# Advances in Radiation Oncology

## The Impact of COVID-19 on brachytherapy during the pandemic: a Rutgers-Robert Wood Johnson Barnabas Health multi-site experience

---Manuscript Draft---

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**Abstract:**

**Purpose/Objectives:** To evaluate whether the COVID-19 pandemic resulted in treatment delays in patients scheduled for or undergoing brachytherapy.

**Materials/Methods:** A retrospective cohort study was conducted across four affiliated sites following local Institutional Review Board approval. Eligibility criteria were defined as all patients with cancer whose treatment plan included brachytherapy during the COVID-19 pandemic from 2/24/2020 to 6/30/2020. Treatment delays, cancellations, alterations of fractionation regimens and treatment paradigm changes were evaluated.

**Results:** A total of 47 patients were eligible for analysis. The median age at time of treatment was 62 (Inter Quartile Range 56-70). 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 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 (Std dev=13.9) and 14 days (IQR=5.75-23.75), respectively. For cervical cancer patients, the mean and median overall treatment time defined as time from start of EBRT to end of brachytherapy were 56 and 49 days, respectively.

**Conclusions:** Despite the challenges the healthcare system faced during the pandemic, it is reassuring to report that 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 oncological outcomes.
Title: The Impact of COVID-19 on brachytherapy during the pandemic: a Rutgers-Robert Wood Johnson Barnabas Health multi-site experience

Short title: Impact of COVID-19 on brachytherapy during the pandemic

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Conflict of interest: none

Data sharing: Research data are stored in an institutional repository and will be shared upon request to the corresponding author.
Summary:
The COVID-19 pandemic resulted in radiation treatment delays and interruptions during the early months of the crisis. Despite the challenges and the shortage of medical resources, most patients with gynecological cancers were able to receive their treatments as planned. Patients with prostate cancer who did not receive brachytherapy boosts were treated with EBRT +/- ADT. Longer follow-up is needed to assess the impact of COVID-19 on oncological outcomes.
Abstract:

Purpose/Objectives: To evaluate whether the COVID-19 pandemic resulted in treatment delays in patients scheduled for or undergoing brachytherapy.

Materials/Methods: A retrospective cohort study was conducted across four affiliated sites following local Institutional Review Board approval. Eligibility criteria were defined as all patients with cancer whose treatment plan included brachytherapy during the COVID-19 pandemic from 2/24/2020 to 6/30/2020. Treatment delays, cancellations, alterations of fractionation regimens and treatment paradigm changes were evaluated.

Results: A total of 47 patients were eligible for analysis. The median age at time of treatment was 62 (Inter Quartile Range 56-70). 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 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 (Std dev=13.9) and 14 days (IQR=5.75-23.75), respectively. For cervical cancer patients, the mean and median overall treatment time defined as time from start of EBRT to end of brachytherapy were 56 and 49 days, respectively.

Conclusions: Despite the challenges the healthcare system faced during the pandemic, it is reassuring to report that 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 oncological outcomes.
**Introduction:**

The COronaVirus Disease-19 (COVID-19) caused by the novel SARS-CoV-2 (severe acute respiratory syndrome corona virus 2) has resulted in a global pandemic. As of June 29th, 2020, with over 2.5 million cases and over 126,000 deaths (1), the United States ranks number one in the world for the highest number of cases. New York and New Jersey were the most heavily impacted states during the early months of the pandemic. The World Health Organization (WHO) and officials from the Centers for Disease Control and Prevention (CDC) have implemented recommendations for physical distancing, increased hand hygiene, use of masks and restrictions on travel and social gatherings. Mandatory quarantines, banned social gatherings, closing of non-essential businesses, schools and borders as well as 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 4th and the second on March 5th. On March 9th, The Governor of New Jersey Philip Murphy declared a state of emergency and a stay-at-home Executive Order was implemented from March 21st until June 9th, 2020. Elective and non-urgent surgeries and procedures were cancelled from March 19th to May 28th, 2020, resulting in postponed cancer treatments, as well as diagnostic and therapeutic oncological procedures. Published data during the pandemic suggested that patients with cancer and COVID-19 may have worse outcomes (2-4); however, these findings are preliminary and may be the result of confounding factors (5). We anticipate that during the pandemic, many brachytherapy procedures have been postponed or cancelled. The American Brachytherapy Society published guidelines on strategies for risk mitigation on May 1st, 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.

Materials and Methods:

A retrospective cohort study was conducted to collect clinical, pathologic, radiologic, demographic, and treatment parameters across four affiliated sites following local Institutional Review Board approval. Eligibility criteria were defined as patients with cancer who received or were scheduled to receive brachytherapy as part of their treatment course during the COVID-19 pandemic from 2/24/2020 to 6/30/2020. Patients treated during that time 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, pre-screening 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, as part of the initiatives within the respective hospitals. Telemedicine visits were implemented initially for follow-ups and
then for consultations as well. The therapist’s 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:
Records of 47 eligible patients from 2/24/2020 to 6/30/2020 were reviewed. The median age at the time of treatment was 62 (Inter Quartile Range (IQR)= 56-70). Patient and treatment characteristics are detailed in Table 1. A majority of the patients, 28 out of 47 (59.6%), had either respiratory, vascular or both comorbidities. In the entire cohort, a total of 3 (6.4%) patients 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 were symptomatic. 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 (Standard deviation (Std dev) =13.9) and 14 days (IQR=5.75-23.75), respectively.

Gynecological cancers:
Most of the cohort had gynecological cancers: 24 and 15 patients had endometrial and cervical cancers, respectively. Within the endometrial cohort who received adjuvant treatment, four patients cancelled their vaginal cuff brachytherapy in fear of contracting the virus during the COVID-19 pandemic, of which 2 patients cancelled their EBRT as well. Six patients had treatment
delays. The mean and median number of treatment days delayed for those 6 patients who had a treatment interruption were 14.8 days (Std dev=15.4) and 10.5 days (IQR=5.75-21.75).

All patients with cervical cancer received their treatments as planned; however, 4 out of 15 patients (26.7%) had treatment interruption during their course. Two patients experienced significant delays (over 20 days) due to COVID-19 infection meanwhile, the other two 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. She missed only one day of treatment and resumed treatments since she was mildly symptomatic. The department implemented strict measures to treat her as described in the Discussion section. The mean and median number of treatment delays for the 4 patients who experienced interruptions was 18.5 days (Std dev= 12.9) and 20.5 days (IQR=5.75-29.25). Eleven cervical cancer patients (73.3%) were able to complete their treatments within 8 weeks. The mean and median overall treatment time (OTT) defined as time from start of EBRT to end of brachytherapy were 56 (Std Dev=19.0) and 49 days (IQR=44-56.5), respectively.

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

A total of seven patients with prostate cancer who were planned to receive brachytherapy were treated across the four hospitals. However, only 3 (43%) of the 7 were actually able to undergo brachytherapy. Six patients elected to undergo EBRT followed by brachytherapy boost for unfavorable intermediate and high-risk disease. Since elective surgeries were cancelled within our system during the pandemic, four patients were treated with EBRT +/- androgen deprivation therapy (ADT) only. Two patients with high-risk prostate cancer were able to receive their HDR brachytherapy boost by interrupting the EBRT and delivering the HDR brachytherapy boost before the closure of the operating room. One patient on clinical trial was treated with prostate HDR brachytherapy monotherapy two days before the WHO declared the COVID-19 a pandemic on March 11th 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 March 2020 in the United States, there were limited data and information 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 three 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 (Std dev=13.9) and 14 days (IQR=5.75-23.75), respectively. It is interesting to note that although a majority of the patients studied had vascular and/or respiratory comorbidities, deeming them in the high-risk category if infected with SARS-CoV-2, most 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 there is limited data on the optimal timing of vaginal cuff brachytherapy (VBT) after surgery for uterine cancer, the experts recommend delivering VBT in ≤ 8 weeks after surgery but no more than 12 weeks (11). Four patients cancelled their brachytherapy and
despite many phone calls, opted not to resume treatment. Of these, one patient with endometrial cancer stage FIGO 2018 IBG3 interrupted her EBRT and cancelled her brachytherapy due to fear of contracting the SARS-CoV-2.

Cervical cancer:

Given the importance of OTT on pelvic control and overall survival (12-15) for cervical cancer, every effort should be made to deliver the entire course of treatment in less than 55 days (13, 16, 17). More recent data from the retroEMBRACE recommended an even shorter overall treatment time. Indeed, the overall treatment time correlated with local control and an increase in overall treatment time 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 available 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 developed COVID-19 and were symptomatic, which delayed their treatment course. The first patient had diffuse bilateral lung infiltrates on CT imaging compatible with COVID-19 infection which delayed her start
date by 20 days. Once she 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 due to COVID-19 disease and then refusal to come in because of fear of getting re-infected. Ultimately, the patient agreed to resume treatment after testing negative. Due to poor compliance, her brachytherapy course was interrupted. The third patient developed COVID-19 at the beginning of her treatment course. Since she was mildly symptomatic, radiation treatments were not interrupted, however Cisplatin was suspended.

Prostate cancer:

It appears that 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 3-6 months (6, 11). For patients with high-risk prostate cancer, continuing or initiating ADT is recommended until brachytherapy can be delivered. If a patient is requiring a brachytherapy boost, initiating ADT and delaying 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 out of 6 patients were able to receive their HDR brachytherapy boost before the closure of the OR. The remaining four patients were treated with EBRT +/- ADT.

In order to safely treat COVID-19 positive patients and ensure safety of all other patients and staff in our department, strict measures were taken as detailed below:
1) **Scheduling measures:**

   a. COVID-19 positive patients were treated at the end of the day after all the other patients left the department.

   b. COVID-19 positive patients were asked to wait in their car and were escorted by the chief therapist through the backdoor to bypass the waiting room.

   Patient changed in the treatment room.

   c. Therapist’s schedules were staggered to limit exposure

   d. Physicians and physicists worked from home on non-clinic days.

2) **Screening measures:**

   a. Pulse Oximeter ready was done before every treatment for COVID-19 patients.

   b. Temperature check for all patients and staff upon arrival in the department daily.

3) **Protection measures:**

   a. Patients were provided surgical masks upon entering the hospital.

   b. Physician and staff wore personnel protective equipment (PPE) including N95 mask, gown, gloves and protective eyewear for each visit.

   c. Deep cleaning including ultra-violet light was done after completion of treatment.

4) **Changes made to clinic flow:**

   a. On treatment visits were done virtually, if possible.

   b. Follow-up appointments were done via telemedicine.

   c. Telemedicine and/or in-person consultations were offered to patients
5) **Testing:**

a. Before the start of brachytherapy, patients underwent COVID-19 testing.

b. Patients were treated as outpatient with Per Os 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 to ensure optimal oncological treatments delivery during the pandemic were in retrospect mostly in line with the recommendations made by the ABS on May 1\(^{st}\) 2020 except a few nuances as detailed below (6).

Based on our experiences we recommend that clinicians who are caring for patients planned for brachytherapy can consider the following to mitigate treatment delays:

1. Gynecological cancers:

   i. For COVID-19 negative and asymptomatic or mildly symptomatic COVID-19 positive patients:

      1. Proceed with EBRT with minimal interruptions

      2. Favor outpatient brachytherapy procedures with PO or conscious sedation.

      3. Limit the number of fractions to 3-4.

      4. For inoperable endometrial cancer, EBRT alone is acceptable especially in morbidly obese patients with significant comorbidities.

   ii. For symptomatic COVID-19 positive patients:
1. Delay treatment until asymptomatic or mildly symptomatic
   a. Endometrial cancer: delay 8-12 weeks after surgery is reasonable.
   b. Avoid delaying patients with medically inoperable endometrial cancer with vaginal bleeding or poor histologies such as carcinosarcoma, papillary serous and clear cell carcinoma since the risk of progression/recurrence is high.
   c. Cervical cancer: delay between 1-2 weeks is reasonable as long as OTT < 8 weeks for cervical cancer. If patients are mildly symptomatic proceed with brachytherapy with PO or conscious sedation anesthesia and appropriate PPE for staff. Delaying brachytherapy by 10-14 days and increasing the dose by 5 Gy for each week delayed as recommended by the ABS (6) should be limited to symptomatic patients requiring hospitalization for COVID-related complications since increasing the dose by 5 Gy while respecting the GEC-ESTRO dose constraints is difficult to achieve.

2. Follow strict measures as outlined above to limit exposure and ensure patient and staff safety.
2. Prostate cancer:

   i. For COVID-19 negative and asymptomatic or mildly symptomatic COVID-19 positive patients:

   1. For unfavorable intermediate risk and high-risk prostate cancer, begin with EBRT +/- ADT and consider EBRT or stereotactic body radiation therapy boost (SBRT) if no operating room availability for HDR brachytherapy boost.

   2. For low-risk prostate cancer, favor hypofractionated regimens and SBRT.

   3. For salvage radiation, proceed with ADT and initiate radiation therapy after 8 weeks.

   ii. For symptomatic COVID-19 patients:

   1. Delay treatment for 6-8 weeks up to 12 weeks.

   2. Offer ADT during delay for unfavorable intermediate and high-risk disease.

   3. 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 those patients given the numerous side effects which 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 of the brachytherapy treatments to the patients with minimal treatment delays and cancellations. Brachytherapy for gynecological tumors was completed in the majority of cases, however most of the prostate brachytherapy boosts were cancelled due to closure of the OR. Patients who became infected with SARS-CoV-2 contracted the virus in the community. Despite the challenges the healthcare system faced during the pandemic, it is reassuring to report that most patients with cancer were safely treated. Long-term follow-up is needed to assess the impact of COVID-19 and treatment interruptions on oncological outcomes.
References:


radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer.


Table 1. Patient and treatment characteristics.
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