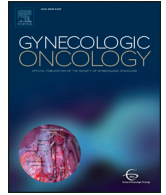




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Underutilization of brachytherapy and disparities in survival for patients with cervical cancer in California

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HIGHLIGHTS

- Brachytherapy after chemoradiation for locally advanced cervical cancer constitutes the standard of care.
- There are declining national trends for the utilization of brachytherapy.
- Patients not treated with a boost after chemoradiation have worse survival outcomes.
- Understanding disparities, access, and interventions to increase the receipt of brachytherapy is needed.

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ABSTRACT

Purpose. The treatment for locally advanced cervical cancer is external beam radiation (EBRT), concurrent chemotherapy, and brachytherapy (BT). We investigated demographic and socioeconomic factors that influence trends in BT utilization and disparities in survival.

Methods. Using the California Cancer Registry, cervical cancer patients FIGO IB2–IVA from 2004 to 2014 were identified. We collected tumor, demographic and socioeconomic (SES) factors. We used multivariable logistic regression analysis to determine predictors of use of BT. Using Cox proportional hazards, we examined the impact of BT vs EBRT boost on cause specific (CSS) and overall survival (OS).

Results. We identified 4783 patients with FIGO stage 11% IB2; 32% II, 54% III, 3% IVA. Nearly half (45%) of patients were treated with BT, 18% were treated with a EBRT boost, and 37% had no boost. Stage II and III were more likely to be treated with BT ($p = 0.002$ and $p = 0.0168$) vs Stage IB2. As patients aged, the use of BT decreased. Using multivariate analysis, BT impacted CCS (HR 1.16, $p = 0.0330$) and OS (HR 1.14, $p = 0.0333$). Worse CSS was observed for black patients ($p = 0.0002$), low SES ($p = 0.0263$), stage III and IVA ($p < 0.0001$). Black patients, low and middle SES had worse OS, ($p = 0.0003$).

Conclusions. The utilization of BT in locally advanced cervical cancer was low at 45%, with a decrease in CSS and OS. Black patients and those in low SES had worse CSS. As we strive for outcome improvement in cervical cancer, we need to target increasing access and disparities for quality and value.

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1. Background

Cervical cancer affects over 12,000 women in the United States with 4200 deaths annually. The standard of care for these patients consists of

radiation, external beam radiation (EBRT) with chemotherapy (CRT) followed by brachytherapy (BT). Furthermore, patterns of care studies established the essential role of BT in the management of cervical cancer, and linked its use to improvements in pelvic control and disease-free survival [1]. Image guided BT is a key component in the treatment of cervical cancer as it allows for dose escalation to the tumor while minimizing dose to surrounding critical organs at risk such as the sigmoid, bladder, and rectum. A typical BT application is shown in Fig. 1, and dose distribution in Fig. 2 [2].

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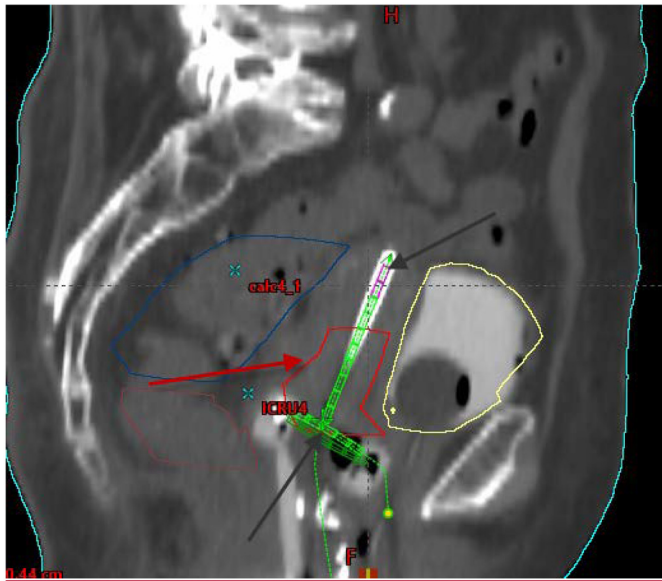


Fig. 1. A cervical cancer patient with brachytherapy equipment placed into the cervix and uterus. The red arrow points to the cervical tumor on the CT planning image. The black arrows point to the radiation after loading equipment. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

There has been decrease in utilization trends of BT, and potential disparities of the use of BT, with detrimental effects on cause specific (CSS) and overall survival (OS) [3–8]. A recent study looking at the Surveillance, Epidemiology, and End Results (SEER) database showed a downward trend in BT usage from 68% in 1988 to 45% in 2010, [3] with a subsequent decline in CSS and OS based on a propensity score matched cohort. A national cancer database (NCDB) report showed a decrease in BT utilization, from 96.7% to 86.1%, with a subsequent survival detriment. Another SEER analysis showed significant geographic disparities in the delivery of brachytherapy in the United States [5]. In addition, elderly cervical cancer patients have

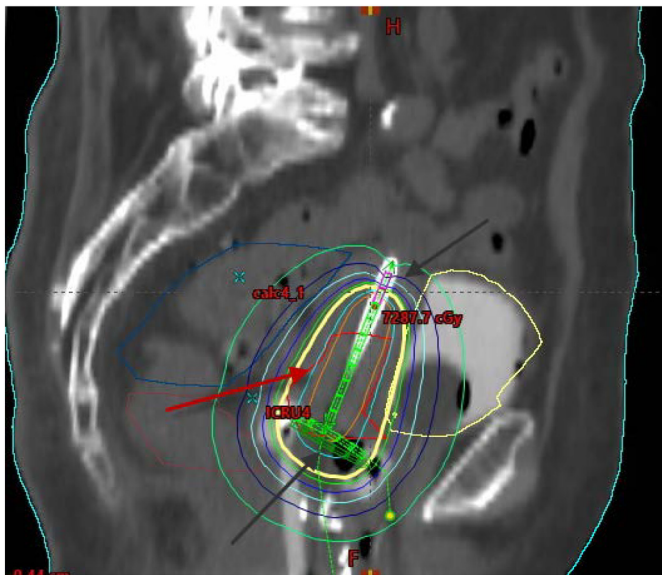


Fig. 2. The dose distribution is overlaying the cervical tumor and radiation equipment, with the isodose lines being the prescribed treatment. The yellow line is the 100% radiation prescription. The bladder, rectum, and sigmoid are spared of the high dose regions with brachytherapy as shown in this figure. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

been found to receive BT less than younger patients, with a resulting increase in cancer specific mortality [8]. However, the NCDB is not a population based registry like the CCR, and therefore the percentage of brachytherapy utilization could be underrepresented. Also the SEER is a sampling of the national trends based on 18 registries and could have inherent selection bias.

Given the disparities on the use of BT reported in the literature, and reported adverse effects on outcomes, we used data from the California Cancer Registry to: 1) examine the utilization trends of BT and potential disparities in survival outcomes based on race, socioeconomic status (SES), or age; and 2) investigate the use of BT on cause-specific (CSS) and overall survival (OS). The goal of our study is to help direct California cervical cancer programs, for better utilization of resources and appropriate allocation.

2. Methods

Women diagnosed with cervical cancer were identified through the California Cancer Registry (CCR), a program of the California Department of Public Health's Chronic Disease Surveillance and Research Branch. The CCR contains demographic, diagnostic, treatment, and outcome information on all reportable cancers diagnosed in California residents since January 1988 and is the single largest population-based state cancer registry in the U.S. The registry is also part of the SEER program through contracts to three of the CCR's Regional Registries and meets all of the quality and completeness standards of the National Cancer Institute SEER program as well as those of the National Association of Central Cancer Registries. Data collected by the CCR are used to develop strategies and policies for the prevention, treatment, and control of cancers. To date the CCR has collected detailed information on over 7 million cases of cancer among Californians, and >175,000 new cases are added annually.

Women included in this study were diagnosed with microscopically confirmed stage IB2-IVA cervical cancer in California between 2004 and 2014. Stage at diagnosis was based on the International Federation of Gynecology and Obstetrics (FIGO) system. Only first primary tumor cases were included, and patients diagnosed at autopsy or by death certificate only were excluded from analysis. All patients in the study received EBRT as part of the first course of treatment. We then assessed whether patients were treated with a radiation boost; women were categorized as having received BT, EBRT boost, or no boost. Women with unknown or missing radiation boost information were excluded from the study ($n = 34$).

We examined trends in the use of BT by demographic and tumor characteristics, including age at diagnosis, race/ethnicity, year of diagnosis, SES, stage at diagnosis, histology, and tumor grade. Neighborhood-level SES was based on U.S. Census data, including educational attainment, occupation type, employment rate, median household income, poverty level, median rent, and house values. For cases diagnosed 2004–2005, SES was computed using census-block group data from the Census 2000 Summary File. For patients diagnosed 2006–2014, SES was determined from the 2007–2011 American Community Survey. These two data sources were combined to form quintiles at the block group level across the state [9,10]. Tumor histologic subtype was classified according to the International Classification of Diseases for Oncology, third edition, as squamous cell carcinoma (codes 8050–8130) adenocarcinoma (codes 8140–8490), or other.

Multivariable logistic regression was used to identify predictors of BT compared to no boost. Cox proportional hazards regression was used to estimate the impact of BT on CCS and OS. Follow-up time for mortality was calculated as the number of days between the date of diagnosis and date of death through the end of the follow-up period (December 31, 2014). Censoring was accounted for patients who were alive at the follow-up date or were lost to follow-up. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

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