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Authors

Tseng, Yolanda D
Paciorek, Alan T
Martin, Neil E
et al.

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Original Article

Impact of National Guidelines on Brachytherapy Monotherapy Practice Patterns for Prostate Cancer

Yolanda D. Tseng, MD[1]; Alan T. Paciorek, BS[2]; Neil E. Martin, MD, MPH[3]; Anthony V. D'Amico, MD, PhD[3]; Matthew R. Cooperberg, MD, MPH[2]; and Paul L. Nguyen, MD[3]

BACKGROUND: In 1999 and 2000, 2 national guidelines recommended brachytherapy monotherapy (BT) primarily for treatment of low-risk prostate cancer but not high-risk prostate cancer. This study examined rates of BT use before and after publication of these guidelines, as compared with 4 other treatment options. **METHODS:** From 1990 to 2011, 8128 men with localized prostate cancer (≤ T3cN0M0) were treated definitively within the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry with 1 of 5 primary treatments: BT, external beam radiotherapy (EBRT), EBRT with androgen deprivation therapy, EBRT+BT, or radical prostatectomy. Men were categorized into low-, intermediate-, and high-risk groups based on the guidelines' risk-group definitions. Within each risk group, logistic regression was used to estimate odds ratios (OR) comparing BT with other treatment options between the 1990-1998 and 1999-2011 periods, adjusting for age, disease characteristics, and clinic type. **RESULTS:** In total, 1117 men received BT alone for low- (n = 658), intermediate- (n = 244), or high-risk disease (n = 215). BT comprised 6.1% of all treatments in 1990-1998 versus 16.6% in 1999-2011 ($P < .01$). The odds of BT use remained increased after adjusting for potential confounders (OR = 3.06; $P < .001$) and was seen among low- (OR = 4.52; $P < .001$), intermediate- (OR = 2.67; $P < .001$), and even high-risk groups (OR = 2.11; $P < .001$). **CONCLUSIONS:** National guidelines did not appear to influence practice patterns, as BT monotherapy use increased relative to other treatments from the 1990-1998 to 1999-2011 periods in unfavorable risk groups including men with high-risk prostate cancer. ***Cancer*** **2014;120:824–32.** © *2013 American Cancer Society.*

KEYWORDS: brachytherapy, prostate cancer, guidelines, public health policy, radiotherapy.

INTRODUCTION

Although permanent prostate brachytherapy (BT) monotherapy is an established treatment option for low-risk prostate cancer,[1-4] its appropriateness for men with intermediate- or high-risk disease is less well defined. Historically, these patients were not considered suitable candidates given that the higher predicted risk[5] of extraprostatic disease may not adequately be treated with BT alone.

These concerns were in part confirmed by a large, observational cohort study published in 1998. Among the 1872 men treated with either BT monotherapy or radical prostatectomy (RP), biochemical outcomes were similar among men with low-risk disease, but inferior among men who received BT monotherapy for intermediate- or high-risk disease.[6] In 1999, the American Brachytherapy Society (ABS) published its recommendations that BT monotherapy was an appropriate treatment for low-risk patients, but required supplementation with external beam radiotherapy (EBRT; ie, EBRT+BT) if used as definitive treatment for high-risk disease.[7] They recommended that intermediate-risk patients be evaluated on a case-by-case basis. In the 2000 National Comprehensive Cancer Network (NCCN) practice guidelines, BT monotherapy was recommended only for low-risk disease.[8]

Several retrospective studies have since suggested that biochemical and even prostate-specific survival outcomes are not significantly different among men who received BT monotherapy for intermediate-risk disease, as compared with RP[9] or EBRT.[10,11] Given conflicting retrospective studies[12] and lack of prospective, randomized data to guide physicians on the relative benefit of BT monotherapy, we evaluated within a large US-based registry the impact of the 1999[7] and 2000[8] national guidelines on BT monotherapy utilization for definitive treatment of localized prostate cancer.

Corresponding author: Yolanda D. Tseng, MD, Harvard Radiation Oncology Program, 75 Francis Street, ASB L2, Boston, MA 02115; Fax: (617) 632-4247; ydtseng@partners.org

[1]Harvard Radiation Oncology Program, Boston, Massachusetts; [2]Department of Urology, University of California, San Francisco, California; [3]Department of Radiation Oncology, Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, Massachusetts

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MATERIALS AND METHODS

Database, Patient Cohort, and Variables

Data were reviewed from Cancer of Prostate Strategic Urologic Research Endeavor (CaPSURE), a longitudinal, observational database of men with biopsy-proven prostate adenocarcinoma. Eligible patients are consecutively recruited at 36 community, 3 academic, and 3 Veterans Administration (VA) institutions, treated per their clinicians' usual practices, and followed until death or withdrawal from the study. Each patient provides written informed consent under local and central institutional review board supervision. Additional details regarding methodology have been previously reported.[13]

As of our analysis, 14,242 men were enrolled in CaPSURE. Of these, 8128 (57%) had clinically localized prostate cancer (clinical stage $\leq$ T3cN0M0) at the time of diagnosis, had complete staging information (clinical tumor stage [cT], Gleason score, and prostate-specific antigen [PSA]), and were treated definitively with primary BT, RP, EBRT, EBRT with androgen deprivation therapy (ADT), or EBRT+BT during either the period before (1990 to 1998) or after (1999 to 2011) publication of the national guidelines.

From the CaPSURE database, we extracted the following variables that could influence physician, clinic, and/or patient preferences or recommendations for BT monotherapy: year of primary treatment, practice site location (west, south, northeast, midwest United States) and type (academic, VA, or community), number of comorbid conditions, clinical tumor stage, Gleason score of diagnostic biopsy, serum PSA, age at diagnosis, ethnicity, body mass index, education level, household income, and insurance type.

Definition of Risk Groups

To evaluate adherence to the 1999 and 2000 national practice guidelines, we tested differences in rates of BT monotherapy use relative to other treatments between the 1999-2011 and 1990-1998 time periods (temporal trends). To adjust for the potentially confounding effects of disease risk factors, we stratified by the low-, intermediate-, and high-risk groups defined by both ABS[7] and NCCN.[8] Given that the intermediate-risk group is a broad but heterogeneous group and that a subset of patients within this group may adequately be treated by BT monotherapy,[14] we subdivided the group into 2 categories: favorable- and unfavorable-intermediate. We based definitions for these subgroups on a patterns-of-care survey among prostate BT experts[15] and on the eligibility criteria for RTOG 0232,[14] a phase 3 study evaluating the role of supplemental EBRT with BT for intermediate-risk disease. The 2 resources are not completely in agreement, so in this analysis conservative criteria from each were used; patients who had only Gleason sum 3+4 or only PSA level of 10 to 20 were designated as favorable-intermediate, whereas patients who had both of these criteria or Gleason sum 4+3 were unfavorable-intermediate.

Statistical Analysis

Participants eligible for BT were described using the selected sociodemographic, clinical, and disease variables. Differences across all 5 primary treatment types were tested using the F-test for continuous variables or Pearson chi-square test. Differences between patients treated with BT monotherapy and 1 of the 4 other treatment types were tested using the Cochran-Mantel-Haenszel chi-square test, Pearson chi-square test, or *t* test.

We hypothesized that among intermediate and high-risk patients, BT monotherapy use relative to other treatments would decrease after publication of the 1999 and 2000 national guidelines given that the guidelines discouraged BT monotherapy for treatment of high-[7,8] and intermediate-risk[8] disease. To test this hypothesis, rates of BT monotherapy use compared to either all other treatment types or a single type were compared across the 2 time periods, 1999-2011 and 1990-1998, using a logistic regression model that was adjusted for age, grade, stage, PSA level, and practice site type. To further control for site-to-site variability, the models were stratified by each practice site, which produced more robust standard errors. Trends across years within either time period were tested using the same multivariate logistic regression models but with treatment year as a linear variable. Then the data were divided using the 4 risk groups (low, favorable-intermediate, unfavorable-intermediate, or high), and all the regression models were tested again within each risk group.

We explored potential factors that might explain our study's observed deviations from national guidelines, in particular among men with intermediate- and high-risk disease. The proportion of unfavorable-intermediate or high-risk cases treated with BT monotherapy was plotted against each individual practice site's BT treatment volume. BT treatment volume was defined as the proportion of a clinic's patients that were treated with any BT (BT alone, BT+ADT, or EBRT+BT). All tests of statistical significance were 2-sided. All analyses were performed with SAS software, version 8.2 (SAS Institute, Cary, NC).

RESULTS

Disease, Clinical, and Sociodemographic Characteristics

Among the 8128 men in the CaPSURE database who were treated from 1990 through 2011 in this analysis, 1117 (14%) received BT monotherapy as definitive treatment. Table 1 summarizes demographic, disease, and socioeconomic characteristics by primary treatment group. Men who received BT monotherapy had lower risk disease, as measured by the composite risk or individually by grade, stage, or PSA, compared with men treated with any 1 of the 4 other definitive therapies (all $P < .001$). Men treated with BT monotherapy were younger than men treated with EBRT or EBRT+ADT, and older than men treated with RP (all $P < .001$).

Using the available covariates, men treated with BT monotherapy differed the most from men treated with RP; patients treated with BT monotherapy had lower risk disease, were older, had more comorbid conditions, had lower socioeconomic status based on income and education, were less likely to have private health care insurance, and more likely to be from the southern United States (all $P < .001$). We could detect no significant differences between men who received BT monotherapy and men who received EBRT+BT with respect to all characteristics (all $P > .05$) except risk and region; BT monotherapy patients had lower risk disease and were more likely to be from the South (both $P < .001$). Men treated with BT monotherapy differed from men treated with EBRT or EBRT+ADT in that they had lower risk disease (all $P < .001$), were younger (both $P < .001$), had higher income (versus EBRT $P = .017$, versus EBRT+ADT $P = .014$), and were more likely to have private insurance (both $P < .001$).

Temporal Utilization of BT Monotherapy

BT monotherapy comprised 6.1% of all definitive treatments in 1990-1998, which increased to 16.6% in 1999-2011 (Fig. 1; $P < .01$). Crude treatment rates of BT monotherapy compared to EBRT, EBRT+ADT, or RP were higher in the later period (all $P < .0001$; Table 1). Adjusting for risk, age, and clinic site type, the odds of BT monotherapy use in the later period increased by 3 times (OR = 3.06; 95% confidence interval [CI] = 2.52-3.72; $P < .0001$). Increased use occurred not only among the low-risk group (OR = 4.52; $P < .001$), but also among favorable-intermediate (OR = 2.58; $P < .001$), unfavorable-intermediate (OR = 2.43; $P < .001$), and high-risk groups (OR = 2.11; $P < .001$). In general, BT monotherapy increased over time relative to EBRT and RP for all risk groups (all $P < .01$; Table 2) and relative to EBRT+ADT only among the low-risk group ($P < .01$). These results were similar when the cohort was dichotomized so that patients treated in 1999 and 2000 were included in the early time period (ie, when national guidelines were published; 1990-2000 versus 2001-2011), although the odds ratios were smaller. Adjustment for number of comorbid conditions also did not significantly affect these results.

Although rates of BT monotherapy use relative to EBRT or RP increased significantly across all risk groups from the earlier to later period, BT monotherapy use decreased linearly within the 1999-2011 time period with respect to EBRT (OR = 0.89; 95% CI = 0.84-0.94) and RP (OR = 0.92; 95% CI = 0.92-0.98). Compared to RP, BT monotherapy rates were stable among the low-risk (OR = 0.99; 95% CI = 0.94-1.03) and favorable-intermediate risk groups (OR = 0.99; 95% CI = 0.92-1.06), but nonsignificantly decreased in the unfavorable-intermediate risk (OR = 0.90; 95% CI = 0.79-1.02) and significantly decreased among the high-risk group (OR = 0.83; 95% CI = 0.75-0.91). Compared to EBRT, rates nonsignificantly decreased among the low-risk (OR = 0.94; 95% CI = 0.86-1.01), favorable-intermediate-risk (OR = 0.89; 95% CI = 0.78-1.02), and unfavorable-intermediate-risk groups (OR = 0.85, 95% CI = 0.72-1.01) and significantly decreased among the high-risk group (OR = 0.77; 95% CI = 0.65-0.92).

Site-to-Site Variability of BT Monotherapy Utilization

We investigated what factors might drive the observed practice deviations from national practice guidelines, in particular among unfavorable-intermediate and high-risk men. The proportion of unfavorable-intermediate and high-risk patients treated with BT monotherapy widely differed across the 40 practice sites, ranging from 0% to 64% (Fig. 2). Clinics that treated a higher proportion of their patients with any BT tended to use BT monotherapy for treatment of unfavorable-intermediate or high-risk men (Fig. 3).

DISCUSSION

In this patterns-of-care study from a large, US-based registry of men with prostate cancer, BT monotherapy for definitive treatment of localized prostate cancer significantly increased from the 1990-1998 to 1999-2011 time periods, in particular relative to EBRT and RP. The temporal trends and disease and demographic characteristics of patients who received BT are consistent with prior studies

TABLE 1. Univariate Analysis of Sociodemographic and Clinical Characteristics of Men by Treatment Group

Characteristic	BT alone N = 1117		EBRT+BT N = 313		EBRT alone N = 596		EBRT+ADT N = 613		RP N = 5489		Pearson *P*
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	
Age at diagnosis, y											
Mean (SD)	68.1	(7.3)	68.3	(6.9)	70.7	(6.2)	70.7	(6.6)	61.3	(6.9)	<.01[a]
Race											<.01
Caucasian	989	(89)	278	(89)	531	(89)	486	(80)	4833	(88)	
African American	80	(7)	23	(7)	53	(9)	106	(17)	486	(9)	
Other	47	(4)	12	(4)	11	(2)	16	(3)	144	(3)	
Unknown	1		0		1		5		26		
Comorbid conditions											<.01
None	97	(12)	27	(12)	74	(15)	63	(14)	991	(23)	
1	215	(27)	47	(20)	116	(24)	109	(23)	1358	(31)	
2	225	(28)	71	(30)	124	(25)	134	(29)	1094	(25)	
3-11	258	(32)	89	(38)	173	(36)	158	(34)	936	(21)	
Unknown	322		79		109		149		1110		
BMI											<.01
<25	210	(27)	57	(25)	169	(38)	130	(30)	1092	(26)	
25-29.9	380	(49)	111	(48)	202	(45)	221	(50)	2191	(52)	
≥30	190	(24)	64	(28)	74	(17)	89	(20)	893	(21)	
Unknown	337		81		151		173		1313		
Gleason score											
2-6	901	(81)	105	(34)	407	(68)	234	(38)	3807	(69)	<.01
7	179	(16)	159	(51)	139	(23)	242	(39)	1357	(25)	
8-10	37	(3)	49	(16)	50	(8)	137	(22)	325	(6)	
PSA (ng/mL)											<.01
<10	955	(85)	202	(65)	386	(65)	307	(50)	4459	(81)	
10-20	133	(12)	83	(27)	143	(24)	172	(28)	765	(14)	
>20	29	(3)	28	(9)	67	(11)	134	(22)	265	(5)	
Clinical tumor stage											<.01
T1	620	(56)	109	(35)	252	(42)	257	(42)	2835	(52)	
T2	492	(44)	194	(62)	312	(52)	313	(51)	2574	(47)	
T3	5	(<1)	10	(3)	32	(5)	43	(7)	80	(1)	
Risk group											<.01
Low	658	(59)	38	(12)	219	(37)	97	(16)	2490	(45)	
Favorable intermediate	164	(15)	65	(21)	97	(16)	105	(17)	853	(16)	
Unfavorable intermediate	80	(7)	59	(19)	81	(14)	89	(15)	682	(12)	
High	215	(19)	151	(48)	199	(33)	322	(53)	1464	(27)	
Household income, $											<.01
<20,000	130	(19)	48	(22)	92	(23)	97	(24)	331	(8)	
20,000-50,000	308	(45)	103	(48)	189	(48)	178	(45)	1404	(36)	
>50,000	251	(36)	63	(29)	115	(29)	122	(31)	2186	(56)	
Unknown	428		99		200		216		1568		
Education level											<.01
High school or less	352	(45)	122	(51)	227	(48)	227	(50)	1503	(35)	
College	275	(35)	72	(30)	167	(35)	142	(31)	1811	(42)	
Graduate	162	(21)	43	(18)	82	(17)	84	(19)	1010	(23)	
Unknown	328		76		120		160		1165		
Insurance											<.01
Medicare	184	(16)	51	(16)	112	(19)	186	(30)	445	(8)	
Medicare plus	438	(39)	139	(44)	330	(55)	240	(39)	1360	(25)	
Private	440	(39)	99	(32)	119	(20)	112	(18)	3368	(61)	
VA	29	(3)	17	(5)	9	(2)	8	(1)	106	(2)	
Other	26	(2)	7	(2)	26	(4)	67	(11)	210	(4)	
Region of United States											<.01
West	142	(13)	49	(16)	61	(10)	64	(10)	790	(14)	
South	371	(33)	42	(13)	104	(17)	91	(15)	888	(16)	
Northeast	429	(38)	130	(42)	377	(63)	335	(55)	2515	(46)	
Midwest	175	(16)	92	(29)	54	(9)	123	(20)	1296	(24)	
Year of treatment											<.01
1990-1998	133	(12)	25	(8)	347	(58)	150	(24)	1537	(28)	
1999-2011	984	(88)	288	(92)	249	(42)	463	(76)	3952	(72)	

Abbreviations: ADT, androgen deprivation therapy; BMI, body mass index; BT, brachytherapy; EBRT, external beam radiotherapy; PSA, prostate-specific antigen; RP, radical prostatectomy; SD, standard deviation; VA, Veterans Administration.
[a] F-test

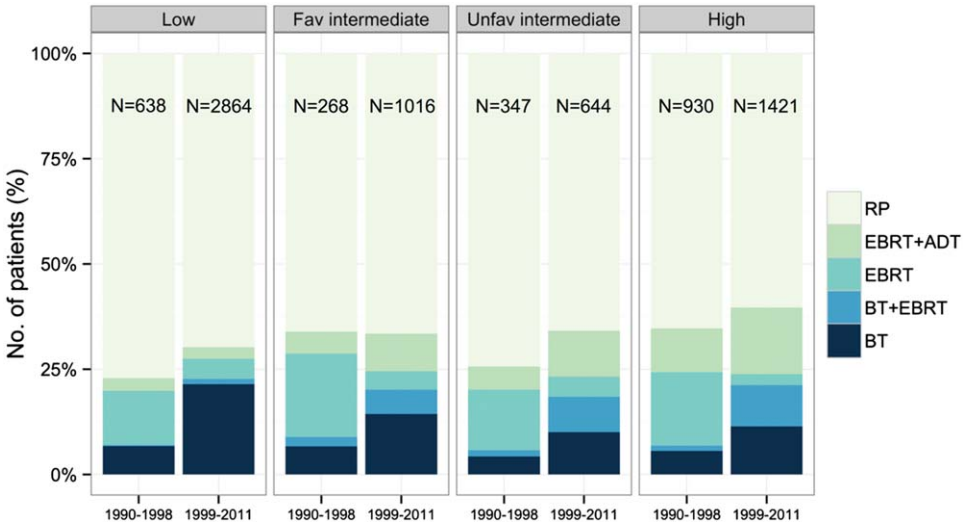

Figure 1. Relative utilization of each primary treatment type is shown between the 2 time periods, stratified by risk group. Abbreviations: ADT, androgen deprivation therapy; BT, brachytherapy; EBRT, external beam radiotherapy; RP, radical prostatectomy.

TABLE 2. Temporal Use of Brachytherapy Monotherapy Relative to EBRT+BT, EBRT alone, EBRT+ADT, or RP (ie, Reference Groups), Adjusting for Site Type, Age, PSA, Clinical Tumor Stage, and Gleason Score[a]

	Period of Treatment (1999-2011 Versus 1990-1998)		
BT Versus	Adjusted Odds Ratio	95% Confidence Interval	*P*
Low risk			
EBRT+BT	0.57	0.11-3.02	.51
EBRT alone	9.69	5.89-15.95	<.01
EBRT+ADT	3.11	1.38-6.98	<.01
RP	4.89	3.26-7.33	<.01
Favorable-intermediate risk			
EBRT+BT	1.24	0.42-3.62	.68
EBRT alone	9.56	4.44-20.56	<.01
EBRT+ADT	1.46	0.59-3.56	.40
RP	3.67	1.99-6.76	<.01
Unfavorable-intermediate risk			
EBRT+BT	0.72	0.21-2.45	.60
EBRT alone	9.78	3.67-26.04	<.01
EBRT+ADT	1.34	0.49-3.62	.55
RP	3.68	1.60-8.43	<.01
High risk			
EBRT+BT	0.28	0.14-0.57	<.01
EBRT alone	14.42	8.30-25.05	<.01
EBRT+ADT	1.37	0.85-2.21	.18
RP	2.69	1.79-4.03	<.01

Abbreviations: ADT, androgen deprivation therapy; BT, brachytherapy; EBRT, external beam radiotherapy; PSA, prostate-specific antigen; RP, radical prostatectomy; VA, Veterans Administration.

[a] Results are stratified by low- (N = 3502), favorable-intermediate (N = 1284), unfavorable-intermediate (N = 991), and high-risk subgroups (N = 2351). An adjusted odds ratio (AOR) >1 means an increased odds of brachytherapy monotherapy use compared to the reference group.

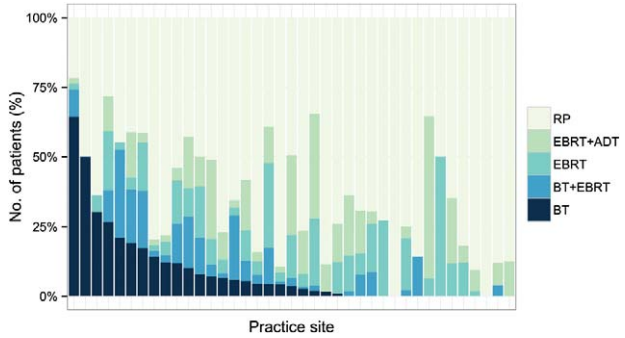

Figure 2. Relative utilization of brachytherapy monotherapy for unfavorable-intermediate or high-risk patients by clinic site (n = 40). Abbreviations: ADT, androgen deprivation therapy; BT, brachytherapy; EBRT, external beam radiotherapy; RP, radical prostatectomy.

from the Surveillance, Epidemiology, and End Results (SEER) cancer registry[16] and a 1999 patterns-of-care survey of radiation oncology facilities.[17] When evaluated by risk group, BT monotherapy use increased over time among men with low-risk disease. This finding is not wholly unexpected, because BT monotherapy for low-risk disease is readily recommended by national practice guidelines[3,7,8] and is cost-effective.[10]

More provocative is that treatment of high-risk groups increased, despite recommendations to the contrary from 2 national practice guidelines in 1999[7] and 2000.[8] Of note, this increased utilization was not sustained across all high-risk groups; compared with EBRT and RP, BT monotherapy use among high-risk men

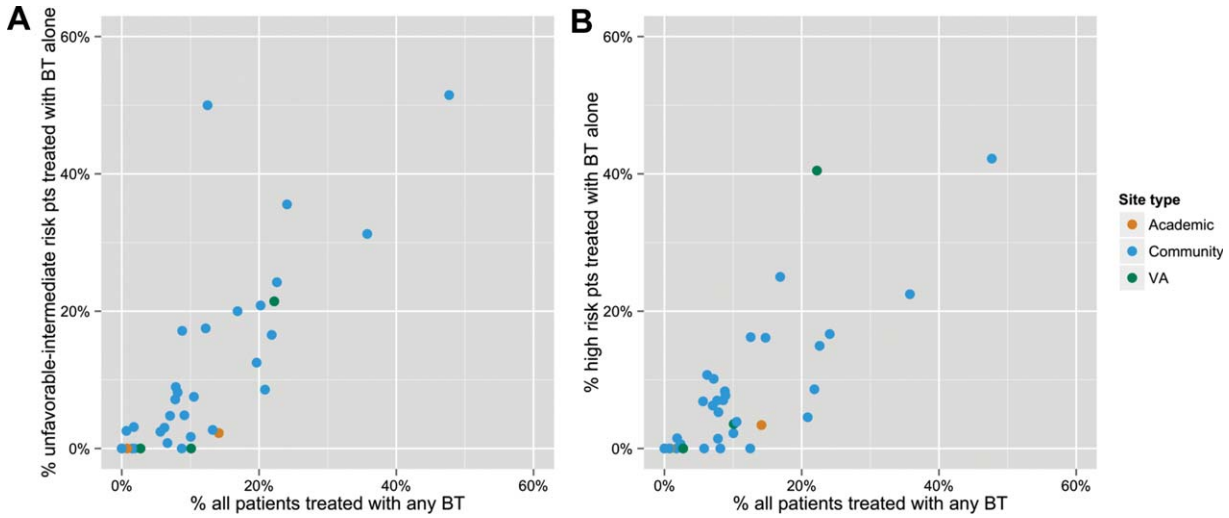

Figure 3. Scatter plots show proportion of men with (A) unfavorable-intermediate or (B) high-risk disease who were treated with brachytherapy (BT) monotherapy at a clinic site versus each clinic site's BT treatment volume. Brachytherapy treatment volume was defined as the proportion of all patients treated at a clinic site (academic, community, or Veterans Administration [VA]) who received any BT (ie, monotherapy or with supplemental external beam radiotherapy).

decreased linearly within the 1999-2011 time period. Clinical practice guidelines (CPGs), which synthesize the pertinent literature, are created to limit practice variations toward evidence-based treatments.[18] However, CPGs have not always been successfully adopted among physicians.[19] A contemporary, SEER-based study reported increased use of BT for accelerated partial breast irradiation (aPBI) between 2000 and 2007. Based on the American Society of Radiation Oncology (ASTRO) consensus guidelines, 65.8% of women who received aPBI BT were classified as cautionary or unsuitable candidates, and use within these 2 categories increased over time.[20] Deviation from CPGs is likely multifactorial and in part based on the quality of the guidelines and/or supporting evidence, characteristics of target health care professionals and practice settings, patient-related factors, and regulation.[18]

In the case of management of localized prostate cancer, choosing the "best" treatment is complicated by the absence of randomized data comparing the efficacy and toxicity of BT monotherapy with EBRT, EBRT+BT, EBRT+ADT, and/or RP. Although BT monotherapy appears to be at least as efficacious as RP or EBRT for men with low-risk disease,[9,12] results are mixed but generally poor for high-risk men treated with BT monotherapy. Relapse-free survival at 8 years was 48% in a multi-institutional series[21] and ranged from 60% to 90% at 12 years in other series.[22,23]

The literature is even more heterogeneous for BT monotherapy treatment of intermediate-risk disease. Poorer outcomes initially seen in some series[6] but not others[9,11] may in part be secondary to the quality of BT implants, which has been shown to affect biochemical outcome.[21] Furthermore, retrospective, observational data suggest that some[24] but not all[25] intermediate-risk patients may be safely treated with BT monotherapy; the RTOG 0232 trial, which evaluates the role of supplemental EBRT to BT for men with either PSA of 10 to 20 and Gleason score < 7 or Gleason score 7 with PSA < 10, is currently addressing this question in a prospective and randomized setting.[14] Although no consensus definition exists, similar favorable intermediate-risk men have also been identified by expert prostate brachytherapists as potential candidates for BT monotherapy.[15] Therefore, although BT monotherapy use increased among intermediate-risk men, a proportion of these men may comprise the favorable subset that is increasingly being accepted as a standard in practice.

This highlights an important, dynamic role of CPGs. In situations where prospective, randomized data does not exist, CPGs also should evolve to represent existing beliefs or values.[18] The updated 2012 ABS guidelines reflect this in their recommendation that intermediate-risk patients with favorable features may be treated with BT monotherapy.[3] Of note, the 2013 NCCN guidelines[4] still does not endorse use of BT monotherapy for treatment of intermediate-risk disease. In our study, however, increased BT monotherapy use among intermediate-risk men was not exclusively driven by treatment of favorable-intermediate risk disease; use also increased among the unfavorable-intermediate risk group. Furthermore,

although the increased use among favorable-intermediate risk men could in part reflect changes in Gleason grading that occurred in the late 1990s and early 2000s, it would not be able to explain the increased use among men with Gleason 4+3 and other intermediate-risk features (ie, unfavorable-intermediate risk group).

In the absence of strong scientific evidence, treatment of localized prostate cancer has been categorized as preference-sensitive care[26] in which a patient's values of the perceived benefits and harms may drive treatment selection. Therefore, patient preference may have contributed to the temporal trends seen with BT monotherapy. Patients may prefer a single treatment and/or the perceived side-effect profile. Although patient convenience, measured in some studies as distance to a radiotherapy facility, has explained some variations in treatment received such as use of mastectomy versus breast-conserving surgery and radiotherapy,[27] this has not necessarily been the case for BT utilization. In the study by Hattangadi and colleagues,[20] location outside of a metropolitan area was associated with decreasing (rather than increasing) odds of receiving aPBI BT for breast cancer; similarly, urban residence (versus nonurban) was a predictor of BT and BT+EBRT use among men being treated for localized prostate cancer.[28]

Finally, physician and possibly clinic preferences may drive BT monotherapy use. The odds of BT monotherapy utilization compared with all other treatments increased with age (OR = 1.11). This could be due to physicians' perceptions that older patients may not tolerate a long EBRT treatment course or a surgical procedure such as RP. At the same time, we observed considerable site-to-site variability for treatment of unfavorable-intermediate and high-risk patients (Fig. 2). Although the factors that contribute to this are unknown, we hypothesized that a site's BT experience (assessed using the proportion of all patients treated with any BT) could influence treatment decisions. Although exploratory in nature, clinics that treated a larger proportion of all patients with prostate cancer with any BT also treated a higher proportion of unfavorable-intermediate and high-risk patients with BT monotherapy. These observations require confirmation in other large, population-based registries.

Aligning treatment practices with those of CPGs is an active area of research. Basing CPGs on better quality data (ie, prospective, randomized) would likely promote concordance among CPGs and provide more weight with recommendations. When mature, data from RTOG 0232[14] will help clarify who may be an appropriate BT monotherapy candidate. Few studies have evaluated how practicing physicians including urologists and radiation oncologists view and utilize national guidelines. In a survey-based study of Canadian oncologists, 41% reported using guidelines routinely or most of the time, and 20% felt that they were too rigid to apply to individual patients.[29] These results cannot be extrapolated to our US-based study, but they are consistent with our findings that physicians may not be using guidelines in their treatment of men with high-risk prostate cancer. Finally, patients can be better educated with decision aids, which are designed to help them understand likely outcomes for each treatment option and the level of scientific uncertainty. A systematic review of trials demonstrates that patient decision aids improved both a patient's realistic perception of benefits and harms and the agreement between a patient's values and the option chosen.[26] Together, these interventions may reduce the variability in BT monotherapy used, in particular among patients who may not be the most appropriate candidates.

Although BT monotherapy use increased from the 1990-1998 to 1999-2011 time periods across all risk groups, it is important to note that there is some evidence of a decrease in BT monotherapy use across years within the 1999-2011 period, especially in the higher risk groups. This may reflect a slow acceptance of CPGs into clinical practice; prior studies have observed that on average, it takes 17 years for results of a randomized controlled trial to be implemented in the community.[30] However, this decline also coincides with the timing of Medicare reimbursement for intensity-modulated radiotherapy and the rise of robotic-assisted RP. Therefore, the relative decline in BT monotherapy during this period may also be secondary to increased utilization of newer technology,[31,32] although our dataset does not provide the information to make such inferences.

Our study has several strengths. The CaPSURE registry provides detailed data on a large, representative sample of US men with prostate cancer and is drawn from various site types including VA, academic, and community practices. A few points require further consideration. Physicians may consider other disease characteristics such as percent of positive biopsies and presence of perineural invasion when deciding if a patient is a suitable candidate for BT monotherapy,[15] but this is not reflected in the risk groups that we used for our analysis. Nonetheless, using the risk groups defined by the ABS in 1999 and NCCN in 2000 permitted us to directly compare whether BT monotherapy use was concordant with the aforementioned guidelines. We subdivided the intermediate-risk group into favorable and unfavorable categories based on

general consensus among expert brachytherapists[15] and the eligibility requirements for the ongoing RTOG 0232 trial.[14] However, these definitions have not been validated, and future studies are required to determine whether these subcategories are meaningful in predicting long-term biochemical outcome or prostate cancer–specific mortality. Finally, although we looked at whether BT monotherapy treatment patterns were concordant to practice guidelines, arguably a more important endpoint is to evaluate whether treatment patterns are associated with improved outcomes such as disease control, overall survival, and lower toxicity. These endpoints were not evaluated in our study and deserve future study.

Conclusions

Within a large, US-based cohort, brachytherapy monotherapy for treatment of localized prostate cancer increased from the 1990-1998 to 1999-2011 periods across low, intermediate, and high-risk groups, despite 2 national guidelines published in 1999 and 2000 recommending BT monotherapy preferentially for low-risk patients and advising against it for high-risk disease. These results suggest that clinical practice guidelines did not significantly change treatment decisions, in particular for the treatment of men with high-risk disease. They also highlight the importance of having prospective, randomized data to help define practice guidelines and minimize treatment variation. However, follow-up studies are required to evaluate other potential factors that influence deviations from guidelines including patient preference and site-to-site variability.

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CONFLICT OF INTEREST DISCLOSURES

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