

Research Letter

General Anesthesia for Pediatric Radiation Therapy in the Era of COVID-19



Michael J. LaRiviere, MD,^{a,b,*} Yash B. Shah, BS,^{a,b,c}
Elizabeth R. Cummings, CRNP,^{a,b} Kelly Clegg, RN,^{a,b} Abigail Doucette, MPH,^a
Brian P. Struyk, MD,^{d,e} Robert A. Lustig, MD,^{a,b} Goldie Kurtz, MD,^{a,b} and
Christine E. Hill-Kayser, MD^{a,b}

^aDepartment of Radiation Oncology, University of Pennsylvania, Philadelphia, Pennsylvania; ^bDepartment of Radiation Oncology, Children's Hospital of Pennsylvania, Philadelphia, Pennsylvania; ^cSidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania; ^dDepartment of Anesthesiology and Critical Care, University of Pennsylvania, Philadelphia, Pennsylvania; ^eDepartment of Anesthesiology and Critical Care Medicine, Children's Hospital of Pennsylvania, Philadelphia, Pennsylvania

Received December 13, 2021; accepted February 17, 2022

Abstract

Purpose: Managing pediatric patients requiring daily general anesthesia (GA) for radiation therapy (RT) in the setting of COVID-19 is complex, owing to the aerosolizing nature of GA procedures, the risk of cardiopulmonary complications for infected patients, and the treatment of immunocompromised oncology patients in a busy, densely populated radiation oncology clinic.

Methods and Materials: We developed an institutional protocol to define procedures for COVID-19 testing and protection of patients, caregivers, and staff, hypothesizing that this protocol would allow patients requiring GA to be safely treated, minimizing COVID-19 transmission risk to both patients and staff, and at the same time maintaining pre-COVID-19 patient volumes. All patients underwent COVID-19 testing before their first treatment and thrice weekly during treatment. For patients who tested positive for COVID-19, RT was delivered in the last end-of-day treatment appointment. A negative pressure room was used for GA induction and recovery, and separate physician/nurse teams were designated for in-room versus out-of-room patient management.

Results: Seventy-eight pediatric patients received RT under GA, versus 69 over the same prior year timeframe, and 2 patients received 2 courses of RT under GA, for a total of 80 courses. The mean age was 4.9 years (range, 0.5-19.0 years) and 41 of 78 (52.6%) were male. Two patients (2.6%) received 2 courses of RT under GA, establishing a total of 80 courses. The mean number of treatment fractions was 22.2 (range, 1-40). Two of 78 patients (2.6%) tested positive for COVID-19; both were asymptomatic. Both patients completed treatment as prescribed. Neither patient developed cardiopulmonary symptoms complicating anesthesia, and neither patient experienced grade 3+ acute radiation toxicity.

Conclusions: With careful multidisciplinary planning to mitigate COVID-19 risk, pediatric RT with GA was carried out for a large patient volume without widespread infection and without increased toxic effects from either GA or RT.

© 2022 The Authors. Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Sources of support: This work had no specific funding.

Disclosures: none.

Declaration of competing interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data sharing statement: Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

*Corresponding author: Michael J. LaRiviere, MD; E-mail: michael.lariviere@penncmedicine.upenn.edu

<https://doi.org/10.1016/j.adro.2022.100929>

2452-1094/© 2022 The Authors. Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The COVID-19 pandemic has disrupted clinicians' approach to the diagnosis and management of cancer. Radiation oncology, in particular, has required adaptations to balance the competing demands of providing life-saving daily treatments to patients who may be immunocompromised and at increased risk of severe COVID-19 infection¹ with the protection of staff who treat patients who have confirmed COVID-19 infection. Common protective precautions include screening all hospital entrants, regularly testing patients, requiring masks for patients and caregivers, enforcing social distancing, minimizing time spent in public spaces, enforcing mandatory staff use of personal protective equipment (PPE), and limiting the number of staff who interact with patients with suspected or confirmed COVID-19.^{2,3} With the emergence of the delta variant and the specter of new COVID-19 variants on the horizon, evaluating these precautions brings a renewed urgency.⁴ Novel variants' high rate of transmission and potential to infect vaccinated individuals demand evidence-based precautions to protect vulnerable patients with cancer.⁵

Pediatric patients treated with radiation therapy (RT) require additional unique precautions, particularly if they require daily general anesthesia (GA) if their age or developmental stage prevents them from maintaining the treatment position during RT setup and treatment. Anesthesia induction and recovery involve potentially aerosol-generating procedures that have the potential to increase the risk of viral transmission to nearby staff and patients.⁶⁻⁹ Although the degree to which these procedures generate clinically significant aerosols is not well understood,⁶⁻⁹ odds of viral transmission are estimated to be elevated 6.6 times during intubation.¹⁰ Moreover, supraglottic airway devices, including laryngeal mask airways commonly used for pediatric GA, may actually be *more* aerosolizing than endotracheal intubation.^{11,12} COVID-19 infection may introduce additional cardiopulmonary risks among patients receiving GA, as even clinically asymptomatic patients may have computed tomography imaging evidence of pulmonary injury,¹³ and GA may interfere with normal immune function.¹⁴

Given the risks and challenges associated with treating pediatric patients with COVID-19 under GA, our tertiary academic center developed and implemented a detailed, systematic testing and management protocol to reduce the risk of COVID-19 transmission among patients and staff. We hypothesized that this protocol would allow patients requiring GA to be safely treated, minimizing COVID-19 transmission risk to both patients and staff, at the same time maintaining pre-COVID-19 patient volumes to allow for the continuation of essential and timely radiation treatments.

Methods and Materials

Pediatric patients treated under GA through the Children's Hospital of Philadelphia and the University of Pennsylvania from March 1, 2020, to January 29, 2021, were identified. Structured data were extracted from Penn Medicine's Oncology Research and Quality Improvement Datamart, a clinical data repository that sources data from multiple databases, including the Penn Medicine Epic Clarity database (Epic Systems Corporation, Verona, WI) and Varian Aria database (Varian Medical Systems, Palo Alto, CA).

On March 1, 2020, institutional COVID-19 precautions for these patients were developed by the department of radiation oncology in conjunction with the division of infectious diseases and environmental health and radiation safety (Figs. E1 and E2). All patients underwent COVID-19 polymerase chain reaction testing 3 times per week, initiated before the first treatment and continued throughout the treatment course, with results typically available within 4 to 6 hours. Testing was initially conducted by nasopharyngeal swab but later transitioned to anterior nasal swab. Adult caregivers were not COVID-19 tested, but all hospital entrants underwent verbal screening. Only asymptomatic caregivers were allowed entry. Staff and patient protections still treated asymptomatic caregivers of patients who tested positive for COVID-19 as potentially COVID-19 positive themselves. As directed by hospital-wide guidelines, only a single adult caregiver was permitted for each patient. For patients with confirmed cases of COVID-19, only the same caregiver was allowed to accompany the patient through the duration of the treatment under COVID-19 precautions.

All patients who were COVID-19 positive and their caregivers were required to wear masks and gloves during the duration of the visit, unless, for the patient, radiation setup and treatment required their removal. The number of rooms or corridors occupied by each patient was minimized, as the patient was escorted directly from the parking lot to the GA induction/recovery room, to the treatment vault, and vice versa.

Staff "expanded PPE" included gown, gloves, eye protection, and N95 masks or, when N95s were initially unavailable, powered air purifying respirators (PAPRs) (Fig. E1). PAPR use required additional staff to ensure correct donning and doffing. Separate physician and nurse teams were designated for in-room versus out-of-room patient management. When exiting patient rooms, in-room staff were required to doff PPE in the anteroom. Staff "modified expanded PPE" included gown, gloves, eye protection, and surgical masks.

Patients who were COVID-19 positive were treated in the final evening appointment slot each day to allow the facility to remain empty after treatment, until they were cleaned overnight. Because the usual induction and

recovery rooms lacked negative pressure ventilation, a separate negative pressure room was designated for both GA induction and recovery. Physician anesthesiologists, rather than certified registered nurse anesthetists, were responsible for patients who were COVID-19 positive.

Patients who were COVID-19 positive were treated according to the COVID-19–positive patient management protocol described in detail in Figure E2. Specific steps are outlined for preprocedure preparation, patient arrival, and patient treatment. Briefly, preprocedure preparation requires the therapy manager to notify the nursing supervisor that the hospital-based rapid response/code call may require activation, and the therapy manager prepares PPE supplies for the rapid response/code call team. Before patient arrival, the children’s hospital/pediatric team huddles. During patient arrival, 2 children’s hospital/pediatric nurses, wearing modified expanded PPE, meet the patient at a designated entrance, which 1 nurse designated “clean” for elevator operation, door opening, and so on. The patient and caregiver then wear mask and gloves and are escorted through a designated path and elevators directly to the negative pressure room. Under patient treatment, the anesthesia induction protocol details the use of expanded PPE, and which staff may remain in the negative pressure room during induction. In the next patient treatment subsection, transport to treatment room, the children’s hospital/pediatric anesthesia team transports the patient to the treatment room, where 2 “dirty” radiation therapists wear expanded PPE, and 2 “clean” radiation therapists remain in the control room with modified expanded PPE. The “dirty” radiation therapists wait in the designated “dirty” area outside of the treatment room, and

re-enter for multifield treatments or at the end of treatment. As staff gained experience with these procedures, the protocol was amended to require only 2 rather than 4 radiation therapists – the first remains “dirty” and the second alternates between “dirty” and “clean” with PPE donning and doffing. The third patient treatment subsection describes transport to recovery room, where the patient is brought back to the negative pressure room. To ensure fully functional negative pressure, the children’s hospital/pediatric anesthesia team must wait 4 minutes before beginning the extubation sequence. Additional anesthesia team members, wearing modified expanded PPE, wait outside of the negative pressure room in case of emergency. No less than 15 minutes after extubation, after the patient has recovered from anesthesia, the caregiver is escorted to the negative pressure room. The final patient treatment subsection outlines the steps for patient departure. Briefly, after 2 nurses escort the patient and caregiver back to the exit via the designated route, the negative pressure, recovery, and treatment rooms are cleaned, environmental services and physics are notified of room closure time, and therapy managers are notified. Therapy managers ensure the treatment room is clean before resuming treatments the next morning.

Results

Seventy-eight pediatric patients received RT under GA, compared with 69 patients over the same timeframe the previous year (Table 1). For the present cohort, the mean age was 4.9 years (range, 0.5-19.0 years) and 41 of 78

Table 1 Patient characteristics.

Patients treated	78 (vs 69 over prior year timeframe)
Total RT courses	80
Mean age (range)	4.9 y (5.5 mo-19.0 y)
Sex	52.6% (41/78) male 47.4% (37/78) female
Mean treatment fractions (range)	22.2 (1.0-40.0)
Modality	Proton therapy 48.8% (39/80) Photon 22.5% (18/80) Both 28.8% (23/80)
Target	Chest, abdomen, pelvis 30% (24/80) Craniospinal axis 26.3% (21/80) Brain 21.3% (17/80) Total body 11.3% (9/80) Head and neck 6.3% (5/80) Other 5% (4/80)
COVID-19 positive	2.6% (2/78)

Abbreviation: RT = radiation therapy.

(52.6%) were male. Two patients (2.6%) received 2 courses of RT under GA, establishing a total of 80 courses. Nine of 80 (11.3%) courses involved total body irradiation, 24 (30.0%) were delivered to the chest, abdomen, and/or pelvis, 21 (26.3%) to the craniospinal axis, 17 (21.3%) to the brain, 5 (6.3%) to the head/neck, and 4 (5%) to other sites. Sixty-four of 80 (80%) courses were delivered with curative intent, with 39 (48.8%) using proton therapy, 18 (22.5%) using photons, and 23 (28.8%) using both modalities. The mean number of treatment fractions was 22.2 (range, 1-40). Two of 78 patients (2.6%) tested positive for COVID-19, although both were asymptomatic.

The first patient who was COVID-19 positive was a 3-year-old girl with high-risk neuroblastoma. Her simulation was initially delayed by 8 days because she had a known household contact with COVID-19, and the delay was not expected to affect disease-related outcomes. RT was ultimately initiated 15 days after simulation, but the patient herself tested positive for COVID-19 after the first fraction of RT. A 2-day treatment interruption was required to finalize and implement institutional COVID-19 guidelines. Including the weekend and an additional missed fraction for nil per os (NPO) violation, resumption of treatment was delayed by a total of 5 days. Proton therapy to 21.6 Gy/12 fx for this patient then continued without incident. The only toxic effects noted were grade 1 anorexia and grade 2 alopecia. Approximately one-third of staff members wore PAPRs owing to limited N95 supply, fit test failures, or personal preference. Because eye protection was not yet routinely used, 17 staff were quarantined because of exposure on treatment day 1, but no further staff exposures occurred after precautions for this positive test were implemented.

The second patient who was COVID-19 positive was a 3-year-old boy with relapsed medulloblastoma, not previously treated with radiation, who tested positive on initial COVID-19 testing, requiring a 1-day treatment delay to implement COVID-19 precautions. The patient was treated as COVID-19 positive with appropriate precautions implemented for the following 10 days of treatment. Proton craniospinal irradiation and boost to a cumulative dose of 54 Gy/30 fx was well tolerated, with only grade 1 dermatitis, cough, voice alteration, anorexia, fatigue, and grade 2 alopecia noted. No staff exposures were recorded. As the supply of N95 masks had improved when he underwent treatment, all staff members wore N95 masks. On-treatment visits were held via telemedicine for patient 1 and in-person for patient 2. No caregivers screened positive, and neither patient presented for treatment without the designated parent. Both patients were managed with laryngeal mask airways for GA. Neither patient developed cardiopulmonary symptoms complicating GA, and neither patient experienced grade 3+ acute radiation toxicity.

Discussion

To our knowledge, this is the first publication of a protocol to facilitate the continued, safe RT treatment of pediatric patients under GA in the midst of the COVID-19 pandemic. With careful multidisciplinary planning to mitigate the risk of transmission, pediatric RT with GA was carried out for a large patient volume without widespread infection or increased toxicities from either GA or RT. Only 2 patients from a large cohort tested positive for COVID-19, both at the beginning of the RT course (infection not thought to be related to RT). With the institutional COVID-19 guidelines finalized and implemented after the first patient tested positive, treatment delay was reduced for the second patient who was COVID-19 positive. Staff exposures were minimized, and although staff quarantines were initially required, no positive cases were identified among staff.

The COVID-19 pandemic has introduced significant challenges for health care systems worldwide, leading to clinically meaningful interruptions in the management of patients with cancer¹⁵ as well as increased COVID-19–related intensive care unit admissions and deaths among this group.¹⁶ Implementation of our protocol was instrumental in allowing treatments for all children receiving GA to continue with minimal delay or interruption, while at the same time minimizing their risk of transmitting or contracting COVID-19. Our volume of children treated with GA was actually 13% higher compared with the same timeframe the prior year. By contrast, 85% of practices across the United States saw decreased patient volume several months into the COVID-19 pandemic, with an average volume of 68% versus baseline.¹⁷ Moreover, these practices treat primarily adult patients, with no GA.

Although this report is the first to describe a specific protocol for RT in pediatric patients receiving GA, others have published recommendations that are relevant to this patient cohort. For instance, in April of 2020, Johns Hopkins radiation oncology department published guidelines that described selected pediatric patients as high priority and for whom RT should be continued even in the setting of COVID-19 infection.¹⁸ In July of 2020, The European Society of Paediatric Oncology published recommendations for the delivery of RT for pediatric patients.¹⁹ Although GA was not specifically discussed, our management of both patients who were COVID-19 positive was consistent with the authors' recommendations that (1) neuroblastoma should be treated with standard dose/fractionation schedules when possible, and (2) radiation for medulloblastoma should not be delayed.

Staff were generally highly receptive to the implementation of this protocol and gained comfort with it over time. There were no notable points of contention in the development of this protocol in collaboration with the infection prevention and control and radiation safety

teams, as radiation therapists, nurses, and physicians felt that given the risks of COVID, they should proceed as directed by these groups despite certain challenges, which are noted in the following sections. Notably, correct donning and doffing of PPE was initially challenging. Based on additional input from the infection prevention and control team, and as supplies of appropriate PPE stabilized after shortages early in the pandemic, the donning/doffing sequence was streamlined. The staffing required by the original protocol was difficult to maintain in the setting of pandemic-related staffing shortages. Although the required number of anesthesiologists (2) and nurses (2) has remained unchanged, the protocol was amended to require fewer radiation therapists (2 vs 4) to be present for each COVID-19 + GA treatment. As our department has robust processes in place for the review and implementation of new procedures, staff felt that, when sufficient time was allowed to schedule appropriate staffing levels, to procure the requisite supplies, and to rearrange treatment time schedules – specifically requiring at least 2 days to prepare – this protocol was fairly straightforward to implement.

In addition to staff, patients and families have experienced challenges related to this protocol. Because GA requires patients to be NPO, and because patients who are COVID-19 positive require end-of-day treatment times, adherence to NPO instructions is particularly unpleasant for these children. Another point of contention has been clearance from COVID-19 precautions, as our departmental and adult hospital requirements differ from the children's hospital's requirements. Our practice has been to follow the more conservative protocol that treats patients as COVID-19 positive for a longer period.

GA is a staff-, time-, and resource-intensive procedure, and access to GA may be limited. Before the COVID-19 pandemic, in the setting of higher patient volumes or limited GA staffing, the pediatric radiation oncology team led multidisciplinary communication among the radiation therapy, anesthesia, and nursing teams to triage patients by clinical need, delaying treatment start dates if clinically acceptable. In the setting of COVID-19, this multidisciplinary discussion now includes the infection prevention and control team. After this protocol was implemented, our department assembled a radiation oncology COVID-19 committee, which includes a pediatric radiation oncologist, to discuss the triage and management of any patient with COVID-19 requiring treatment. A similar committee could be developed to triage access to GA if this becomes a more limited resource.

Safe and timely management of pediatric patients who require RT under GA is seeing renewed importance in light of the multiple variants that have emerged since this patient cohort was analyzed, namely the delta and omicron variants, and there remains concern that novel, more virulent COVID-19 variants may develop. Indeed, although the delta variant did not appear to cause more

severe disease among children, it caused a marked increase in cases and hospitalizations: among children who were hospitalized between June 20, 2021, and July 31, 2021, approximately 23.2% required intensive care unit admission, 9.8% required ventilator support, and 1.8% died.²⁰ Likewise, the omicron variant was even less severe for children, with 10.4% of hospitalized patients under 18 requiring intensive care unit admission and 0 requiring ventilator support; no children died during the omicron surge between December 26, 2021, and January 15, 2021.²¹

Our protocol presents a standardized approach to prevent transmission of a highly infectious respiratory disease for children who require GA for RT. This protocol may be adapted to reflect institution-specific considerations and requirements. Key limitations include the fact that, as only 2 patients tested positive for COVID-19 and both patients were asymptomatic, it is difficult to conclude whether our findings regarding patient and staff safety will generalize to a larger population. Future directions include validation of this approach in the setting of the delta and omicron variants, future COVID-19 variants, and any other novel respiratory virus outbreaks. To improve on this work, we propose the development of a consortium of institutions treating pediatric patients who are COVID-19 positive under GA, to efficiently share information about disease transmission and protocol failures. With this rapid information sharing in place, protocol updates can be made and evaluated in real-time to allow for the continued treatment of pediatric patients with cancer.

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.adro.2022.100929](https://doi.org/10.1016/j.adro.2022.100929).

References

1. Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: A multicenter study during the COVID-19 outbreak. *Cancer Disc*. 2020;10:783–791.
2. Karasu D, Kilicarslan N, Ozgunay SE, Gurbuz H. Our anesthesia experiences in COVID-19 positive patients delivering by cesarean section: A retrospective single-center cohort study. *J Obstet Gynaecol Res*. 2021;47:2659–2665.
3. Aksu C, Cesur S, Kus A, Toker K. General anesthesia practices during the COVID-19 pandemic in Turkey: A cohort study with a national survey. *Cureus*. 2020;12:e10910.
4. Li Q, Zhan X, Wang J, Lu H. Considerations and guidance to control the rebound in COVID-19 cases. *Biosci Trends*. 2021;15:341–344.
5. Luo CH, Morris CP, Sachithanandham J, et al. Infection with the SARS-CoV-2 delta variant is associated with higher infectious virus loads compared to the alpha variant in both unvaccinated and vaccinated individuals [preprint]. *medRxiv*. <https://doi.org/10.1101/2021.08.15.21262077>. accessed April 6, 2022.

6. Klompas M, Baker M, Rhee C. What is an aerosol-generating procedure? *JAMA Surg.* 2021;156:113–114.
7. Weissman DN, de Perio MA, Radonovich Jr LJ. COVID-19 and risks posed to personnel during endotracheal intubation. *JAMA.* 2020;323:2027–2028.
8. Wilson NM, Marks GB, Eckhardt A, et al. The effect of respiratory activity, non-invasive respiratory support and facemasks on aerosol generation and its relevance to COVID-19. *Anaesthesia.* 2021;76:1465–1474.
9. Hamilton GS. Aerosol-generating procedures in the COVID era. *Respirology.* 2021;26:416–418.
10. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: A systematic review. *PLoS One.* 2012;7:e35797.
11. Brewster DJ, Chrimes N, Do TB, et al. Consensus statement: Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group. *Med J Aust.* 2020;212:472–481.
12. Lim WY, Wong P. Supraglottic airways in the management of COVID-19 patients. *Anaesth Crit Care Pain Med.* 2020;39:589–590.
13. Mills GH. Respiratory complications of anaesthesia. *Anaesthesia.* 2018;73(suppl 1):25–33.
14. Macfarlane AJR, Harrop-Griffiths W, Pawa A. Regional anaesthesia and COVID-19: First choice at last? *Br J Anaesth.* 2020;125:243–247.
15. Xie J, Qi W, Cao L, et al. Predictors for fear of cancer recurrence in breast cancer patients referred to radiation therapy during the COVID-19 pandemic: A multi-center cross-section survey. *Front Oncol.* 2021;11: 650766.
16. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. *Lancet Oncol.* 2020; 21:335–337.
17. Wakefield DV, Sanders T, Wilson E, et al. Initial impact and operational response of radiation oncology practices to the COVID-19 pandemic in the United States, Europe, and Latin America. *Int J Radiat Oncol Biol Phys.* 2020;108:1402–1403.
18. Wright JL, Alcorn SR, McNutt T, et al. An integrated program in a pandemic: Johns Hopkins radiation oncology department. *Adv Radiat Oncol.* 2020;5:666–672.
19. Janssens GO, Mandeville HC, Timmermann B, et al. A rapid review of evidence and recommendations from the SIOPE radiation oncology working group to help mitigate for reduced paediatric radiotherapy capacity during the COVID-19 pandemic or other crises. *Radiother Oncol.* 2020;148:216–222.
20. Delahoy MJ, Ujamaa D, Whitaker M, et al. Hospitalizations associated with COVID-19 among children and adolescents—COVID-NET, 14 states, March 1, 2020–August 14, 2021. *Morbidity and Mortality Weekly Rep.* 2021;70:1255.
21. Iuliano AD, Brunkard JM, Boehmer TK, et al. Trends in disease severity and health care utilization during the early omicron variant period compared with previous SARS-CoV-2 high transmission periods - United States, December 2020–January 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71:146–152.