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COVID-19 Rapid Communication

Mitigating the impact of COVID-19 on oncology: Clinical and operational lessons from a prospective radiation oncology cohort tested for COVID-19 [☆]



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ABSTRACT

Background and purpose: The COVID-19 pandemic warrants operational initiatives to minimize transmission, particularly among cancer patients who are thought to be at high-risk. Within our department, a multidisciplinary tracer team prospectively monitored all patients under investigation, tracking their test status, treatment delays, clinical outcomes, employee exposures, and quarantines.

Materials and methods: Prospective cohort tested for SARS-CoV-2 infection over 35 consecutive days of the early pandemic (03/19/2020–04/22/2020).

Results: A total of 121 Radiation Oncology patients underwent RT-PCR testing during this timeframe. Of the 7 (6%) confirmed-positive cases, 6 patients were admitted (4 warranting intensive care), and 2 died from acute respiratory distress syndrome. Radiotherapy was deferred or interrupted for 40 patients awaiting testing. As the median turnaround time for RT-PCR testing decreased from 1.5 (IQR: 1–4) to ≤ 1 -day ($P < 0.001$), the median treatment delay also decreased from 3.5 (IQR: 1.75–5) to 1 business day (IQR: 1–2) [$P < 0.001$]. Each patient was an exposure risk to a median of 5 employees (IQR: 3–6.5) through prolonged close contact. During this timeframe, 39 care-team members were quarantined for a median of 3 days (IQR: 2–11), with a peak of 17 employees simultaneously quarantined. Following implementation of a “dual PPE policy,” newly quarantined employees decreased from 2.9 to 0.5 per day. **Conclusion:** The severe adverse events noted among these confirmed-positive cases support the notion that cancer patients are vulnerable to COVID-19. Active tracking, rapid diagnosis, and aggressive source control can mitigate the adverse effects on treatment delays, workforce incapacitation, and ideally outcomes.

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Introduction

Since its outbreak in December 2019 [1], the novel coronavirus (SARS-CoV-2) and associated respiratory disease (COVID-19) have led to a global pandemic, adversely impacting healthcare across the world [2]. The field of oncology faces particular challenges, as reports from Wuhan indicate that cancer patients are more vulnerable to COVID-19 and carry a greater risk of morbidity and death [3]. These data are corroborated by reports from Italy [4–6], in which radiotherapy (RT) departments have also been impacted [7,8], and data from New York City [9]. As such, patients undergoing active cancer treatment—including surgery, chemotherapy or radiation—are deemed highly susceptible to severe illness from COVID-19 [10,11].

Neither a vaccine nor a targeted therapy for COVID-19 exists, but early detection through intensive screening measures [3] may mitigate poor outcomes among these patients [12]. Additionally, the pandemic has necessitated adoption of non-traditional care approaches—such as planned deferrals and delays—to minimize travel to healthcare facilities [10] and thus contain viral exposure and spread [1]. However, cancer patients pose a unique challenge [13]: in addition to the risk of infection, there are hazards associated with undertreatment among patients with active disease [14]. Many malignancies warrant early diagnosis and treatment for favorable outcomes. Delays and interruptions of RT, for example, are associated with disease progression and increased mortality among patients with thoracic, gynecologic, and head-and-neck cancers. Therefore, an optimal balance need be maintained between treatment deferrals and protection against COVID-19 exposure.

Recognizing these challenges, our department established a tracer team to prospectively monitor all patients under investigation (PUI) and track their screening test status, treatment delays, and employees quarantined. This initial report provides insight on the early clinical and operational impact of the COVID-19 pandemic on ambulatory cancer care and may provide guidance for subsequent risk-mitigation strategies.

Materials and methods

Study population and RT policy for PUIs

This prospective cohort encompassed all patients who: (a) were evaluated for, had received, or were undergoing RT at our large academic cancer center; and (b) who also underwent RT-PCR testing for SARS-CoV-2 infection, over 35 consecutive days from 03/19/2020 to 04/22/2020. Testing indications were as follows: active fever or respiratory symptoms (55%), pre-procedure screening (30%), epidemiologic risk factors such as travel (11%), and radiographic findings (4%). Among PUIs actively scheduled for RT, our departmental policy was to pause treatment pending final RT-PCR test results. Several follow-up patients underwent testing early in the pandemic, prior to implementation of operational changes to minimize non-urgent clinic appointments. These included: (a) deferring routine visits by ≥ 2 months; (b) transitioning toward telemedicine platforms; and (c) referring patients to local oncology providers for management. Collectively, these changes decreased the volume of routine clinic visits (and testing associated with such appointments).

PUI tracer team

The team was composed of representatives from each care team provider group— including physicians, advanced practice providers, nurses, physicists, and radiation therapists—and worked closely with employee health services, infection control, and human resources staff. All PUIs were prospectively monitored from initial screening presentation, tracking their test date, result, impact on RT course, and clinical outcomes. Interruptions and resumptions of RT were coordinated with provider teams. In addition, the team traced patient points-of-contact to identify all clinical staff at potential exposure risk. Care team members were contacted directly with instructions and referred to employee health services. Staff quarantine status (including start, end, and return-to-work dates), were monitored.

Institutional screening and personal protective equipment (PPE) measures

Widespread screening for fever and/or respiratory symptoms was implemented for all employees and patients entering our

institution. When indicated, several locations were available for nasopharyngeal swab collection and in-house RT-PCR testing: five sites for patients and four designed for employees. Notably, our institution has been recognized as a state leader in hospital-based testing, accounting for a significant proportion across Texas. Halfway through this prospective study period, our institution implemented a “dual PPE” policy, requiring both employees and patients to wear surgical masks while on-site. Employees also donned additional PPE—such as gowns, gloves, respirators, and/or goggles—as indicated by the Centers for Disease Control and Prevention (CDC) guidelines.

Results

A total of 121 Radiation Oncology patients underwent RT-PCR testing during this timeframe. By treatment site, these included: 19 breast, 17 thoracic, 17 head/neck, 15 CNS, 14 gynecologic, 13 lymphoma, 11 gastrointestinal, 10 genitourinary, and 5 sarcoma patients. Of seven confirmed-positive cases, six patients (86%) were admitted including four (57%) warranting intensive care, and two (29%) died from acute respiratory distress syndrome (ARDS):

- (1) 61-year-old African American woman from Louisiana on investigative anti-PD-L1 and PARP-inhibitor therapy for metastatic rectal cancer involving lungs, peritoneum, and brain, seen for follow-up of brain metastases status-post radiosurgery with stable disease. Five days later she presented to the emergency room (ER) with cough, dyspnea, and desaturation to 91% on room air. Chest CT demonstrated diffuse bilateral heterogeneous consolidative and ground glass opacities (GGOs) [Fig. 1]. RT-PCR test was positive. She developed ARDS without improvement on antimicrobials plus non-rebreather and was transitioned to comfort care per advanced directive (DNR/DNI), dying one week into hospital admission.
- (2) 83-year-old African American woman from Texas was undergoing post-operative chemo-RT with cisplatin for Stage IIIB endometrial cancer. Following fraction 7 of 25, she presented to the ER, febrile to 39.2 °C with altered mental status and desaturation to 91% on room air. Chest X-ray demonstrated bilateral lung radiopacities. RT-PCR returned as positive. She developed ARDS, with desaturation to 40% despite non-rebreather. Per advanced directive (DNR/DNI), she was transitioned to comfort care and died five days into hospital admission.
- (3) 74-year-old Caucasian man from Texas undergoing definitive hypo-fractionated RT for recurrent retroperitoneal leiomyosarcoma. Following fraction 7 of 15, he developed fever of 39.2 °C along with productive cough. He presented to our outpatient screening clinic, and both the patient and his wife tested positive. Subsequently, he was admitted to a local intensive care unit (ICU) for ARDS and maintained on ventilator support for 14 days prior to discharge. The remaining RT fractions were aborted due to significant mid-course interruption (>4 weeks). Follow-up CT nearly 2 months later still showed bilateral lung GGOs (Fig. 1).
- (4) 63-year-old Caucasian woman from Texas presented for definitive stereotactic ablative radiotherapy (SABR) for recurrent adenocarcinoma of the left upper lobe. CT-on-rails, obtained prior to delivery of first fraction, revealed new multifocal GGOs of the bilateral lungs, as compared to her initial planning scan from CT-simulation 20 days prior [15,16]. Although asymptomatic, she tested positive in the ER, and treatment was aborted. The patient returned one

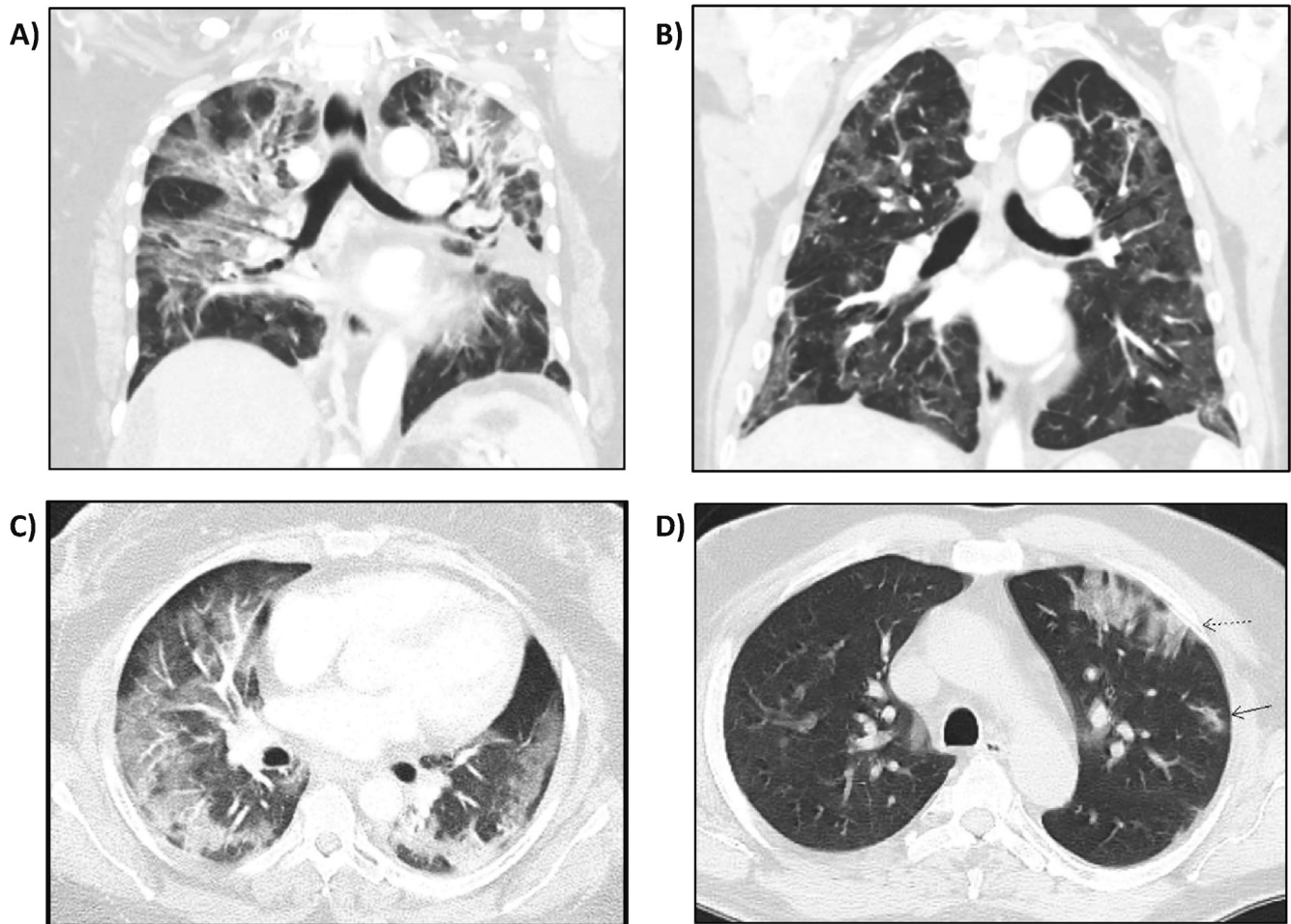


Fig. 1. Chest CTs of confirmed-positive patients demonstrating diffuse bilateral ground-glass opacities characteristic of COVID-19 [15,16]: (A) 61-year-old woman with metastatic rectal cancer died one week into admission from acute respiratory distress syndrome (ARDS); (B) 74-year-old man with recurrent retroperitoneal leiomyosarcoma, admitted to intensive care for ARDS requiring ventilator for 14 days, with bilateral GGOs resolving on follow-up CT nearly 2 months later; (C) 43-year-old woman with metastatic breast cancer admitted with ARDS requiring 15 L on non-rebreather; and (D) 62-year-old man with pineal melanoma, on ipilimumab/nivolumab, febrile to 38.9 °C without respiratory complaints.

month later for repeat CT-simulation and treatment re-planning, remaining completely asymptomatic in the interim. Imaging demonstrated resolution of prior GGOs and confirmed stable lung malignancy, for which she successfully underwent SABR.

- (5) 43-year-old African American woman from Texas with metastatic breast cancer status-post radiosurgery of brain metastases, recently started on bevacizumab for radiation necrosis. She presented to the ER with progressive dyspnea, and chest CT demonstrated new bilateral peripheral GGOs (Fig. 1). RT-PCR returned as positive. She developed ARDS requiring 15 L on non-rebreather but recovered and was discharged seven days into admission.
- (6) 62-year-old Caucasian man from Texas being considered for consolidative RT of pineal melanoma with small-volume progression on ipilimumab/nivolumab. He presented to the ER, febrile to 38.9 °C without respiratory complaints. CT demonstrated patchy peripheral GGOs (Fig. 1), and RT-PCR was positive. During a six-day admission, he recovered from a mild dry cough with 2 L nasal cannula requirement. The patient returned one month later for reconsideration of RT. CT Chest demonstrated interval decrease in bilateral lung opacities, but MRI brain revealed progression with numerous metastases, leptomeningeal spread, and obstructive hydrocephalus, for which he received whole-brain RT.

- (7) 91-year-old Caucasian woman from Louisiana undergoing definitive chemo-RT with cisplatin for Stage IVA high-grade vaginal serous carcinoma. Following fraction 17 of 33, she presented to the ER with sinus bradycardia and heart rate of 30–40, but otherwise asymptomatic without fever, respiratory symptoms, or concerning chest CT. RT-PCR testing returned positive, and she was briefly admitted for three days. Two weeks later, she returned for verification simulation and successfully completed the remainder of her RT course

Overall, RT was delayed or interrupted for a total of 40 patients (33%) while awaiting test results. As the median turnaround time for RT-PCR decreased from 1.5 (IQR: 1–4) day (03/19/2020–03/30/2020) down to ≤1-day (03/31/2020–04/22/2020) [Mann-Whitney-Wilcoxon; $P < 0.001$], the median treatment delay also decreased from 3.5 (IQR: 1.75–5) business days (03/19/2020–03/30/2020) down to 1 business day (IQR: 1–2) [Mann-Whitney-Wilcoxon; $P < 0.001$] [Fig. 2].

Each patient was a potential exposure risk to a median of 5 employees (IQR: 3–6.5) through close contact. During this time-frame, 39 care-team members were quarantined for a median of 3 days (IQR: 2–11) [Fig. 3], with a peak of 17 employees out simultaneously (Fig. 2). Radiation therapists were the most commonly affected personnel group, accounting for 15 staff quarantines (38%) [Fig. 3]. No employee tested positive due to exposure.

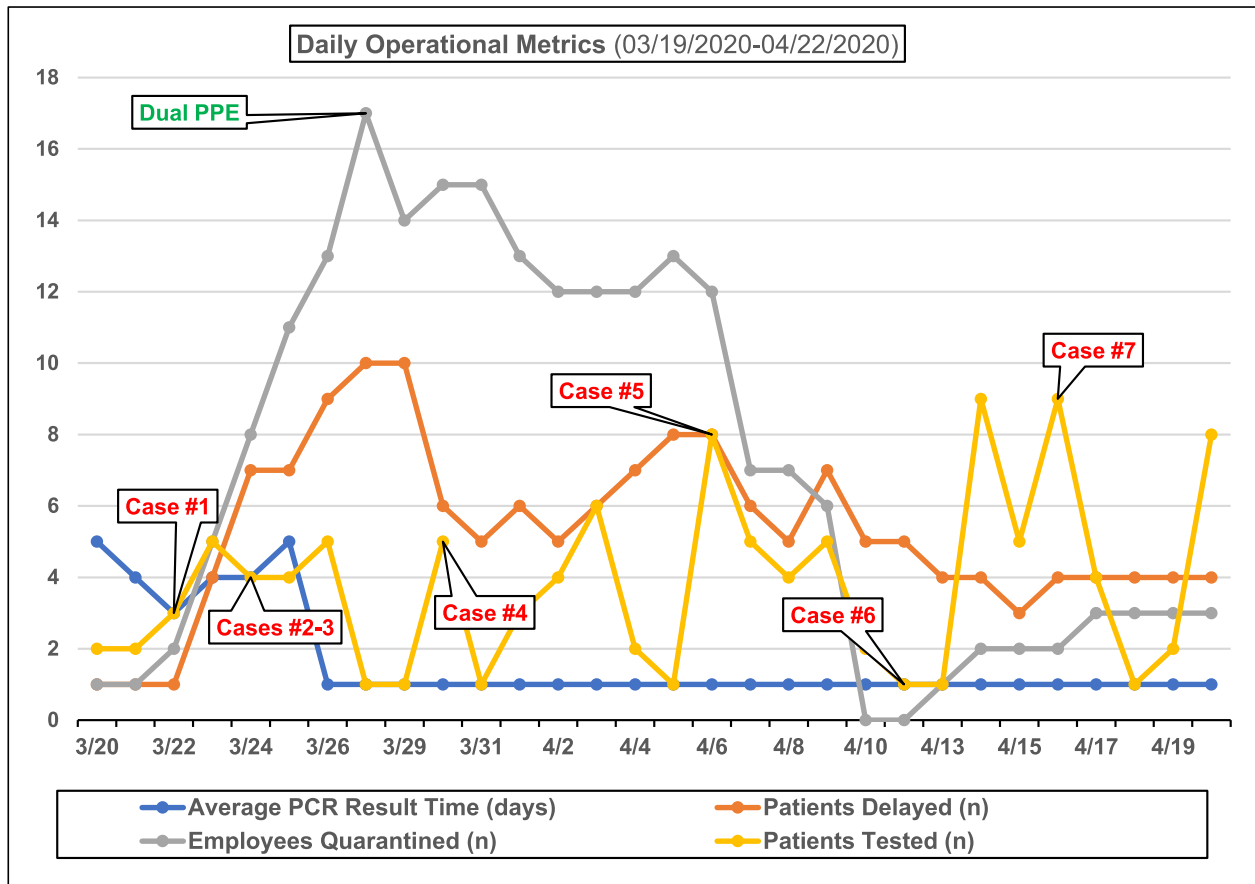


Fig. 2. RT was delayed or interrupted for 40 patients awaiting test results. As the median turnaround time for RT-PCR decreased from 1.5 (IQR: 1–4) to ≤ 1 -day (Mann-Whitney–Wilcoxon; $P < 0.001$), the median treatment delay also decreased from 3.5 (IQR: 1.75–5) to 1 business day (IQR: 1–2) [Mann-Whitney–Wilcoxon; $P < 0.001$]. Staff quarantines peaked at 17 employees out simultaneously but decreased following implementation of a “dual PPE policy” (for both patients and providers).

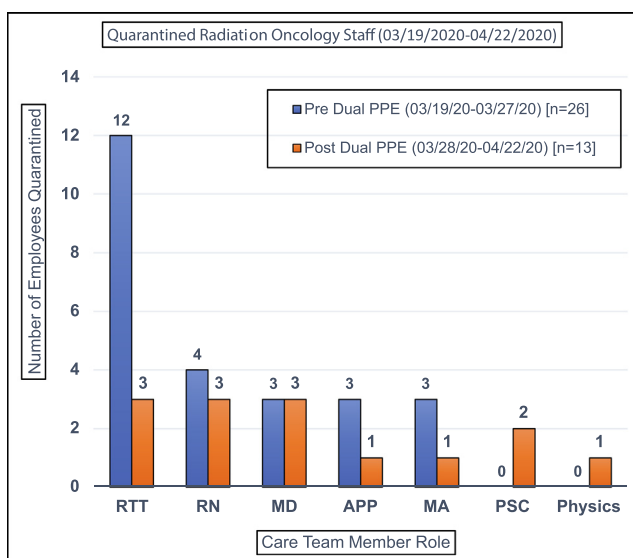


Fig. 3. During this timeframe, 39 care team members were quarantined for a median of 3 days each (IQR: 2–11), with radiation therapists most commonly affected. Following implementation of a “dual PPE policy” (for patients and providers), the number of newly quarantined employees decreased six-fold from 2.9 to 0.5 daily.

During the initial weeks of this analysis, staff were not wearing PPE for asymptomatic patients and were required to self-quarantine following exposure to confirmed-positive patients

according to CDC guidance. However, implementation of a “dual PPE policy” (for both patients and providers) imparted additional employee protection, shifting exposures into the low-risk category and eliminating extended quarantines post-exposure. Following this “dual PPE policy,” the number of newly quarantined employees decreased six-fold from 26 (03/19/2020–03/27/2020) to 13 (03/28/2020–04/22/2020), or 2.9 to 0.5 per day [Fig. 2].

Discussion

To summarize, this preliminary report provides insight on the early clinical and operational impact on ambulatory oncology due to the COVID-19 pandemic, as well as guidance on optimal management strategies for cancer patients in this setting. The poor outcomes noted among these confirmed-positive cases support the notion that cancer patients are particularly susceptible to this disease, corroborating initial reports from Wuhan [3], Italy [4–6], and New York City [9], and supporting the approach of pausing RT for PUIs pending test results. Additional data are warranted to refine treatment strategies for this vulnerable patient population, particularly regarding potential interactions with ongoing cancer therapies such as chemotherapy, immune checkpoint inhibitors, and RT [17].

Intensive screening measures are instrumental among this population due to the relative immunosuppressed state of many oncologic patients; however, presentation patterns of COVID-19 may be altered in cancer patients due to oncologic treatments or malignancy itself. This hypothesis is supported by the wide heterogeneity of clinical presentations observed among our seven confirmed-

positive cases: four patients (57%) initially lacked respiratory symptoms, two of whom (28.5%) presented without fever as well. However, six patients (86%) had radiographic presentations characteristic for COVID-19, with typical findings of bilateral parenchymal and consolidative opacities with peripheral lung distribution [18,19]. Indeed, the diagnostic utility of chest CT has been demonstrated for primary detection of COVID-19, with reports indicating higher sensitivity than RT-PCR (particularly among early and likely asymptomatic cases) [20]. Rapid assessment tools such as imaging can supplement standard screening measures to facilitate early diagnosis and isolation protocols while awaiting laboratory confirmation [15,16].

Upon suspicion for COVID-19, patients actively receiving RT should defer subsequent fractions pending RT-PCR test result. For confirmed-positive cases, the appropriate quarantine interval prior to restarting RT remains moot; however, our department has adapted the CDC-recommended non-testing approach for ending transmission-based precautions within the healthcare setting [21,22]. Note that the CDC also detailed a test-based approach requiring two consecutive negative test results (collected ≥ 24 h apart), but this resource-intensive strategy may lack feasibility depending on available testing capacity. Alternatively, the non-testing approach for patients with symptoms recommends passage of: (a) ≥ 3 days following recovery (defined as improvement of respiratory symptoms and resolution of fever); as well as (b) ≥ 10 days since initial symptom presentation [21,22]. Regarding asymptomatic patients, the CDC similarly recommends a ≥ 10 -day interval from positive test result. Note that this ≥ 10 -day timeframe was revised from the initial recommendation of ≥ 7 -days, based on emerging data of viral shedding duration [21,22]. Due to concerns that stricter guidelines may be indicated for cancer patients actively undergoing treatment, our department has conservatively extended these recommendations to ≥ 14 -days from the appearance of symptoms (and ≥ 14 -days from positive test result for asymptomatic patients) prior to resuming RT, without a need for re-testing.

One limitation of this report is the relatively modest number of patients tested during the initial pandemic at our center, which reflects a combination of variables. The most prominent contributing factor is the geographic heterogeneity of the pandemic: even within the United States, the incidence and trajectory of COVID-19 cases has consistently remained lower in Houston, TX as compared to Northeastern cities such as New York, NY or Boston, MA [23]. Across our department, early proactive efforts were also made to decrease treatment volume, through encouragement of shorter hypo-fractionated courses and two-week intervals between simulation and treatment start (when clinically feasible). Along with a decrease in multidisciplinary referrals, these changes culminated in a 26% reduction in treatment volume noted across seven of our RT centers during April 2020 [24]. In addition, rigorous screening and isolation practices further reduced the number of patients warranting testing. For example, our out-of-state patients were instructed to self-quarantine and self-monitor for ≥ 14 days before presenting to our department for visit or treatment.

RT is an integral component of many treatment regimens but entails frequent close contact with multiple providers over several weeks; therefore, our center has taken aggressive measures to reduce exposures among patients and care teams. In addition to infection-related outcomes, the continued use of rapid diagnostic and aggressive source control measures can help mitigate adverse effects on treatment delays and workforce incapacitation. While face masks were not initially recommended by the CDC for brief patient interactions, the dual PPE policy further decreases viral transmission among our high-risk patients and minimizes workforce impact. Treatment delays and employee exposures are probable among suspected patients, but can be addressed with active

tracking, rapid RT-PCR testing, and a dual PPE approach. Our team has continued tracking and monitoring of patients tested, treatment delays, and employees quarantined as a result of the COVID-19 pandemic, in order to regularly assess the impact of operational changes over time.

Declaration of interest

The authors report no conflicts of interest, financial or otherwise, to disclose with respect to this work. Outside of the respective work, Dr. Percy Lee is a medical advisory board member for Viewray and reports research funding and honorarium from AstraZeneca and Varian, respectively. Dr. Prajnan Das reports honorarium from Adlai Nortye and from MD Anderson Cancer Center Madrid Spain, again outside of the respective work.

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