**ABSTRACT**

**PURPOSE:** To analyze rates of brachytherapy use for prostate cancer over time and evaluate patient characteristics, demographics and factors predictive for its utilization.

**METHODS:** Data was retrospectively analyzed from the National Cancer Database (NCDB) for patients with localized prostate cancer treated between 2010 and 2015. Patients were included if they had biopsy confirmed localized adenocarcinoma of the prostate, were treated with radiation as definitive local therapy, and were at least 18 years old. Utilization rates of external beam radiation (EBRT), brachytherapy (BT) and combination (EBRT + BT) were evaluated over time. Univariable (UVA) and backwards elimination multivariable (MVA) analysis were performed to determine characteristics predictive for brachytherapy use.

**RESULTS:** We analyzed 178,837 patients with localized adenocarcinoma of the prostate treated between 2010 and 2015 with radiation therapy. During this period, the use of EBRT increased from 67% to 78%, BT (both monotherapy and combination with EBRT) decreased from 33% to 22%, BT monotherapy decreased from 25% to 16% and EBRT + BT decreased from 8% to 6%. Age >70, government funded insurance or lack of insurance, intermediate or high-risk disease and treatment at an academic center were associated with significantly lower utilization of brachytherapy (all \( p < 0.001 \)), while higher median zip code income was associated with increased use (\( p = 0.02 \)). On multivariable analysis patients who were younger, had private insurance, were lower NCCN risk category and treated in non-academic cancer centers, had a higher rate of brachytherapy utilization. Notably, on both UVA and MVA brachytherapy practice decreased with increasing year of diagnosis (OR 0.881, 95% CI 0.853–0.910, \( p < 0.001 \)).

**CONCLUSION:** Rates of brachytherapy utilization for the treatment of prostate cancer continue to decrease over time. Treatment at an academic center was associated with reduced likelihood of brachytherapy use. This has significant implications for the training of future radiation oncology residents/fellows and direct consequences for both our patients and healthcare expenditure. © 2021 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

**Keywords:** Prostate cancer; Radiation; Brachytherapy; Health-care expenditure

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**Introduction**

In the United States, prostate cancer is the most common cause of noncutaneous malignancy in men, and the second most common cause of cancer related death. There are multiple treatment modalities that can be used to treat localized prostate cancer; including: surgery, external beam radiation (EBRT), brachytherapy (BT), and androgen deprivation therapy (ADT) [1]. Although these treatment options lead to similar oncologic outcomes, they differ in terms of toxicity profile and healthcare cost [2].

The use of brachytherapy for the treatment of low-risk prostate cancer is well established [3-4]. Over time the indications for brachytherapy have evolved with developing literature. Data from PROSTQA and ProtecT trials have shown that radiation may be associated with a more favorable toxicity profile compared to radical prostatectomy. While radiation was associated with higher rates of urinary irritation and rectal toxicity, lower rates of urinary
incontinence and sexual dysfunction were reported when compared to radical prostatectomy [5-6]. In these trials, the factors that were most determinant of overall satisfaction after localized treatment were sexual function, vitality and urinary continence, favoring the radiation side effect profile [5]. These studies solidify the role of brachytherapy for the treatment of low-risk prostate cancer.

Recent compelling evidence has shown that the use of brachytherapy as a boost after EBRT provides a biochemical control benefit for patients with intermediate and high-risk prostate cancer. Patients who received a brachytherapy boost were twice as likely to be free of biochemical failure at median follow-up of 6.5 years [7]. However, there was a substantially higher risk of severe urinary toxicity associated with brachytherapy boost. This study influenced the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) to revise their guidelines to include the recommendation for brachytherapy boost as an option for all eligible intermediate and high-risk prostate cancer patients [8,9]. Additionally, recent data has shown promising results for the use of brachytherapy as salvage for localized recurrent disease, demonstrating both safety and efficacy of its utilization [10-11].

Despite this growing body of literature demonstrating expanding indications for the use of brachytherapy, multiple prior studies have shown that over time rates of brachytherapy utilization have been decreasing in the United States [12-14]. The purpose of this study is to evaluate more recent trends of brachytherapy use in the United States and determine factors predictive for its utilization.

Methods

The National Cancer Database (NCDB) was queried for patients treated for localized prostate cancer from 2010 to 2015. Patients were included if they met the following criteria: 18 years of age or older, diagnosed with locoregionally confined adenocarcinoma of the prostate (ICD morphology code 81440) between the years of 2010 and 2015. We included locoregionally confined disease to mirror the paper by Mahmood et al. in order to make a meaningful comparison between their study cohort and our own, providing a longitudinal evaluation of brachytherapy trends over time [12]. We chose to start our data collection from 2010 to provide an update from the previously reported data by Mahmood et al., which looked at brachytherapy trends from 2004 to 2009. Patients were excluded if they had M1a, M1b or M1c disease. Patients without T-stage, PSA and Gleason score were excluded ($n = 323,679$). The study was deemed IRB-exempt.

In order to evaluate treatment trends over time, we initially assessed all patients who met the above criteria and were treated with definitive local therapy. This included surgical intervention or radiation therapy (“beam radiation,” “radioactive implants,” “combination of beam with implants or isotopes,” or “radiation, not otherwise specified [NOS]”). Rates of each treatment modality (surgery and radiation) were compared based on year of diagnosis to evaluate treatment trends over time.

Subsequently, patients who were treated with radiation therapy alone were analyzed to further evaluate radiation modality utilization over time. In recent years, the NCDB began collecting data on treatment technique for brachytherapy (low-dose rate (LDR) vs high-dose rate (HDR) vs not otherwise specified (NOS)) and EBRT (Intensity-modulated radiation (IMRT), vs three-dimensional conformal radiation (3D-CRT), vs protons, vs stereotactic body radiation (SBRT), vs NOS) and we compared treatment techniques utilization rate, both for subtypes of brachytherapy and EBRT.

Univariate logistic regression analysis was performed to determine if patient demographic information or tumor characteristics were predictive of brachytherapy utilization over time, using Wald χ² test to determine significance. The following variables were included: year of diagnosis, age, race, median income by zip code, insurance provider, treatment facility type, T-stage, PSA, Gleason score, NCCN risk grouping, and type of radiation received. Median income and age were divided into categories for analysis ($≤$63k and $>$63k) and ($≤$70 and $>$70), respectively. Race was broken down into categories (white, black, and other). Year of diagnosis was evaluated as a continuous variable and all other variables were evaluated as categorical variables. Subsequently, backwards elimination multivariable analysis was run using logistic regression analysis, while evaluating the same variables listed above. All results are reported as an odds ratio (OR) for brachytherapy use with 95% confidence intervals, based on a p-value of 0.05 demonstrating significance. All statistical analysis was completed using SPSS software version 26.

Results

A total of 645,932 patients with localized adenocarcinoma of the prostate diagnosed between 2010 and 2015 were included. Fig. 1 summarizes the distribution of treatment modality used for the years 2010 to 2015. The total number of patients diagnosed with prostate cancer has decreased by 2.2% from 2010 to 2015. Similarly, the number of patients treated with either surgery or radiation have decreased from 2010 to 2015 by 3.4% and 3.9%, respectively. However, the number of patients being observed with no intervention has increased by 6.1% over the same time period.

Subsequently, the cohort of patients who only received radiation treatment were analyzed, in order to evaluate trends in different radiation modalities. There were a total of 178,837 patients with locoregionally confined prostate adenocarcinoma treated with radiation therapy during this time period. Most patients (96%) had N0 disease, only 1.5% had N1 and the remaining 2.5% were Nx. The me-
The median age of this cohort was 67 years (29–90). According to NCCN risk stratification, 22% had low-risk disease, 42% intermediate-risk and 36% high-risk (Table 1) [1].

The most common radiation modality used was EBRT (72%), 7% of patients received EBRT and brachytherapy, 20% brachytherapy alone and 1% radiation, NOS. Further breakdown evaluating treatment technique showed that most patients who received EBRT, were treated with IMRT (68%) or EBRT, NOS (25%). Less common techniques were 3D-conformal (2%), protons (2%) or SBRT (3%). For patients who received brachytherapy, LDR was most often utilized (55%), followed by HDR (25%) and brachytherapy, NOS (20%).

During the period from 2010 to 2015, the use of EBRT (with or without BT) increased from 67% to 78%, while BT (with or without EBRT) decreased from 33% to 22%. BT monotherapy decreased from 25% to 16% and EBRT + BT decreased from 8% to 6% (Fig. 2). The decline in use of brachytherapy was associated with a 10% increase (38% to 48%) in the use of androgen deprivation therapy (ADT) from 2010 to 2015. Evaluating brachytherapy trends alone from 2010 to 2015, LDR use increased from 50% to 58%, HDR use increased from 24% to 27% and brachytherapy NOS decreased from 26% to 15%. The use of brachytherapy at academic centers specifically, decreased from 27.7% to 20.8% from 2010 to 2015.

Patient and tumor characteristics were evaluated using univariable analysis to determine predictors for the utilization of brachytherapy. Multiple independent factors were found to be significantly predictive for lower rates of brachytherapy utilization, including age >70 (OR 0.545, 95% CI 0.533–0.558, p <0.001), government funded insurance (OR 0.607, 95% CI 0.594–0.620, p <0.001) or lack of insurance (OR 0.407, 95% CI 0.368–0.449, p <0.001), intermediate (OR 0.438, 95% CI 0.427–0.449, p <0.001) or high-risk disease (OR 0.202, 95% CI 0.196–0.208, p <0.001) and treatment at an academic center (OR 0.889, 95% CI 0.856–0.923, p <0.001). Conversely, higher median zip code income was associated with increased use (OR 1.026, 95% CI 1.004–1.049, p = 0.02). Race was not significantly predictive of brachytherapy utilization.

On multivariable analysis, patients who were younger, had private insurance, with lower NCCN risk category, or treated in non-academic cancer centers had a higher rate of brachytherapy utilization. Notably, on both UVA and MVA brachytherapy practice decreased with increasing year of diagnosis (OR 0.881, 95% CI 0.853–0.910, p <0.001). The results of multivariable analysis are summarized in Table 2.

Discussion

A previous SEER analysis of the utilization of brachytherapy for the treatment of localized prostate cancer in the United States showed that utilization peaked in 2005 at 44.5% of radiation treatment delivered and subsequently decreased to 38% by 2009 [12]. Our study shows that brachytherapy treatment has continued to decline, reaching a low of 22% in the year 2015.

We found that patients with private insurance were more likely to receive brachytherapy compared to patients with government associated insurance policies. Additionally, patients from zip codes with higher median income were more likely to receive treatment with brachytherapy. This suggests that patients from lower socioeconimic backgrounds unfortunately have less access to prostate brachytherapy, which is concordant with prior studies [15].
Additionally, our study has shown that patients treated at an academic center are significantly less likely to receive brachytherapy. This has important implications for the future utilization of brachytherapy as a treatment modality. Resident education is dependent on ample case load at academic centers in order to develop the skillset to deliver safe and efficacious brachytherapy treatment [16]. Orio et al. showed that academic practices performing an average of ≤1 brachytherapy cases per month increased from 56.4% to 73.7% and practices performing an average of ≥1 cases per week decreased from 2004 to 2012, representing a significant decline in case load [17]. With fewer patients being treated with BT, the next generation of radiation oncologists will not have the necessary skills for brachytherapy to be a viable treatment option.

What factors may be causing the decreased utilization of brachytherapy? The answer to this question is likely multifactorial. The practice of brachytherapy requires a comprehensive infrastructure, including operating room space, time, specialized equipment including appropriate shielding, in addition to available ancillary staff and medical personal involving nursing, anesthesia, radiology, dosimetry and medical physics. This provides a larger barrier to entry compared to clinics who routinely offer external beam radiation therapy. Additionally, fee for service reimbursement models have evolved to favor the use of EBRT, further de-incentivizing the development of a brachytherapy practice [18].

Insufficient education during residency training due to lack of case load, inadequate requirements, and large variability in training programs has led many graduating residents to feel unequipped and uncomfortable treating with brachytherapy independently. In a recent study surveying post-graduate year 4 and 5 radiation oncology residents, 59% of residents felt that caseload was the greatest barrier to achieving proficiency and only 54% felt comfortable practicing independently [19]. Although the current ABR requirement for interstitial cases has recently increased from 5 to 7, this is still largely inadequate to develop proficiency in the practice of brachytherapy. Additionally, there is a steep learning curve that requires frequent practice and centers with small or infrequent volumes may find it difficult to maintain this skill set.

On a more positive note, an increasing number of patients are being observed for early stage localized prostate cancer, which is likely contributing to some extent to the decline in brachytherapy use. However, we are seeing a disproportionate decline in brachytherapy compared to an increase in EBRT use. This may be due to improved EBRT techniques such as SBRT and proton therapy. But, this is unlikely to provide the entire explanation, as we know from this study that these techniques only account for 5% of the EBRT being delivered. Additionally, this has significant implications for healthcare expenditure, as studies have shown that the cost of EBRT is almost double the cost of brachytherapy treatment [20]. Additionally, our study shows that the use of ADT increased by 10% over the period of time that brachytherapy use has shown a decline. The NCCN recommends 18–36 months of ADT for patients receiving EBRT alone and only 12–36 months for patients who are treated with brachytherapy boost [1]. Since the cost of ADT can reach up to $20,000 in the first year alone, and has significant impact on patient quality of life, brachytherapy use provides a benefit from both a financial and quality of life perspective [21-22].

The radiation oncology alternative payment model (APM) is a new model for reimbursement that focuses on value-based care. This model incentivizes brevity of
treatment in the setting of equivalent outcomes and patient satisfaction, reversing the previous incentives of increased fractionation. Prostate brachytherapy is cost effective and convenient as a result of shorter treatment duration. Therefore, there is a significant potential for brachytherapy utilization to increase within this new repayment model [22]. However, with declining utilization this potential may be blunted.

The American Brachytherapy Society (ABS) has recognized the declining use of brachytherapy and has implemented several programs to help provide learning opportunities to develop proficiency. There is a brachytherapy workshop that takes place annually and requires attendees to register with both a radiation oncologist and physicist. This requirement increases the chance of creating a new successful brachytherapy program and 80% of teams have implemented prostate brachytherapy within 6 months of the training [23]. Additionally, there is a “300 in 10” initiative, which aims to train 30 competent brachytherapists each year, over a 10-year period of time. With continued focus on the trend of brachytherapy utilization we can advocate for the allocation of resources towards brachytherapy training and skill development.

Several limitations to the current analysis need to be acknowledged. The present study was not able to account for other factors that could have contributed to decreased utilization including prostate size, pre-treatment urinary function, or other contradictions to prostate brachytherapy. The type of brachytherapy (HDR vs. LDR) was not included in the dataset. Furthermore, there are other inherit biases with the NCDB, including the fact that it is not a true representation of the US population [24].

### Conclusion

Rates of brachytherapy utilization for the treatment of prostate cancer continue to decrease over time. Government paid insurance, lower median income by zip code and treatment at an academic center were associated with reduced likelihood of brachytherapy use. This has significant implications for the training of future radiation oncology residents/fellows and direct consequences for both our patients and healthcare expenditure.

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Conflicts of interest

None of the authors have any conflicts of interest to disclose.

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