

Scientific Article

The Impact of COVID-19 on Brachytherapy During the Pandemic: A Rutgers-Robert Wood Johnson Barnabas Health Multisite Experience



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Abstract

Purpose: This study aimed to evaluate whether the coronavirus disease of 2019 (COVID-19) pandemic resulted in treatment delays in patients scheduled for or undergoing brachytherapy.

Methods and Materials: A retrospective cohort study was conducted across 4 affiliated sites after local institutional review board approval. The eligibility criteria were defined as all patients with cancer whose treatment plan included brachytherapy during the COVID-19 pandemic from February 24, 2020 to June 30, 2020. Treatment delays, cancellations, alterations of fractionation regimens, and treatment paradigm changes were evaluated.

Results: A total of 47 patients were eligible for the analysis. Median patient age at the time of treatment was 62 years (interquartile range, 56-70 years). Endometrial, cervical, and prostate cancers were the most common sites included in this analysis. Three patients (6.4%) with cervical cancer were diagnosed with COVID-19 during the course of their treatment. Interruptions of external beam radiation therapy (EBRT), cancellations of EBRT, cancellations of brachytherapy, and treatment delays due to COVID occurred in 5 (10.6%), 3 (6.4%), 8 (17%), and 9 (19%) patients, respectively. The mean and median number of days delayed for patients who experienced treatment interruptions were 16.3 days (standard deviation: 13.9 days) and 14 days (interquartile range, 5.75-23.75 days), respectively. For patients with cervical cancer, the mean and median overall treatment times defined as the time from the start of EBRT to the end of brachytherapy were 56 and 49 days, respectively.

Conclusions: Despite the challenges the health care system faced during the pandemic, most patients with cancer were safely treated with minor treatment delays and interruptions. Long-term follow up is needed to assess the impact of COVID-19 and treatment interruptions on oncologic outcomes.

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Introduction

The coronavirus disease of 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in a global pandemic. As of June 29, 2020, with >2.5 million cases and >126,000 deaths,¹ the United States ranks number 1 in the world for the highest number of cases. New York and New Jersey were the most heavily affected states during the early months of the pandemic. The World Health Organization and officials from the Centers for Disease Control and Prevention implemented recommendations for physical distancing, increased hand hygiene, the use of masks, and restrictions on travel and social gatherings. In addition, mandatory quarantines; banned social gatherings; the closing of nonessential businesses, schools, and borders; and restrictions on travel have been put in place by federal governments around the world.

The first positive case in New Jersey was announced on March 4, 2020, and the second on March 5, 2020. On March 9, 2020, the Governor of New Jersey, Philip Murphy, declared a state of emergency, and a stay-at-home executive order was implemented from March 21, 2020, until June 9, 2020. Elective and nonurgent surgeries and procedures were canceled from March 19, 2020, to May 28, 2020, resulting in postponed cancer treatments and diagnostic and therapeutic oncologic procedures. Published data during the pandemic suggested that patients with cancer and COVID-19 may have worse outcomes²⁻⁴; however, these findings are preliminary and may be the result of confounding factors.⁵ We suspect that many brachytherapy procedures were postponed or canceled during the pandemic. The American Brachytherapy Society published guidelines on strategies for risk mitigation on May 1, 2020.⁶ However, before the implementation of these guidelines, radiation oncology departments managed the crisis as best as possible during the initial peak of the crisis.

The goal of this study is to evaluate whether the COVID-19 pandemic resulted in treatment delays in patients scheduled for or undergoing brachytherapy or if alternative approaches were applied at 4 academic institutions in New Jersey during the peak of the pandemic.

Methods and Materials

A retrospective cohort study was conducted to collect clinical, pathologic, radiologic, demographic, and treatment parameters across 4 affiliated sites after local institutional review board approval. The eligibility criteria were patients with cancer who received or were scheduled to receive brachytherapy as part of their treatment course during the COVID-19 pandemic between February 24, 2020, and June 30, 2020. Patients treated during that time

Table 1 Patient and treatment characteristics

| Factor | n | % |
|---|------------|------|
| Age, median (25th-75th percentile = interquartile range) | 62 (56-70) | |
| Comorbidities | | |
| None | 19 | 40.4 |
| Respiratory (eg, asthma, chronic obstructive pulmonary disease) | 1 | 2.1 |
| Vascular (eg, heart disease, diabetes, hypertension) | 23 | 49 |
| Respiratory and vascular | 4 | 8.5 |
| Human immunodeficiency virus infection status | | |
| Negative | 44 | 94 |
| Positive | 3 | 6 |
| Cancer site | | |
| Endometrial cancer | 24 | 51 |
| Cervical cancer | 15 | 32 |
| Prostate cancer | 7 | 15 |
| Lower extremity sarcoma | 1 | 2 |
| Type of brachytherapy planned/delivered | | |
| Vaginal cuff brachytherapy | 25 | 53 |
| Intracavitary brachytherapy gynecology | 11 | 23.5 |
| Interstitial brachytherapy gynecology | 4 | 8.5 |
| Interstitial brachytherapy prostate | 7 | 15 |
| Chemotherapy | | |
| None | 23 | 49 |
| Androgen deprivation therapy | 5 | 10.6 |
| Concurrent chemoradiation | 16 | 34 |
| Adjuvant chemotherapy | 3 | 6.4 |
| External beam radiation therapy | | |
| No | 16 | 34 |
| Yes | 31 | 66 |

who decided to cancel or interrupt their treatment course, as well as patients who changed their treatment options due to the pandemic, were included. Treatment delays, cancellations, alteration of fractionation regimens, and treatment paradigm changes were evaluated. The final cohort included 47 patients eligible for analysis.

The radiation oncology departments enforced strict guidelines during the pandemic, including temperature checks for patients and staff members, prescreening for COVID-19 symptoms before each patient visit, social distancing in the waiting room, limiting visitors, providing surgical masks to patients, as well as personal protective equipment for the staff members, as part of the initiatives within the respective hospitals. Telemedicine visits were implemented initially for follow-up visits and then for consultations as well. Therapist schedules were changed to minimize exposure by alternating morning and afternoon shifts. Descriptive and frequency statistics were used to characterize baseline clinical and treatment characteristics. Mean and median were used to determine treatment delays.

Results

The records of 47 eligible patients between February 24, 2020, and June 30, 2020, were reviewed. Median patient age at the time of treatment was 62 years (interquartile range [IQR], 56-70 years). Patient and treatment characteristics are detailed in Table 1. A majority of patients (28 of 47 [59.6%]) had either respiratory, vascular, or both comorbidities. In the entire cohort, a total of 3 patients (6.4%) with cervical cancer contracted SARS-CoV-2 in the community and were diagnosed with COVID-19 during the course of their treatment, of which 2 patients were symptomatic. Interruptions of external beam radiation therapy (EBRT), cancellation of EBRT, cancellations of brachytherapy, and treatment delays due to COVID occurred in 5 (10.6%), 3 (6.4%), 8 (17%), and 9 (19%) patients, respectively. The mean and median number of days delayed for patients who experienced treatment interruptions were 16.3 days (standard deviation [SD]: 13.9 days) and 14 days (IQR, 5.75-23.75 days), respectively.

Gynecologic cancers

Most patients in the cohort had gynecologic cancers, with 24 and 15 patients suffering from endometrial and cervical cancers, respectively. Within the endometrial cohort of patients who received adjuvant treatment, 4 patients canceled their vaginal cuff brachytherapy in fear of contracting the virus during the COVID-19 pandemic, of whom 2 patients canceled their EBRT as well. Six patients had treatment delays. The mean and median of treatment days delayed for those 6 patients who had a treatment interruption were 14.8 days (SD: 15.4) and 10.5 days (IQR, 5.75-21.75 days).

All patients with cervical cancer received their treatments as planned; however, 4 of 15 patients (26.7%) had a treatment interruption during their course. Two patients experienced significant delays (>20 days) owing to COVID-19 infection and the other 2 patients had treatment interruptions due to non-COVID medical problems (hydronephrosis/acute kidney injury requiring stent placement and pancytopenia due to myelodysplastic syndrome). One patient presented with anosmia and tested positive for COVID-19 infection. However, the patient missed only 1 day of treatment and resumed treatments, as she was only mildly symptomatic. The department implemented strict measures to treat this patient as described in the discussion section. The mean and median of treatment delays for the 4 patients who experienced interruptions was 18.5 days (SD: 12.9) and 20.5 days (IQR, 5.75-29.25 days). Eleven patients with cervical cancer (73.3%) were able to complete their treatments within 8 weeks. The mean and median overall treatment time (OTT), defined as the time from the start of EBRT to

the end of brachytherapy, were 56 days (SD: 19.0 days) and 49 days (IQR, 44-56.5 days), respectively.

To limit patient and personnel exposure, the number of intracavitary brachytherapy fractions was limited to 4 in the midst of the pandemic for 7 patients. Interstitial brachytherapy was not impacted and delivered per our standard (inpatient over 3 days for a total of 5 fractions).

Prostate cancer

A total of 7 patients with prostate cancer who were scheduled to receive brachytherapy were treated across the 4 hospitals. However, only 3 patients (43%) were actually able to undergo brachytherapy. Six patients elected to undergo EBRT followed by a brachytherapy boost for unfavorable intermediate- and high-risk disease. Since elective surgeries were canceled within our system during the pandemic, 4 patients were treated with EBRT with or without androgen deprivation therapy (ADT) only. Two patients with high-risk prostate cancer received their high-dose rate (HDR) brachytherapy boost by interrupting the EBRT and delivering the HDR brachytherapy boost before the closure of the operating room. One patient enrolled in a clinical trial was treated with prostate HDR brachytherapy monotherapy 2 days before the World Health Organization declared the COVID-19 a pandemic on March 11, 2020.⁷

Other primary sites

Interstitial HDR brachytherapy for lower extremity sarcoma was delivered without interruption to a single patient with recurrent sarcoma.

Discussion

When the pandemic began in the United States in March 2020, limited data and information were available about the management of cancer treatments during the COVID-19 crisis. This study reports the impact of COVID-19 on brachytherapy across 4 institutions in New Jersey during the early months of the pandemic. Despite the various challenges presented, most patients were able to receive their treatments as planned with few interruptions. Six patients (13%) had significant treatment delays (>7 days), of which 3 delays were due to COVID-19 infection. Interruptions of EBRT, cancellation of EBRT, cancellations of brachytherapy, and treatment delays due to COVID occurred in 5 (10.6%), 3 (6.4%), 8 (17%), and 9 (19%) patients, respectively. The mean and median number of days delayed for patients who experienced treatment interruptions were 16.3 days (SD: 13.9) and 14 days (IQR, 5.75-23.75 days), respectively. Of note, although a majority of the patients studied had vascular and/or respiratory comorbidities, placing them in

the high-risk category if infected with SARS-CoV-2, most patients still proceeded with treatment and did not try to delay or cancel out of fear. Several publications from experts in brachytherapy tackled the challenges of delivering brachytherapy during the pandemic and made recommendations for risk mitigations.^{6,8-11}

Endometrial cancer

Although only limited data exist on the optimal timing of vaginal cuff brachytherapy after surgery for uterine cancer, experts recommend delivering vaginal cuff brachytherapy in ≤ 8 weeks after surgery but no more than 12 weeks.¹¹ Four patients canceled their brachytherapy, and despite many phone calls, opted not to resume treatment. Of these, one patient with endometrial cancer stage International Federation of Gynecology and Obstetrics 2018 grade IBG3 interrupted her EBRT and canceled her brachytherapy due to fear of contracting the SARS-CoV-2.

Cervical cancer

Given the importance of OTT on pelvic control and overall survival¹²⁻¹⁵ for cervical cancer, every effort should be made to deliver the entire course of treatment in < 55 days.^{13,16,17} More recent data from the retro-EMBRACE study recommended an even shorter OTT. Indeed, the OTT correlated with local control and an increase in OTT beyond 7 weeks required an additional 5 Gy to compensate for loss of local control.¹⁵ Despite the challenges we faced, especially from March through June 2020 during the pandemic, including shortages of personal protective equipment, limited medical resources, limited access to the operating room and anesthesia support, limited transportation for patients, and shortage of COVID-19 testing kits, all patients with cervical cancer were able to complete their treatments with minor delays. Two patients experienced significant treatment delays due to synchronous medical problems. Although these delays were not directly related to COVID-19, they were further compounded due to the significant impact on medical resources and patient care access.

Three patients became infected with COVID-19 and were symptomatic, which delayed their treatment course. The first patient had diffuse bilateral lung infiltrates on computed tomography imaging compatible with COVID-19 infection, which delayed her start date by 20 days. Once the patient tested negative, treatment was started and completed within 8 weeks. The second patient tested positive for COVID-19 shortly after beginning her chemoradiation course. Treatments were interrupted for 4 weeks owing to COVID-19 and then refusal to come in because of fear of getting reinfected. Ultimately, the patient agreed to resume treatment after testing negative.

Due to poor compliance, her brachytherapy course was interrupted. The third patient became infected with COVID-19 at the beginning of her treatment course. Because she was mildly symptomatic, radiation treatments were not interrupted; however, treatment with cisplatin was suspended.

Prostate cancer

Definitive treatment for prostate cancer can be postponed without impact on clinical outcomes.¹⁸⁻²² Experts have suggested that prostate cancer treatment can safely be deferred for 3 to 6 months.^{6,11} For patients with high-risk prostate cancer, continuing or initiating ADT is recommended until brachytherapy can be delivered. If a patient requires a brachytherapy boost, initiating ADT and delaying the start of EBRT is recommended.¹¹ In our small cohort, we were able to deliver the entire course of EBRT to all patients with prostate cancer without delays. Two of 6 patients received their HDR brachytherapy boost before the closure of the operating room. The remaining 4 patients were treated with EBRT with or without ADT.

To safely treat COVID-19-positive patients and ensure the safety of all other patients and staff members in our department, strict measures were taken. COVID-19-positive patients were treated at the end of the day after all the other patients had left the department. COVID-19-positive patients were asked to wait in their car and escorted by the chief therapist through the backdoor to bypass the waiting room and change in the treatment room. In addition, therapist schedules were staggered to limit exposure, and physicians and physicists worked from home on nonclinic days.

Moreover, a pulse oximeter reading was done before every treatment for COVID-19-positive patients, as well as a daily temperature check for all patients and staff members upon arrival in the department. Patients were provided surgical masks upon entering the hospital. Physicians and staff members wore personnel protective equipment, including an N95 mask, gown, gloves, and protective eyewear, for each visit. Deep cleaning, including ultraviolet light, was done after completion of treatment.

On-treatment visits were done virtually, if possible, and follow-up appointments via telemedicine. Telemedicine and/or in-person consultations were offered to all patients. In addition, before the start of brachytherapy, patients underwent COVID-19 testing. Patients were treated as an outpatient with PerOs medication or brought to the operating room for Smit Sleeve insertion for the first fraction.

The strategies we employed to prevent the spread of the virus and ensure optimal oncologic treatment delivery during the pandemic were in retrospect mostly in line with

the recommendations made by the American Brachytherapy Society on May 1, 2020, except for a few nuances.⁶ Based on our experiences, we recommend that clinicians who care for patients planned for brachytherapy can consider the following to mitigate treatment delays.

For COVID-19-negative and asymptomatic or mildly symptomatic COVID-19-positive patients with gynecologic cancers, proceed with EBRT with minimal interruptions. Favor outpatient brachytherapy procedures with PerOs or conscious sedation, and limit the number of fractions to 3 to 4. For inoperable endometrial cancer, EBRT alone is acceptable especially in morbidly obese patients with significant comorbidities. For symptomatic COVID-19-positive patients, delay treatment until the patient is asymptomatic or mildly symptomatic. For patients with endometrial cancer, a delay of 8 to 12 weeks after surgery is reasonable. Avoid delaying patients with medically inoperable endometrial cancer with vaginal bleeding or poor histologies, such as carcinosarcoma, papillary serous, and clear cell carcinoma, because the risk of progression/recurrence is high.

For patients with cervical cancer, a delay between 1 to 2 weeks is reasonable as long as the OTT is <8 weeks. If patients are mildly symptomatic, proceed with brachytherapy with PerOs or conscious sedation anesthesia and appropriate personal protection equipment for staff. Delaying brachytherapy by 10 to 14 days and increasing the dose by 5 Gy for each week delayed as recommended by the American Brachytherapy Society⁶ should be limited to symptomatic patients who require hospitalization for COVID-related complications because increasing the dose by 5 Gy while respecting The Groupe Européen de Curiethérapie- European Society for Radiotherapy & Oncology dose constraints is difficult to achieve. Follow these strict measures as outlined to limit exposure and ensure patient and staff member safety.

For COVID-19-negative and asymptomatic or mildly symptomatic COVID-19-positive patients with unfavorable intermediate- and high-risk prostate cancer, begin with EBRT with or without ADT and consider EBRT or stereotactic body radiation therapy boost if no operating room is available for an HDR brachytherapy boost. For patients with low-risk prostate cancer, favor hypofractionated regimens and stereotactic body radiation therapy. For salvage radiation, proceed with ADT and initiate radiation therapy after 8 weeks. For symptomatic COVID-19-positive patients with prostate cancer, delay treatment for 6 to 8 weeks up to 12 weeks. Offer ADT during the delay for unfavorable intermediate- and high-risk disease. For low- and favorable intermediate-risk patients, proceed with definitive treatments unless patients require hospitalization due to COVID-related complications. ADT is not recommended for these patients given the numerous side effects that can negatively impact quality of life.

Conclusions

During the early months of the pandemic, 4 radiation oncology departments in New Jersey managed to deliver most brachytherapy treatments to patients with minimal treatment delays and cancellations. Brachytherapy for gynecologic tumors was completed in the majority of cases; however, most prostate brachytherapy boosts were canceled due to the closure of the operating room. Patients who became infected with SARS-CoV-2 contracted the virus in the community. Despite the challenges the health care system faced during the pandemic, most patients with cancer were safely treated. Long-term follow up is needed to assess the impact of COVID-19 and treatment interruptions on oncologic outcomes.

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