (1.21–1.44) **
2008	7,157	83.4%		1.70 (1.52–1.89) **	1.63 (1.46–1.82) **
2009	5,969	85.8%		2.06 (1.80–2.34) **	1.95 (1.71–2.23) **
2010	6,596	89.6%		2.71 (2.34–3.13) **	2.60 (2.25–3.02) **
2011	6,435	90.2%		3.06 (2.61–3.59) **	2.95 (2.51–3.46) **
Demographic Characteristics					
Median Income (\$)					
30,000	5,840	81.1%			
30,000–34,999	7,059	82.7%		1.02 (0.95–1.11)	1.02 (0.94–1.11)
35,000–45,999	11,066	84.4%		1.08 (0.99–1.16)	1.07 (0.99–1.17)
46,000	15,336	83.4%		1.06 (0.99–1.14)	1.04 (0.96–1.13)
Unknown	1,534	83.6%		1.03 (0.91–1.17)	0.96 (0.81–1.13)
Insurance Status					
Medicaid	1,166	80.5%			
Not Insured	620	85.3%		0.97 (0.75–1.25)	0.96 (0.71–1.30)
Medicare	25,642	82.8%		0.79 (0.64–0.97) *	0.84 (0.66–1.08)
Commercial Insurance	12,730	84.4%		0.87 (0.71–1.08)	0.89 (0.69–1.14)
Unknown	677	83.0%		0.76 (0.59–0.97) *	0.78 (0.58–1.03)
Size of County (Thousands)					
<250	12,471	82.5%			
250	26,794	83.7%		1.08 (0.99–1.18)	1.08 (0.98–1.19)
Unknown	1,570	80.8%		1.13 (0.99–1.28)	1.21 (1.02–1.43) *

*
p-value < 0.05

**
p-value < 0.001

Table 3

Receipt of EBRT Dose 75.6 Gy for High Risk Disease

Characteristic	n	% Receiving EBRT Dose 75.6 Gy	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Clinical Characteristics				
Men with High Risk Disease	32,929	81.1%		
Clinical Stage				
T1	14,838	82.1%		
T2	11,866	81.4%	0.98 (0.93–1.03)	0.99 (0.95–1.05)
T3	4,978	80.1%	0.90(0.84–0.97)*	0.91 (0.83–0.99)*
T4	472	70.3%	0.61 (0.50–0.74)**	0.62 (0.50–0.76)**
X	775	71.7%	0.62 (0.52–0.74)**	0.82 (0.68–0.98)*
PSA				
< 10.0 ng/ml	12,402	82.3%		
10.0 – 20.0 ng/ml	5,827	80.6%	0.94 (0.89–0.99)*	0.96 (0.91–1.02)
> 20.0 ng/ml	13,955	80.6%	0.91 (0.87–0.96)**	0.92 (0.86–0.98)
Unknown	745	76.0%	0.73 (0.61–0.86)**	0.87 (0.73–1.04)
Gleason Score				
2–7	9,451	81.1%		
8–10	22,415	81.2%	1.05 (0.99–1.10)	0.96 (0.90–1.03)
Unavailable	1,063	81.0%	1.04 (0.89–1.21)	1.09 (0.93–1.28)
Comorbidity Index				
None	28,472	81.3%		
Moderate (1)	3,692	80.5%	1.00 (0.94–1.08)	0.94 (0.87–1.01)
High (2)	765	77.4%	0.91 (0.78–1.06)	0.87 (0.74–1.02)
EBRT Treatment Technique				
Non-IMRT Photon Therapy	11,655	73.1%		
IMRT	21,274	85.5%	1.82 (1.66–2.00)**	1.62 (1.48–1.77)**
Androgen Deprivation (ADT)				
ADT not administered	6,945	79.7%		
ADT administered	25,494	81.5%	1.07 (1.003–1.14)*	1.10 (1.03–1.18)
Unknown	490	83.7%	0.98 (0.82–1.18)	1.06 (0.88–1.28)
Treatment Facility				
High-Volume Academic	6,629	83.5%		
Low-Volume Academic	2,918	78.3%	0.79 (0.53–1.17)	0.87 (0.52–1.45)
High-Volume Comprehensive	11,665	84.1%	1.06 (0.73–1.55)	0.99 (0.60–1.64)
Low-Volume Comprehensive	7,295	78.6%	0.84 (0.59–1.19)	0.90 (0.57–1.41)
Community/Other	4,396	76.2%	0.67 (0.47–0.96)*	0.65 (0.41–1.02)
Patient Characteristics				
Age at Diagnosis				
30–49	259	78.0%		

Characteristic	n	% Receiving EBRT Dose 75.6 Gy	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
50–64	7,856	81.3%	1.36 (1.07–1.73) *	1.35 (1.05–1.75) *
65–79	20,829	81.6%	1.40 (1.11–1.79) *	1.34 (1.03–1.74) *
80	3,985	78.7%	1.15 (0.91–1.47)	1.08 (0.83–1.41)
Race				
White	25,623	81.5%		
Black	1,555	80.9%	1.02 (0.96–1.08)	1.03 (0.96–1.10)
Other	1,125	72.6%	0.99 (0.88–1.14)	0.99 (0.86–1.15)
Unknown	459	83.2%	1.10 (0.91–1.35)	1.17 (0.95–1.45)
Year of Diagnosis				
2006	5,686	70.6%		
2007	5,938	77.3%	1.42 (1.31–1.55) **	1.38 (1.27–1.51) **
2008	5,773	81.4%	1.73 (1.57–1.92) **	1.65 (1.49–1.83) **
2009	5,177	84.0%	2.11 (1.89–2.36) **	1.99 (1.78–2.23) **
2010	5,339	86.7%	2.55 (2.25–2.90) **	2.42 (2.12–2.76) **
2011	5,016	88.5%	3.00 (2.59–3.47) **	2.86 (2.46–3.31) **
Demographic Characteristics				
Median Income (\$)				
30,000	5,041	79.8%		
30,000–34,999	6,019	81.2%	1.01 (0.94–1.09)	1.01 (0.93–1.10)
35,000–45,999	8,840	81.6%	1.03 (0.96–1.11)	1.04 (0.95–1.13)
46,000	11,697	81.4%	1.03 (0.95–1.11)	1.02 (0.94–1.11)
Unknown	1,332	80.2%	0.99 (0.87–1.14)	0.99 (0.83–1.21)
Insurance Status				
Medicaid	945	80.3%		
Not Insured	673	78.6%	0.76 (0.61–0.95) *	0.75 (0.59–0.96) *
Medicare	20,646	81.2%	0.92 (0.79–1.06)	0.93 (0.78–1.12)
Commercial Insurance	10,104	81.0%	0.89 (0.77–1.04)	0.90 (0.75–1.08)
Unknown	561	84.8%	1.05 (0.83–1.32)	1.04 (0.82–1.33)
Size of County (Thousands)				
< 250	10,521	81.3%		
250	21,069	81.2%	0.95 (0.88–1.04)	0.95 (0.87–1.04)
Unknown	1,339	79.8%	0.94 (0.82–1.07)	0.94 (0.78–1.13)

* p-value < 0.05

** p-value < 0.001