Cost of palliative external beam radiotherapy (EBRT) use for bone metastases secondary to prostate cancer

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Background Evaluations of the costs of palliative external beam radiation therapy (EBRT) for treatment of bone metastases are limited.

Objective To summarize EBRT lifetime care patterns in deceased men with metastatic prostate cancer treated in a cancer hospital in the United States.

Methods A retrospective review of electronic health records identified deceased adult prostate cancer (ICD-9 185.xx) patients with bone metastases (ICD-9 198.5) and who were treated for bone pain and metastasis management with EBRT between January 1, 1995 and December 17, 2012. Common Procedural Terminology codes were used to identify all EBRT episodes (total billed EBRT services; initial and final evaluation) to calculate length of EBRT treatments and per episode costs (2011 US$). Bootstrapping approximated the 95% confidence interval for final cost estimates.

Results 176 men were identified; 19 (10.8%) had bone metastases in >1 site. Eighty-nine men (50.6%) received >1 EBRT episode (range, 1-6; median, 2), with first episode length ranging from 1-44 calendar days (mean, 13.4; SD, 8.4) at a mean cost of $7,084 (SD, $4,028). About 70% of costs were attributable to hospital charges and 30% to physician charges.

Limitations Small sample size limits broad applicability to large populations of men with prostate cancer.

Conclusion Care costs for EBRT constitute one of many costs that should be taken into account when planning for palliative care of prostate cancer and bone metastasis.

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In spite of early diagnosis and successful primary prostate cancer treatment, a large number of men will experience recurrent disease as metastasis to bone.[1-3] Once metastatic bone disease (MBD) has been diagnosed, prognosis is poor and quality of life may be reduced because of the development of skeletal-related events (SREs). SREs, defined as spinal cord compression, surgery to bone, pathologic fracture, or radiation to bone, are responsible for significant morbidity in prostate cancer patients, and their development may also increase mortality and shorten length of life.[4-7] SRE palliative care options include pain management with corticosteroids, analgesics and opioids, and bone-impacting therapies such as bisphosphonates and/or RANK-ligand inhibitors.[4-6,8-10] Bone stabilization surgery is also used to mitigate the effects of fractures and spinal cord compressions,[11] but bone metastasis treatment with radioisotopes or radiation therapy (RT) to reduce tumor size and prevent impending fractures is recognized as clinically effective.[12-15] Meta-analyses of clinical studies have indicated that up to 70% of patients are likely to benefit from external beam radiation therapy (EBRT), with as many as 25% achieving complete pain relief.[13,15] Therefore, EBRT serves as a mainstay of MBD treatment and palliation.[4]

The high costs of cancer care and treatment of associated morbidities are well documented.[16] However, the extent to which treatment adds value to cancer care is less well understood. Delea[17,18] (breast and lung cancer), Lage[19] (prostate cancer), and Hess[20] (breast and prostate cancer) and their respective colleagues have

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published estimates from administrative claims data of bone metastasis EBRT costs relative to other SRE care. However, only Groot and colleagues[21] have used chart review methods to estimate proportional costs of EBRT compared with all SRE care. Although these studies have added significantly to the understanding of complex medical care costs, only Groot[21] provided lifetime estimates for prostate cancer patients with bone metastases who required multiple episodes of EBRT therapy courses because of ongoing metastatic processes.

Therefore, the specific aim of this retrospective descriptive study was to summarize usual palliative bone EBRT care patterns, quantify lifetime episodes of EBRT care, and estimate total costs of EBRT based on institutional professional and technical charges for services. To identify lifetime episodes and costs, a cohort of deceased men with metastatic prostate cancer was identified via retrospective electronic health record (EHR) review. As such, no hypothesis was tested and no comparison group was created.

Methods

Data source

Data for this study were obtained via a retrospective EHR review of records stored in University of Utah Health Care (UUHC) system's Enterprise Data Warehouse (EDW).[22,23] The EDW is a high-fidelity, long-term, comprehensive, and integrated digital representation of day-to-day operational data that supports clinical systems across the UUHC enterprise, including Huntsman Cancer Hospital (HCH), which is one of 21 National Comprehensive Cancer Network (NCCN)-designated institutions.[24,25] EDW subject records from 1994 to present represent a comprehensive data set, including medical, treatment, diagnostic, nursing care, prescription data (including dispensing records if dispensed from UUHC pharmacies), pharmacotherapeutic data and pharmacy orders, diagnostic radiology and radiation oncology records, billing data, and community clinic outpatient records.

Disease-specific, International Classification of Diseases, 9th revision (ICD-9) diagnosis, and Current Procedural Terminology, 4th Edition (CPT4) procedure codes were obtained from the EDW, and missing data points were collected directly from archived patient EHRs (missing data not imputed). As necessary, the Utah Population Database (UPDB) was accessed for information concerning birth and death dates, including cause of death.[26] In addition, the Utah Cancer Registry[27] was used as a final check on prostate cancer primary and metastatic disease diagnosis dates. The protocol for this study was approved by the HCH Clinical Cancer Investigations Committee, the Resource for Genetic and Epidemiological Research, and the University of Utah Institutional Review Board on April 4, 2012.

Study design and patient identification

Based on preliminary chart review to rule out EDW selection errors (wrong diagnosis, eg, patients diagnosed with bone metastases but ultimately diagnosed with a cancer other than prostate cancer, such as bladder cancer), EBRT charge codes were searched in institutional billing records to preliminarily verify palliative EBRT usage by each patient. This resulted in a semifinal cohort of 446 patients diagnosed with prostate cancer (Index Date, ICD-9 185.xx) and bone metastases (ICD-9 198.5) for EHR review. Patients were excluded if treatment was still being received at time of data collection completion (still alive, thus cannot compute lifetime episodes of EBRT) or if EBRT was received outside of the UUHC-HCH system. All deceased (from any cause, except accidental death or trauma) men with metastatic prostate cancer who had received palliative EBRT to bone in UUHC-HCH system's department of radiation oncology from January 1, 1995 to December 17, 2012 were included in the final study cohort of 176 men (Figure 1) and underwent full EHR review to collect demographic data.

Demographic and clinical characteristics including birth and death dates, age at both primary and metastatic prostate cancer diagnoses, metastases information, and EBRT records were collected as available in both the EHR and the radiation oncologists' patient evaluation record. Comorbidities present before or on the date of bone metastasis diagnosis were used to calculate an adapted Charlson Comorbidity Index (CCI).[28,29] In the past, the University of Utah radiation oncology department held contracts with a local private hospital and a local Veteran's Administration hospital (VA) to provide palliative EBRT services. Thus, of the final study cohort of 176 men, 92 men (52.3%) received both oncology medical management and palliative EBRT management within the UUHC-HCH system. The remaining 84 men (47.7%) were either private hospital (n = 23) or VA (n = 61) patients who had UUHC-HCH EHRs and billing records for EBRT services, yet had little to no medical oncology management information in UUHC-HCH system records except for that recorded by radiation oncologists.

A preliminary review of the radiation oncologist's therapeutic evaluation in the UUHC-HCH EHR was conducted to eliminate patients who did not medically qualify for EBRT to bone or were recommended to have EBRT but refused medical care (n = 63), were recommended to have EBRT but chose to receive EBRT outside of the UUHC-HCH system (n = 32), or who received EBRT but EDW billing (charge) records were missing (n = 7; Figure 1).

Finally, EDW billing records for the final study cohort

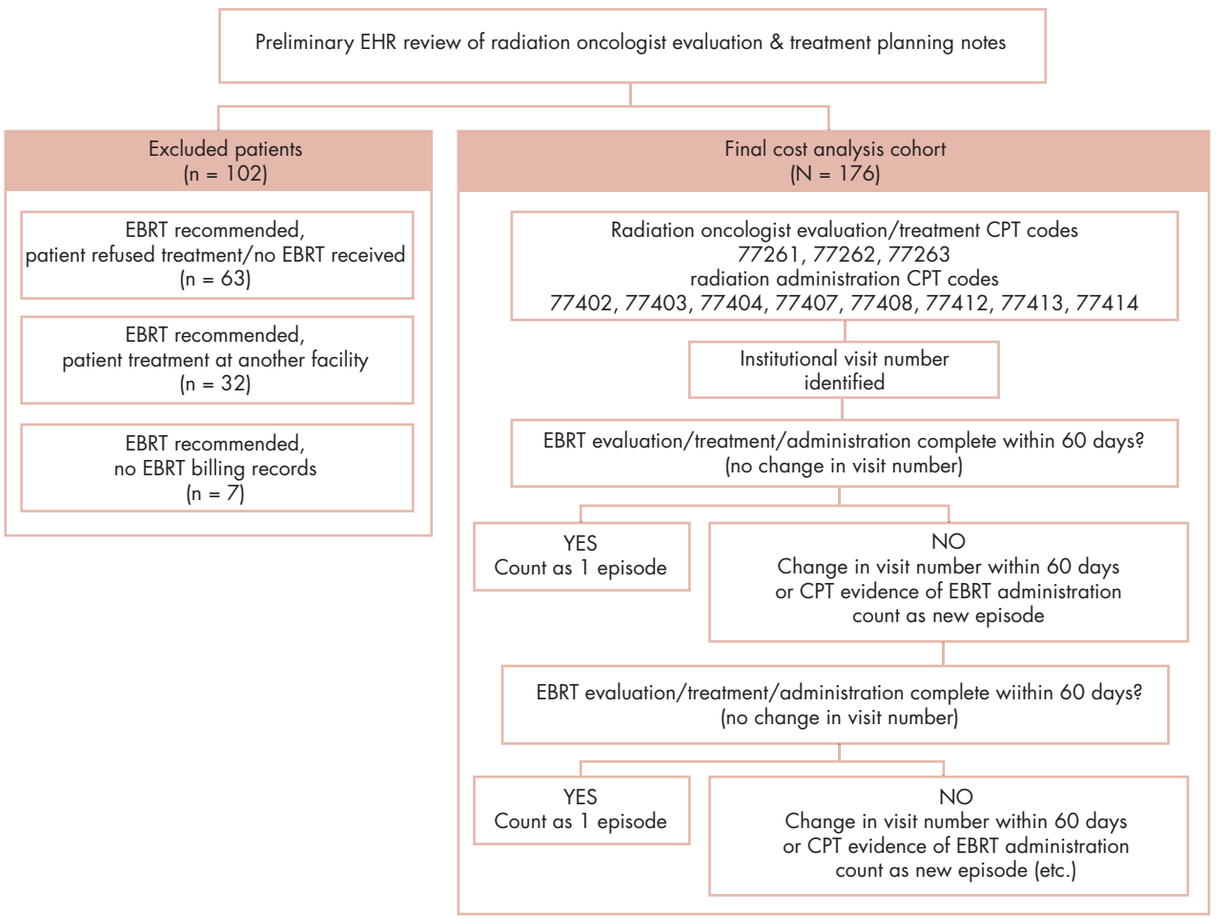

FIGURE 1 Assessment algorithm for EBRT episode of care identification.
CPT, Common Procedural Terminology; EBRT, external beam radiotherapy; EHR, electronic health record

(n = 176) were analyzed via an assessment algorithm (Figure 1) developed to count EBRT episodes of care (defined as "all billed professional and technical EBRT services provided between initial and final evaluation by radiation oncologist") and estimate the length of each EBRT treatment course. Three professional CPT codes (EBRT evaluation and treatment planning) and 8 technical (EBRT administration) codes (Figure 1) were used to identify treatment episodes in conjunction with the unique UUHC-HCH visit/encounter number assigned to each course of treatment. A 60-day gap in treatment was assumed to mean that the episode was completed, unless a next set of radiation oncologist evaluation or radiation administration codes occurred before the end of the 60-day period (if a second, third etc, episodes were to be found). The 60-day gap was based on HCH radiation oncology policy that care episodes not completed within 60 days would require an updated patient evaluation by a radiation oncologist. The hospital-assigned visit/encounter number was also checked against CPT-identified episodes. If the visit number changed and appropriate professional evaluation and technical administration CPT codes were present, then a new episode was identified and counted as such.

Statistical analysis

Descriptive statistics (mean, standard deviation [SD], median, and frequency distributions) were used to describe general demographic characteristics, metastatic prostate cancer variables of interest, and EBRT episode information for the study cohort. Bootstrapping (percentile method)[30] was used to approximate the 95% confidence interval for final EBRT cost estimates (standardized to 2011 US$ using the US consumer price index for medical care[31]). Similar to Groot and colleagues[21] and Delea and colleagues,[17,18]

TABLE 1 Final cohort demographics and clinical characteristics

Demographic/characteristic	Cohort HCH (n = 92)	PH (n = 23)	VA (n = 61)	Overall (N = 176)
Mean age at death = overall survival, years				
Mean (SD)	72.3 (10.8)	72.5 (9.4)	74.8 (8.0)	73.2 (9.8)
Median	73.0	72.0	76.0	74
Range	45-94	55-89	55-89	45-94
Age at primary diagnosis, years				
Mean (SD)	66.2 (10.2)	64.1 (8.2)	67.6 (8.4)	66.4 (9.4)
Median	66.0	63.0	67.0	66
Range	41-91	49-80	46-86	41-91
Age at MBD diagnosis, years				
Mean (SD)	70.4 (11.0)	71.4 (9.4)	73.2 (8.4)	71.5 (10.0)
Median	71.0	70.0	75.0	72
Range	44-93	53-88	51-87	44-93
Time to MBD diagnosis = MBD-free survival, months				
Mean (SD)	51.1 (54.2)	86.9 (64.6)	68.8 (49.9)	61.9 (55.4)
Median	34.0	98	61	50.5
Range	0-268	1-291	0-202	0-291
Time to death, post-MBD diagnosis, months				
Mean (SD)	23.2 (21.0)	13.7 (13.3)	18.5 (20.4)	20.3 (20.2)
Median	18	9	10	14.5
Range	1-118	1-49	0-80	0-118
CCI at bone metastases diagnosis				
Mean (SD)	5.8 (4.2)	6.4 (3.5)	7.3 (3.4)	6.4 (3.9)
Median	4.0	8.0	9	7
Range	0-16	1-13	1-13	0-16
Symptoms at metastatic diagnosis (from chart review)				
All patients[a]				
Bone pain	46 (50.0)	17 (73.9)	38 (62.3)	101 (57.4)
Mental status changes	1 (1.1)	0 (0)	0 (0)	1 (0.6)
Nausea/vomiting	1 (1.1)	0 (0)	0 (0)	1 (0.6)
Headache	3 (3.3)	0 (0)	0 (0)	3 (1.7)
Fatigue (from anemia, etc)	1 (1.1)	0 (0)	0 (0)	1 (0.6)
Weight loss	1 (1.1)	0 (0)	2 (3.3)	3 (1.7)
Urinary symptoms (frequency, hesitancy)	6 (6.5)	0 (0)	3 (4.9)	9 (5.1)
Other	3 (3.3)	2 (7.7)	0 (0)	5 (2.8)
No symptoms	1 (1.0)	0 (0)	0 (0)	1 (0.6)
Metastases sites[b] in addition to bone by ICD-9				
Lung	10 (10.9)	0 (0)	2 (3.3)	12 (6.8)
Liver	13 (14.1)	1 (4.3)	0 (0)	14 (8.0)
Brain	25 (27.2)	3 (13.0)	7 (11.5)	35 (19.9)
Adrenal gland	2 (2.2)	0 (0)	0 (0)	2 (1.1)
Other	21 (22.8)	0 (0)	2 (3.3)	23 (13.1)
Disease sites				
Unique patients	48 (52.2)	3 (13.0)	10 (16.4)	61 (34.7)
>1 site	17 (18.5)	1 (4.3)	1 (1.6)	19 (10.8)
Bone only	44 (47.8)	20 (87.0)	51 (83.6)	115 (65.3)

[a]Patients could present with multiple symptoms at diagnosis. [b]Patients could have multiple metastatic sites.

CCI, Charlson Comorbidity Index ; HCH, Huntsman Cancer Hospital; ICD-9, International Classification of Diseases, 9th revision; MBD, metastatic bone disease; PH, private hospital; SD, standard deviation; VA, Veterans Administration hospital.

EBRT costs were estimated using billed charges.

Results

The final study cohort consisted of 176 deceased men diagnosed with metastatic prostate cancer to bone who had received palliative EBRT at least once (by study design). There were no statistical differences in any demographic or EBRT treatment variables between men whose medical oncology care originated from HCH, the private hospital, or the VA. Overall, the mean age for men in the study cohort (Table 1) was 66.4 years (SD, 9.4; median, 66 years) when diagnosed with prostate cancer, with an average of 5 years (mean, 61.9; SD, 55.4 months; median, 50.5 months) of bone metastases-free survival. Average age at death was 73.2 years (SD, 9.8; median, 74 years). For many men, point of entry for medical evaluation relative to metastatic disease was bone pain (57.4 %, based on patient self-report). Forty-five percent were diagnosed with both prostate cancer and bone metastases within the first 30 days, and 61.4% were diagnosed with both within 1 year (Table 2). A CCI [28,29] calculated at bone metastasis diagnosis averaged 6.4 (SD, 3.9; median, 7). Sixty-five percent (115 of 176 men) of the cohort had bone metastases only (Table 1), and the remaining 61 men also had metastases to the brain (19.9%), liver (8.0%), lung (6.8%), and other areas.

The assessment algorithm used to count EBRT episodes of care and estimate the length of each EBRT treatment course has already been described (Figure 1). Due to inclusion criteria, all patients (N = 176) received at least 1 EBRT treatment episode, and nearly half (49.4%) received only 1 EBRT episode. Although 50.6% (89 of 176 men) received 2 EBRT episodes, fewer than 20% of all patients received 3 or more episodes of EBRT. Thus only data from the first 2 episodes were included in the final EBRT cost analysis, because not enough cases were present in the 3 or more EBRT episode cohort to allow bootstrapping estimations.

For EBRT Episode 1, 19 patients (10.8%) were evaluated by a radiation oncologist and treated the same calendar day (Figure 2). Just over 50% of patients completed EBRT within 14 calendar days, 86% completed within 21 calendar days, 97% completed within 30 calendar days, and all of the patients finished treatment within 44 calendar days. For EBRT Episode 2, 20 patients (22.5%) were evaluated and treated within the same calendar day. Nearly 71% were treated within 2 weeks, 89.9% completed within 21 calendar days, 98.9% completed within 30 calendar days, and all patients completed treatment within 39 calendar days. Reasons for delays during treatment were related to patient preference, chemotherapy administration, and patient hospitalization.

For EBRT Episodes 1 and 2, both length of treatment courses and billing charges (Table 3) were quantified, with all charges standardized to 2011 US$.[31] Bootstrapping (percentile method)[30] was used to approximate the 95% confidence interval (CI) for each variable. For EBRT Episode 1 (N = 176), an average of 13.4 calendar days (bootstrapping 95% CI, 12.5-14.3) was observed as required to complete a course of EBRT. For the 89 men who received a second treatment course, EBRT Episode 2 was completed in an average of 10.7 calendar days (bootstrapping 95% CI, 9.4-12.0**).**

For EBRT Episode 1, mean charges totaled $7,084 (SD, $4,028; bootstrapping 95% CI, $6,641-$7,528). About 70% of costs were attributable to hospital (technical) charges and 30% to physician (professional) charges. For EBRT Episode 2, mean charges totaled $6,760 (SD, $5,559; bootstrapping 95% CI, $5,839-$7,595), with professional-technical proportions remaining the same (30% to 70% split).

Discussion

Increasing restrictions on limited health care resources and recognition of the long-term socioeconomic impact of prostate cancer-related bone metastases have resulted in the need for clearer understanding of the financial costs associated with palliative care, comprehensive cancer treatment, and bone metastatic preventatives. This study attempted to identify all lifetime episodes of EBRT services for MBD-related care among a cohort of US patients who had died from prostate cancer. Use of an EHR-based data warehouse and access to text files that contained radiation oncologist treatment notes permitted study investigators to identify a robust and reproducible cohort of patients who received EBRT as part of a bone metastases palliative care treatment plan. Furthermore, development of an assessment algorithm that linked billing information with EHR records allowed investigators to review the accuracy of EBRT episode identifications. Previous US EBRT cost evaluations have historically relied on administrative claims databases (ie, insurance claims) and CPT code-based algorithms to estimate cost of care during the stated period of study (no lifetime cost estimate) and predominantly for those patients who received 2 or more EBRT episodes. Of note is that the present study identified that 49.4% of cohort patients received only 1 EBRT episode of care, which strongly suggests that a significant number of patients would have been missed in a claims-based study. Equally important, the present study was also able to identify the length (calendar days) required to complete multiple fraction EBRT episodes and by using the EHR, understand why delays may have occurred. This level of detailed understanding would have been unavailable in other published US-based studies.

Institutional charges (worst case costs) were used to estimate the costs of providing EBRT services in this

TABLE 2 Bone metastasis-free survival from time of primary prostate cancer diagnosis (N = 176)

Survival	Frequency, no. of patients (%)	Cumulative frequency, no. of patients (%)
Months (days)		
1 (0-30)	79 (44.9)	79 (44.9)
2 (31-60)	2 (1.1)	81 (46.0)
3 (61-90)	3 (1.7)	84 (47.7)
4 (91-120)	5 (2.8)	89 (50.6)
5 (121-150)	4 (2.3)	93 (52.8)
6 (151-180)	3 (1.7)	96 (54.5)
7 (181-210)	3 (1.7)	99 (56.3)
8 (211-240)	2 (1.1)	101(57.4)
9 (241-270)	0	0
10 (271-300)	5 (2.8)	106 (60.2)
11 (301-330)	0	0
12/1 y (331-365)	2 (1.1)	108 (61.4)
Years (days)		
2 (366-730)	21 (11.9)	129 (73.3)
3 (731-1,095)	13 (7.4)	142 (80.7)
4 (1,096-1,460)	7 (4.0)	149 (84.7)
5 (1,461-1,825)	8 (4.5)	157 (89.2)
6 (1,826-2,190)	4 (2.3)	161 (91.5)
7 (2,191-2,555)	3 (1.7)	164 (93.2)
8 (2,556-2,920)	6 (3.4)	170 (96.6)
9 (2,921-3,285)	2 (1.1)	172 (97.7)
10 (3,286-3,650)	2 (1.1)	174 (98.9)
11 (3,651-4,015)	1 (0.6)	175 (99.4)
12 (4,016-4,380)	0	0
13 (4,381-4,745)	1 (0.6)	176 (100)

cohort, similar to studies by Groot and colleagues[21] and Lage and colleagues.[19] Although an average of nearly $7,084 (SD, $4,028, 2011 US$) represents the highest amount that would have been charged for care (no institutional discounting), analyzed charges also represented an equalized distribution of charges among all prostate cancer EBRT patients, regardless of insurance type and potentially discounted pre-reimbursement amounts. Previous published estimates of per patient EBRT bone metastases treatment costs based on administrative claims data set analyses (ie, insurance claims) from Delea and colleagues for lung cancer (US $7,200 in 2002 and US $10,080 in 2011)[17] and breast cancer (US $6,920 in 2002 and US $9,688 in 2011)[18] are comparable with Lage and colleagues'[19] per patient prostate cancer EBRT estimates (US $5,930 in 2006 and US $7,057 in 2011). In the present study, estimates for Episode 1 per patient EBRT treatment are also within these same estimated ranges. Most similar to the present study is Groot and colleagues's[21] chart review-based estimate of EBRT costs for bone metastatic prostate cancer in the Netherlands at €4,740 per event (€1,998 = $5,585, 2011 US$), with an average of 3 EBRT events (episodes) recorded per patient (present study range, 1-6; median, 2). As Ploquin[32] stated in a literature review of non-US published EBRT cost-estimate studies, until standardized methods of EBRT cost analyses are agreed on, comparisons will not be exact. Therefore, further research is needed to better understand alternative treatment patterns and the comparative costs associated with them.

Some limitations are of note for this study. Small sample size limits broad applicability to large populations of men diagnosed with prostate cancer. For example, although the design of the study was to look at deceased patients with prostate cancer, those in our study cohort may have been sicker and have had higher levels of charges and resource use compared with those who were alive and thus excluded because lifetime EBRT episodes and costs could not yet be calculated. However, a relatively high percentage of men (44.9%) were diagnosed with prostate cancer and bone metastases within 30 days of each other, and thus may have been more ill due to previously undiagnosed prostate cancer. In addition, a possible explanation for the short period between both diagnoses may have come from the use of EHRs and billing records as data collection tools. For example, if a patient complained of severe bone pain but had no previous diagnosis consistent with bone pain, radiographic studies could have indicated that metastatic disease was present. In that patient's billing records, any bone metastasis diag-

TABLE 3 Analysis of EBRT Episodes 1 and 2

EBRT	No. of patients (%)	Mean (SD)	95% CI [a]	Median	Interquartile range 25%	Interquartile range 75%	Minimum	Maximum
Treatment length by Episode, calendar days								
Episode 1	176 (100)	13.4 (8.4)	12.5-14.3	14	7	18	1	44
Episode 2	89 (50.6)	10.7 (8.3)	9.4-12.0	10	4	15	1	39
Charges by episode, 2011 US$								
Episode 1	176 (100)	7,084 (4,028)	6,641-7,528	6,965	3,838	9,684	462	21,097
Professional	145 (82.4)	2,393 (1,014)	2,267-2518	2,257	1,636	3,111	141	7,483
Technical	165 (93.8)	5,470 (2,952)	5,134-5809	5387	3,371	7,119	230	17,409
Episode 2	89 (100)	6,760 (5,559)	5,839-7,595	5,574	2590	9,400	71	29,797
Professional	77 (86.5)	2,021 (1,418)	1,764-2,251	1,719	997	2,718	133	7,572
Technical	84 (94.4)	5,310 (4,256)	4,592-5,964	4,237	2,543	7,241	71	22,225

EBRT, external beam radiotherapy

[a]Bootstrapping 95% confidence interval

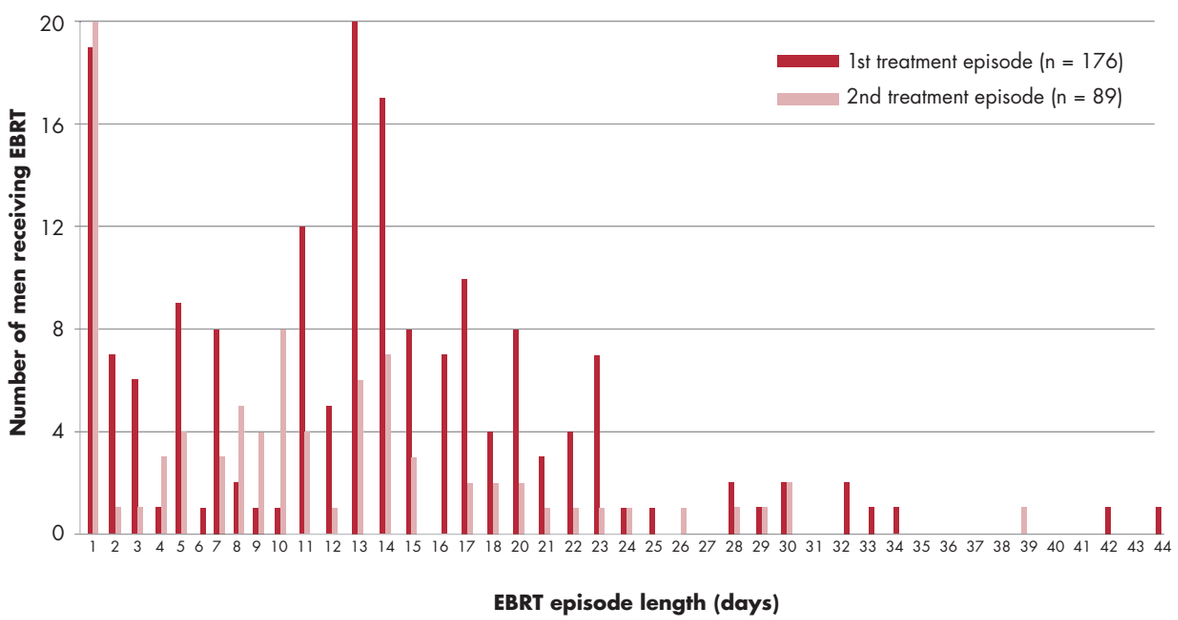

FIGURE 2 Length of EBRT treatment episodes (calendar days).
EBRT, external beam radiotherapy

nosis date would have preceded any cancer diagnosis. Another reason could be that in an older group of men (median age, 66 years), if prostate cancer had never been diagnosed because of lack of screening, bone aches and pains could be assumed as part of a natural aging process until documented as otherwise. In addition, because patient data spanned 1995-2012, some data points (ie, actual fractionation schedules and dosages, radiation oncologist pain medication prescriptions) were unavailable in archived data warehouse records due to incomplete transfer from paper to electronic systems over the timespan included in the study. Patient choice to use services outside of this institution (ie, pharmacies, medical oncology services) also limited collection of data for some patient-specific variables.

Finally, due to small sample size, bootstrapping was used to create statistical confidence intervals to accommodate the skew present in both calendar days per treatment episode and total charges for EBRT services. In addition, radiotherapy for the definitive treatment of prostate cancer has changed significantly with intensity-modulated radiation therapy being standard and the NCCN recommending daily image guidance. For the palliation of bone metastases, randomized trials have shown equivalent pain relief for single fractions such as 8 Gy compared with a 10-fraction regimen of 30 Gy. However, there has not been widespread adoption of hypofractionated regimens. The American Society of Radiation Oncology recommended in 2013 that practitioners should consider hypofractionated courses of RT for the palliation of bone metastases such as 8 Gy in a single fraction. Recommendations such as these and the uptake of short courses of stereotactic body radiosurgery for bony metastatic disease may begin to widely alter practice patterns.

In conclusion, the presented results suggest that EBRT for prostate cancer patients is but one of many costs that must be considered when planning for palliative care of bone metastases and may present a resourcing challenge to both prostate cancer patients and the health care financial system.

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