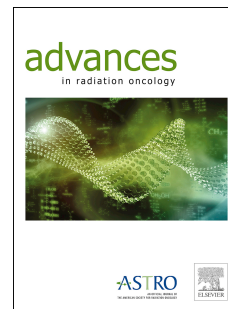


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The Impact of COVID-19 on Radiation Oncology Clinics and Cancer Patients in the U.S.

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Background:

In December 2019, Wuhan, China witnessed the outbreak of the novel coronavirus (SARS-CoV-2) that would soon become an international public health emergency and world pandemic.¹ In the U.S., we are at a time where preparation for healthcare systems is critical. Given the rapidity with which the novel coronavirus (SARS-CoV-2) is spreading, we can expect an increased burden of cancer patients diagnosed with COVID-19 at oncology treatment clinics and a need to address this diagnosis. As of the date of this writing, the U.S. has witnessed an increase in confirmed cases, not far behind the large outbreaks of European countries.^{2,3}

Since the outbreak in Wuhan, Chinese researchers have published on their experience with COVID-19 and have highlighted high-risk groups, including, the elderly and patients with comorbidities, including cancer. In one of the largest series reported from Wuhan, elderly patients were at a higher risk for disease severity with an 8.0% case fatality rate in those aged 70 to 79 years, and 14.8% in those aged 80 years and older.⁴ The case fatality rate for cancer patients in that cohort was notably higher than non-cancer patients at 5.6% versus 2.1% in the whole sample; it must be noted that this series is very small. How these numbers will evolve in the U.S. population remains to be determined. Based on available data, the impact of patients both at risk for and suffering from COVID-19 will be felt throughout oncology clinics. The burden this may have on Radiation Oncology clinics is of particular concern, due to the potential need for screening of patients for daily treatment, treatment interruptions, delays in restarting treatment, and a decreased workforce.

Patients with cancer are known to be at an increased risk for community acquired respiratory viruses, such as influenza, due to their frequently observed immunocompromised state.⁵ The spread of SARS-CoV-2 is of particular concern in this vulnerable population, given the higher case fatality rate seen in Wuhan, and the potentially increased severity of the disease course with COVID-19.^{4,6}

Spread and Prevention of Exposures:

Considering the CDC data available on SARS-CoV-2, it appears to spread by respiratory droplets and contaminated surfaces and requires contact with the bodily fluids or secretions of an infected individual.⁷ Fortunately, modern healthcare facilities are frequently prepared to deal with this route of spread due to experience with other respiratory viruses, like influenza. However, when dealing with a new pathogen for which limited information exists, predicting the efficacy of these measures is difficult. It is therefore imperative that cancer patients are prevented from congregating in areas with potential SARS-CoV-2 carriers, which means controlling exposures in waiting rooms and treatment areas. Guidelines for prevention of other respiratory viral spread in the healthcare setting for cancer patients should be followed^{6,8}, in addition to the continually updated recommendations from the CDC and WHO.^{7,9} This includes screening of patients entering a clinic for symptoms, and immediate isolation and contact precautions for patients suspected to be infected.^{10,11} Some clinics may opt to screen all patients upon immediate entry into the facilities, or even before entering, to decrease exposure risks. For COVID-19, suspicion for infection would be high in patients with fever, cough, shortness of breath and/or a history of recent travel to high-risk areas.⁷ It should be mentioned that guidelines and recommendations are likely subject to change over time as infectious disease and epidemiology experts learn more. As always, please be aware of the requirements of your local and state health departments regarding reporting and regulations.

Furthermore, Radiation Oncology clinics are uniquely taxed by an extra population of patients reporting to waiting rooms for daily radiation treatments. The large number of potential appointments and/or

daily treatments, in addition to a pre-existing disease state, heightens the risk faced by radiation oncology patients. As noted in the SARS outbreak experience in Radiation Oncology clinics, we will continue to have a lag time even if new consultations are postponed due to patients currently on active treatment for weeks at a time.¹² Canceling of elective procedures will only limit the caseload by a fraction in our specialty, and we therefore must maintain efficient protocols of screening and triage to effectively lower risk to patients and staff.

Another consideration is that of shared treatment machines. Members of this patient group are treated on one of a few machines shared amongst many patients daily, depending on the center. It is therefore imperative that radiation oncology clinics review established infection control protocols and adapt as necessary to the unique considerations of SARS-CoV-2, in accordance with CDC recommendations. Screening by front desk staff upon check-in and triage with nursing and physicians is necessary in order to protect patients, and to prevent possible exposures in both waiting rooms and treatment vaults from infected individuals. How to implement screening in the optimal fashion is a question that is evolving rapidly, and triaging patients remotely is vital.¹³ Remote screening has the potential to offset the load of individuals presenting to emergency rooms and clinics, avoiding possible exposures.¹³

Lastly, areas contaminated by a person under investigation (PUI), or confirmed COVID-19 patient, should ideally be decontaminated. Currently, the CDC recommends routine cleaning and disinfection procedures as appropriate for SARS-CoV-2 in the healthcare setting.¹⁴ Unique considerations in Radiation Oncology may include active breathing control devices, handles for arm positioning, and any attachments of the treatment couch that contact the patient. Attention should also be paid to the time of day suspected COVID-19 patients are treated. High-risk patients should be treated at times that facilitate appropriate sterilization and minimize staff and patient exposure. Finally, cognizant efforts must be made to discard or potentially contaminated PPE and/or garments prior to leaving the hospital so as not to carry viral particles outside.

Table 2 provides a selection of strategies to reduce infectious risk to patients and staff members in the clinic. Bass & Washington provide a more thorough array of the unique considerations in their book chapter dedicated to "Infection Control in Radiation Oncology Facilities."²⁷

Impact of Treatment Interruptions:

Radiation Oncologists will also have to prepare for treatment interruptions caused by development of COVID-19 in cancer patients. Patients who test positive for the novel coronavirus will, at a minimum, require a 14-day quarantine per CDC recommendations.¹⁵ At the other end of the spectrum, cancer patients with immunosuppression may require hospitalization and isolation precautions, thereby preventing the continuation of radiation treatments. Data from a report of the clinical characteristics of patients with COVID-19 showed that 6.1% of patients required intensive care, mechanical ventilation or died.¹⁶ Although it is yet unclear how the virus will behave in the US, the situations in China and Italy suggest the burden on hospitals and intensive care units will be significant. Additionally, this study demonstrated that pneumonia and lymphocytopenia were prominent at 91.1% and 83.2%, respectively, which would impact decisions to hold off on treatments pending improvements in the patient's clinical status and immune recovery.¹⁶ These treatment interruptions would be of utmost concern in tumors for which treatment package time significantly impacts outcomes such as head and neck and cervical tumors.^{17,18} However, this is also of concern in lung tumors and other thoracic tumors, for both tumor control and the lungs potentially lying in the path of treatment beams. Treatments would likely need to be paused while monitoring the course of COVID-19 in this setting. Treatment delays may also be due strains on the healthcare system in the setting of a pandemic due to travel restrictions, availability of

workforce, and/or lack of access to hospital care.¹⁹ If possible, travel restrictions for the general public should be tailored for patients with cancer, such as being done currently in Italy.²⁰

Little data exists currently to guide radiation treatment decisions in the setting of a pandemic. However, we may borrow insight from the response of Radiation Oncology clinics during Hurricane Maria. As per Gay et al, mitigating the impact of a natural disaster on cancer patients requires 4 components or “PCOC”: prepare, communicate, operate, compensate.²¹ In preparing, consideration should be made for scenarios which may require delayed treatment starts, or shorter fractionation regimens (i.e. hypofractionation), given that COVID-19 poses a substantial immediate risk for elderly patients. Again, there is a paucity of data to guide these decisions and priority should be given to higher risk tumors (H&N, Cervix, Lung, etc.), which are nicely referenced in the Hurricane Maria review. Overall, the immediate risk of COVID-19 will have to be weighed against the long-term risks associated with their specific cancer diagnosis.

Separately, patients receiving systemic agents including chemotherapy and/or targeted therapies will require input from multi-disciplinary teams. Thus far, there is little data outside of 1 case report from China of an EGFR T790M mutant advanced lung adenocarcinoma patient who was diagnosed with COVID-19, developed pneumonia and then fully recovered.²² He was maintained on Osimertinib during treatment for COVID-19, though radiation treatment was halted after the 9th fraction. Overall, systemic and radiation treatment adjustments will have to be discussed with input from the oncologic specialists and on an individual basis.

Upon recovery from COVID-19, patients will then need to be cleared to return to the clinic. In order to ensure full recovery and no risk for asymptomatic transmission to other patients, a negative PCR test would ideally be required. Per current CDC recommendations on March 12, 2020, “Negative results of an FDA Emergency Use Authorized molecular assay for COVID-19 from at least two consecutive sets of paired nasopharyngeal and throat swabs specimens collected ≥ 24 hours apart” are required before discontinuing home isolation.²³ However, with a surge in demand for testing kits, the ability to do such testing remains unpredictable. If testing is simply not available, the return of recovered patients may be at the discretion of the treating physician, Radiation Oncologist and infection control officials of the hospital.

Screening for In-Person Visits:

In trying to prevent community spread to non-affected cancer patients, some clinics may consider alternatives to in person triage and visits for sick patients as mentioned by the CDC for outpatient facilities.¹¹ This may entail training of front desk staff to screen patients via telephone before scheduling new appointments. For Radiation Oncology clinics, this may also require rescheduling of non-essential follow up visits or diverting these visits to telemedicine if available.¹³ As a large proportion of our patients are elderly, discretion is needed to protect this vulnerable group from exposure. Visits past the 5-year mark for patients with no evidence of disease or concerning symptoms should be considered for rescheduling if all clinical, laboratory, and imaging data suggest low risk for recurrence. This would ideally be at the discretion of the treating physician with appropriate clinically-specific concern. However, in the context of elevated community-spread risk of a new pathogen with considerable elderly fatality rate, it seems prudent to re-evaluate the timing of follow-up visits for clinically NED patients with long-disease free intervals.

Impact of a Decreased Workforce:

We will have to prepare for a shortage of healthcare workers in Radiation Oncology clinics in the near term as well. In the Wuhan outbreak as reported by Wu et al, 63% of health care workers became

infected, and 14.8% of cases in healthcare personnel were severe or critical.⁴ Though, it is too early to predict how this will affect the U.S. workforce, the number is suggestive of a great potential for a shortage of providers. Additionally, some clinicians will remain home to serve as caregivers for others whom are ill. Just as patients are at risk for possible quarantine or hospitalization, so are healthcare workers, and we will need to adapt accordingly. This may mean other measures in addition to the strict travel restrictions being implemented by many institutions, such as identification of back up staff, or consideration for staff teams who can rotate in order to retain a “team” time at all times.¹² Furthermore, thought may be put into essential and non-essential staff as the outbreak grows as done in the SARS experience in Canada.²⁴ Consideration of remote work for non-essential members should be reviewed. As an example, some institutions may ask some members of the dosimetry and or physics teams to work remotely to decrease unnecessary viral transmission. This should also include a strict policy on remaining home when ill- or potentially ill-, to avoid unnecessary exposures to both patients and staff. Data from Wuhan is unavailable regarding oncology staff management during the outbreak. The situation in Italy is evolving rapidly but may serve as a useful model in the coming weeks.

Management of the COVID-19 Positive Patient

The inevitable presentation of a COVID-19 positive patient to a radiation oncology clinic promises to pose significant challenges to the staff, administration, and physician who are charged with not only that patient’s care and well-being, but also the care and well-being of other patients (and staff) in the department. Figure 1 is a diagram depicting a hypothetical triage decision tree for a patient presenting to a radiation oncology clinic with a recent positive test for the COVID-19 virus, informed by attentions to the CDC outpatient guidelines and the Bass & Washington radiation facility infection control textbook chapter.^{11,27}

ASTRO recommends encouraging staff who interface with a high volume of patients, such as therapists, wear non-N95 masks, if available. Droplet precautions are essential for any patient with positive or suspected COVID-10.²⁸ The clinical landscape with respect to the management of COVID-19 patients continues to evolve at a galloping pace and professional societies, including American Society of Radiation Oncology (ASTRO), continue to work to develop useful and evidence-based guidelines for the management and care of patients as that landscape progresses. We encourage clinicians to look to these updated guidelines as they are released for the most up-to-date and informed management information.

Conclusion:

Overall, it is important to remember that Radiation Oncology clinics have always functioned as an interdisciplinary team of support staff, nurses, therapists, dosimetrists, physicists, and physicians, all aiming to help patients ailing from cancer. Heading into the fight with COVID-19, that team nature and vision to protect cancer patients remains critical. As the World Health Organization reminds us during this time: “Be safe, be smart, be kind.”

Updated information on the corona virus from ASTRO can be found at www.astro.org/coronavirus and from the American Society of Clinical Oncology (ASCO) at www.asco.org/asco-coronavirus-information.

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Coronavirus Fast Facts

Virus Name	SARS-CoV-2
Virus Family	<i>Coronaviridae</i>
Virus Type	(+)-ssRNA
Disease Name	COVID-19
Transmission method	Respiratory droplet
Viral incubation period	Median 5 (1-14) days
Duration of infectiousness	~1d post-exposure to ~10 days post symptom resolution
Most Likely Natural Reservoir	Bats/pangolins

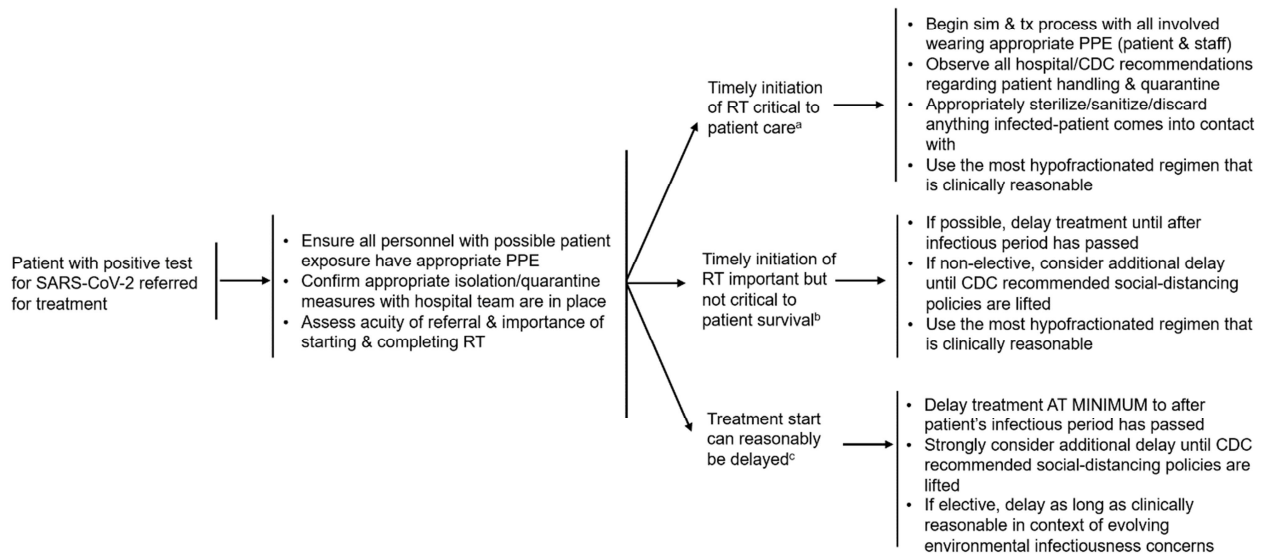
Figure 1 – Characteristics of the SARS-CoV-2 virus responsible for COVID-19 disease^{4,25,26}

Table 2

Example COVID-19 Radiation Oncology Clinic Risk Mitigation Strategies

Screening	<ul style="list-style-type: none"> ● Develop external exposure risk questionnaire for front desk staff to screen patients during time of appointment scheduling & check-in ● Include risk screening questionnaire form with routine review-of-system & medication update form ● Utilize viral-exposure-risk questions in nursing triage
Sanitation	<ul style="list-style-type: none"> ● Increase encouragement and enforcement of hand-washing guidelines ● Implement increased sanitation precautions for simulation/therapy equipment with multiple patient exposure ● Implement QD/BID deep cleaning of sim/therapy equipment with multiple patient exposure ● Remove non-essential items from waiting rooms, such as magazines ● Instruct patients to wash hands upon entry to department ● Transition to online meetings and tumor boards
Containment	<ul style="list-style-type: none"> ● Infected patients who cannot halt/postpone treatment must wear appropriate personal protective equipment during all phases of treatment encounter and be medically quarantined according to CDC/hospital guidelines ● Staff who must interact with patients who cannot halt/postpone treatment must wear appropriate personal protective equipment during all phases of treatment encounter
Exposure	<ul style="list-style-type: none"> ● Clinic staff should be briefed/trained on appropriate COVID-19 testing criteria for their state/hospital and how to direct patients/staff to indicated testing ● Any patient or staff with exposure should be offered testing according to CDC/hospital guidelines ● Consider delay of any unnecessary follow-up for as long as reasonable for the specific patient/clinical scenario ● If a phone call or telemedicine follow-up is sufficient for a patient/clinical scenario, consider that instead of in-person follow-up ● Any patient who presents with recent respiratory symptoms should be offered appropriate mask and counseled on handwashing

Hypothetical Triage Decision Tree for Presentation of Patient with Positive COVID-19 Testing



^a cord compression, significant hemorrhage, very high α/β intact cancers (locally adv gyn, H&N, lung)

^b adjuvant RT after R0 or microscopically positive margins in grossly resected cancers, medium α/β intact cancers

^c elective cases (thalamotomies, BNI \leq IV TGN), low α/β intact cancers (GG2-3 prostate ca, longstanding LGG/meningioma)

Figure 1 – A hypothetical decision tree for the triage of a patient with COVID-19 referred for radiation therapy