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Brief Opinion

An Integrated Program in a Pandemic: Johns Hopkins Radiation Oncology Department

Jean L. Wright, MD,*[,1] Sara R. Alcorn, MD, PhD,[1] Todd McNutt, PhD, Sarah Han-Oh, PhD, Raul Gonzalez, PhD, Lan Lin, PhD, Roberta Anderson, RN, Jennifer Wieworka, RN, Curtiland Deville, MD, Matthew Ladra, MD, Jeffrey Meyer, MD, Russel Hales, MD, Ranh Voong, MD, Amol Narang, MD, Jennifer Vogel, MD, Fariba Asrari, MD, Ana Kiess, MD, Daniel Song, MD, Phuoc Tran, MD, Lawrence Kleinberg, MD, Kristin Redmond, MD, Christina Tsien, MD, Harry Quon, MD, Brandi Page, MD, Victoria Croog, MD, Amanda Walker, MD, Stephen Greco, MD, Marikki Laiho, PhD, and Akila Viswanathan, MD

Department of Radiation Oncology & Molecular Radiation Sciences, Johns Hopkins University, Baltimore, Maryland

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Introduction

The presence of the novel coronavirus (COVID-19) pandemic[1] prompted a structured response across the Johns Hopkins integrated network of radiation oncology facilities in Maryland and the District of Columbia. The department has developed a comprehensive reference document that serves as a resource for our staff and a summary of our response to the pandemic. The document in full has been posted on the American Society for Radiation Oncology "ROhub" web page.[2] We present here several excerpts from the overall program document that we believe may be of interest and can serve as a resource to the radiation oncology community at large. These recommendations are based on current or projected conditions in the Maryland-DC region as of March 25, 2020, and are expected to evolve on an ongoing basis.

Patient treatment priority scales

Attempts should be made to determine whether the risks of pandemic infection outweigh the risks of delaying treatment for that individual patient at the time of consultation. It should be noted that a delay in instituting radiation treatment should be as short as possible. Evidence suggests that even for cancers with typically favorable outcomes, there are higher risk subgroups for whom delays may be detrimental,[3,4] so the decision rests on an assessment of relative risks for an individual patient. Patients receiving care in 2 different centers (eg, external beam at one and brachytherapy at another) should receive special consideration.

Patients will be prioritized for radiation treatment based on the following priority scale, which was adapted from a general framework outlined by Ontario Heath-Cancer Care Ontario[5]:

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* Corresponding author: Jean L Wright, MD; E-mail: jwrigh71@jhmi.edu

[1] J.L.W. and S.A. contributed equally to this work.

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Level 1 (Continue radiation)	Patients already on treatment at the onset of the COVID-19 pandemic will continue treatment unless they become COVID-19 positive (COVID+) or a person under investigation (PUI). Patients who convert to COVID+/PUI status will be placed on a treatment break unless they meet other criteria for urgent treatment. This level allows radiation therapy treatment for emergency and urgent patients for whom alternative management is not possible. Patients with highly symptomatic metastatic disease who are deemed by their physician to have a life expectancy of at least 3 to 6 months and those with rapidly progressing potentially curable cancer will be treated. Please refer to Table 1 for disease site–specific criteria for level 1.
Level 2 (Short delay of radiation acceptable if needed)	Routine situations requiring radiation therapy. Within each disease site, specific recommendations have been made. Patients should be contacted at frequent intervals to ensure they have not progressed to level 1.
Level 3 (Hold radiation)	It may be possible to delay these cases until the pandemic is over or omit radiation altogether. These are patients with benign disease or patients amenable to other therapy first (eg, systemic therapy or surgery when appropriate).

- Level 1 patients will be treated as described in Table 1.
- Level 2 patients will follow a structure determined by the disease site team leader and may have a delay in the initiation of treatment if needed.
- Level 3 patients will receive a video consultation with intervention delayed until after the pandemic has been cleared, if appropriate.

Management of PUI

If a patient becomes a PUI,[6] the following processes will be followed:

- If the patient is on treatment, the patient will be managed as presumptively positive.
- A treatment break should begin and last until the test result has become available.
- Once a negative result has been obtained, treatment may be resumed.
- PUI designated as level 1 may continue treatment and will be managed as COVID+ until proven otherwise, as described below.
- Patients and visitors (if present; only allowed in cases of necessity) should wear a surgical mask when in the health care facility.

Management of COVID+ patients (including level 1 PUI)

Inpatients: COVID+ inpatients will not be treated with radiation therapy until further notice, with decisions made on a case-by-case basis.

Outpatients: Outpatients who are COVID+ or live in the same household as someone who is COVID+ will also be treated as presumptive positive.

- If a COVID+ patient is receiving palliative radiation therapy and the clinical team determines that there is an acceptable medical alternative, radiation treatment can be discontinued at the discretion of the treating physician.
- COVID+ patients will only be treated if they are categorized as level 1.
- Patients should be moved to end-of-day treatment. This should continue for 14 days after positive diagnostic test and 7 days after resolution of symptoms, whichever is longer. Given that the duration of contagiousness of patients who have recovered from COVID-19 is unknown at this time, patients who resume treatment after a break necessitated by COVID-19 infection will also be treated at the end of the day on a single linear accelerator.
- No visitors are permitted, with rare exceptions made for caregivers of the severely impaired.
- Patients should wear surgical masks.
- Patients should enter the facility via a low-volume entrance and move to a dedicated isolation room while waiting for treatment (not in the waiting room). This isolation room should not be used by other oncology patients for the rest of the day.
- Staff should wear appropriate protective equipment (droplet and airborne precautions), which includes double gloves, nonpermeable gown, and a PAPR or fitted N95 with face shield.
- Multiple patients who are COVID+ will be treated sequentially on 1 machine at the end of the business day in each center rather than on multiple machines.
- Because COVID+ patients will be treated at the end of the day and staff will be following best practices to minimize exposure, we have not specifically prohibited staff from rotating to other machines, although this will be avoided when possible.
- Follow-up patient visits should be deferred for at least 2 weeks if feasible. This must be documented in the electronic medical record.

Table 1 Priority levels by disease site

Disease-specific priority scales (COVID-negative patients)	Level 1 (continue radiation)	Level 2 (short delay of radiation if needed)	Level 3 (consider holding radiation)
Breast (see Appendix E1 for more detailed breast guidelines)	Nonmetastatic inflammatory breast cancer Locoregional disease progressing through chemotherapy	All other breast cancer not meeting levels 1 and 3	Patients meeting CALBG/PRIME II criteria for omission of radiation therapy ER+ DCIS for patients meeting criteria from RTOG 9804, particularly if they can take hormone therapy
Central nervous system	High-grade gliomas of brain and spine tumors Benign or other tumors causing or with immediate threat of progressive neurologic symptoms	Symptomatic low-grade glioma Cases where chemotherapy may permit delay of radiation	Asymptomatic meningioma, pituitary adenoma, craniopharyngioma, pilocytic astrocytoma Asymptomatic low-grade glioma after gross total resection Trigeminal neuralgia Schwannomas
Gastrointestinal	Curative-intent anal, esophageal, and gallbladder/bile duct cancers Curative-intent rectal cancer that is medically inoperable	Neoadjuvant/adjuvant pancreas and rectal cancer treatment courses	None
Genitourinary	Curative-intent bladder cancers High-grade prostate cancer not able to receive androgen deprivation Genitourinary small cell carcinoma treated with curative intent Patients in middle of combined brachytherapy and external beam radiation therapy	All other curative-intent prostate cancers Any cases of prostate cancer on androgen deprivation or low-risk prostate cancer cases that have not yet started radiation therapy can be triaged to the bottom of the level 2 patients	None
Gynecologic	Cervical cancer with severe bleeding Locally advanced vulvar or vaginal cancer causing severe pain	Postoperative vulvar cancer Inoperable endometrial cancer Postoperative cervical cancer (can be delayed up to 8 wk postoperatively) After induction chemotherapy, postoperative endometrial cancer (4-wk break allowed after chemotherapy)	Postoperative cases of endometrial cancer to be scheduled for induction chemotherapy or requiring vaginal brachytherapy alone (up to 4-8 wk postoperatively)
Head/neck	All curative cases where treatment with radiation therapy or concurrent chemoradiation is indicated High-risk postoperative cases based on pathologic and intraoperative findings including recurrent well-differentiated extrathyroidal carcinomas	All curative cases where induction chemotherapy is deemed clinically appropriate Intermediate-risk postoperative cases Low-grade unresectable salivary gland malignancies Recurrent parotid/skull base pleomorphic adenoma Medium to large COMS choroidal melanoma or symptomatic choroidal melanoma	Keloids Small COMS choridal melanoma Asymptomatic glomus tumors Slow-growing small basal cell carcinoma with mild or no symptoms, in a patient age >70 y Asymptomatic cutaneous nonpigmented carcinomas located in low-risk anatomic regions

(*continued on next page*)

Table 1 (*continued*)

Disease-specific priority scales (COVID-negative patients)	Level 1 (continue radiation)	Level 2 (short delay of radiation if needed)	Level 3 (consider holding radiation)
		regardless of COMS criteria Symptomatic or secretory paragangliomas Symptomatic cutaneous nonpigmented carcinomas or high-risk postop cutaneous nonpigmented carcinomas	
Lymphoma	Patients with high-grade lymphomas with severe or life-threatening symptoms	Consolidation therapy for high-grade lymphomas Most patients with low-grade lymphomas	Remaining patients with low-grade lymphomas, to be assessed individually
Palliative	Cord compression from histology other than chemotherapy-naïve small cell lung cancer or lymphoma and not amenable to surgical decompression Symptomatic brain metastases not amenable to surgical decompression or brain metastases >5 mm from histologies not anticipated to respond to systemic therapy Malignant airway obstruction not amenable to surgical intervention/stenting. SVC syndrome not amenable to thrombectomy/stenting Acute hemorrhage from primary or metastatic disease not amenable to embolization/other direct intervention Severe pain from primary or metastatic disease not responding to conservative measures Heterotopic bone (at discretion of doctor)	Painful spine metastasis without epidural extension or other immediate risk to the neuraxis Spinal cord compression or spine metastases with epidural disease in patient with chemotherapy-naïve small cell lung cancer or lymphoma who can receive chemotherapy Brain metastases <5 mm anticipated to be responsive to targeted agents or immunotherapy Other metastatic sites causing non–life-threatening symptoms, particularly those that may respond to conservative measures (eg, pain, shortness of breath stable on room air) Patients with stable or minimally symptomatic oligometastatic disease	
Pediatrics	All curable cases where delay of radiation is not possible	All cases where chemotherapy or other interventions can be safely used to delay initiation of radiation therapy	All elective or nonessential radiation cases
Sarcoma	Palliation of extreme pain or uncontrolled bleeding	All other neoadjuvant, adjuvant, and definitive cases	None
Thoracic	Limited-stage small cell lung cancer All patients with nonmetastatic node-positive or rapidly proliferating node-negative thoracic tumors for which the (time-sensitive) goal is cure and where alternative management is not possible	Consolidation of oligometastatic and oligoprogressive lung cancer Stage I NSCLC Postoperative thoracic tumors without residual disease Pulmonary ground glass opacities without solid component	None

Abbreviations: CALGB = Cancer and Leukemia Group B; COMS = Collaborative Ocular Melanoma Study; ER+ = estrogen receptor positive; NSCLC = non small cell lung cancer; RTOG = Radiation Therapy Oncology Group; SVC = superior vena cava.

Table 2 Airflow exchange rate calculations by vault

Machine vault	Measurement*	Airflow exchange per hour	t99% (min)	t99.9% (min)
Primary campus				
Standard LINAC 1	Actual	10.07	27.72	41.14
Standard LINAC 2	Actual	5.94	46.53	69.97
Standard LINAC 3	Actual	5.83	47.39	71.30
Tomotherapy	Actual	16.99	16.60	24.31
Specialty stereotactic	Actual	7.63	36.40	54.39
Regional campus 1				
All standard LINACs	Minimum	12	23.34	34.49
	Maximum	18	15.68	22.94
Tomotherapy	Minimum	10	27.91	41.43
	Maximum	15	18.75	27.55
All proton gantries	Minimum	6	46.07	69.26
	Maximum	12	23.34	34.49
Regional campus 2				
Standard LINAC	Actual	6.5	42.59	63.91
Regional campus 3				
Standard LINAC	Actual	8	34.74	51.86
Regional campus 4				
Standard LINAC	Actual	6.5	42.59	63.91

Abbreviations: LINAC = linear accelerator; t99% = time for 99% airflow exchange; t99.9% = time for full (99.9%) airflow exchange.

* Actual measurements represent airflow measured under standard automatic temperature control and building automation systems settings. Minimum and maximum measurements represent the range of airflow rates delineated according room design specifications; these were not directly measured.

Radiation treatment for patients recovering from COVID-19 infection

Patients may resume treatment without COVID-19 precautions after meeting 1 of the 2 following criteria (extrapolated from the Centers for Disease Control and Prevention's return-to-work criteria for health care personnel[7]):

1. Test-based strategy:
   - Resolution of fever without the use of fever-reducing medications, and
   - Improvement in respiratory symptoms (eg, cough, shortness of breath), and
   - Negative results on a Food and Drug Administration Emergency Use Authorized molecular assay for COVID-19 from at least 2 consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of 2 negative specimens).[8]
2. Non–test-based strategy:
   - At least 3 days (72 hours) have passed since recovery, defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (eg, cough, shortness of breath); and
   - At least 7 days have passed since symptoms first appeared.

Cleaning and equipment management

Cleaning of clinic and treatment areas

During this period, we follow additional precautions above and beyond our normal processes for infection control, wherever possible. All equipment should be cleaned with greater frequency. All treatment areas should be cleaned with 70% alcohol, PDI Super Sani-Cloth, or other Hospital Epidemiology and Infection Control (HEIC)-approved cleaning solutions after each patient, including the linear accelerator couch, the simulator couch, and all door handles or any other items that patients touch routinely. All patients and providers should use hand sanitizer before and after entering the treatment vault. All examination and treatment spaces as well as common spaces within clinics and waiting rooms should undergo thorough cleaning with approved cleaner solutions at least twice a day. Cleaning should include but not be limited to countertops, chair armrests, and other nonfabric surfaces. Given additional risks associated with management of head and neck patients, our specific guidelines for this group are included in Appendix E2.

Airflow exchanges on linear accelerator and proton vaults

If COVID+/PUI patients are treated, full (99.9%) airflow exchange must occur before treatment of the general population during the next business day. To determine the times required for full airflow exchange in each treatment vault, these values were either directly measured by facility staff or estimated using the range of minimum to maximum flow rates from the room design specifications to extrapolate clearance levels. Table 2 summarizes the relevant airflow exchange times for the treatment vaults across our clinical sites. We used these data to select treatment vaults that were most appropriate for treating COVID+/PUI. For example, in a review of data for the East Baltimore site, full airflow exchange times for the vaults of our most versatile linear accelerators ranged from 41.1 to 71.3 minutes; thus, we selected the vault with the shortest exchange time for a treating future COVID+/PUI patients.

Terminal cleaning

After treatment of COVID+/PUI, terminal cleaning procedures must be performed in the machine vault before

Table 3 Guidelines for use of active breathing coordinator

	ABC use guidelines
Central nervous-system	
GI	For GI tumors susceptible to motion, 4DCT will be acquired. Treatment with free-breathing or abdominal-compression approach will be considered for all such patients. ABC is considered clinically necessary when treatment in free breathing or with abdominal compression leads to unacceptably high risk for toxicity (as defined by the treating doctor), and this risk would be substantially lowered with ABC. Specific considerations for the use of ABC include GI cases in which - Expanded lung volumes with ABC will reduce the risk of lung injury for patients with mediastinal disease. - Motion mitigation with ABC will lead to significant dose reductions in the abdomen or chest. In such cases, free-breathing or abdominal-compression approaches may be particularly useful alternatives.
Lymphoma	As per treatment guidelines for tumor location
Thoracic	ABC is clinically necessary for - Any reirradiation case where the anticipated toxicity will be reduced with ABC. - Any conventionally fractionated case where a plan that meets minimum safety requirements cannot be achieved except with ABC. - Any hypofractionated or SABR plan that cannot meet normal tissue safety objectives or will not be well visualized on cone beam computed tomography without the use of ABC.
Sarcoma	As per treatment guidelines for tumor location
Pediatrics	4DCT will be acquired in patients large enough for tracing to be obtained when there is a concern for susceptibility to motion. ABC will be considered clinically necessary and will be used in cooperative patients where ABC significantly reduces dose to organs at risk.
Breast	ABC technique will be used very judiciously and be considered clinically necessary only in cases with cardiac mean dose >4 Gy or lung V20 >40% when free-breathing techniques are used. In general, we should seek alternative approaches to ABC, including IMRT/VMAT, to meet dose objectives.

Abbreviations: 4DCT = 4-dimensional computed tomography; ABC = active breathing coordinator; GI = gastrointestinal; IMRT = intensity modulated radiation therapy; VMAT = volumetric modulated arc therapy.

treatment of the general population. We recommend that this be performed in the morning of the next business day before the scheduled first patient to minimize exposure for the staff responsible for the terminal cleaning.

Active breathing coordinator procedures

Based on current information from manufacturers and product suppliers, our active breathing coordinator (ABC) system's single-use mouth piece/tube with attached ViroMax filter has >99.99% filtration efficiency for viral particles and is reported to be effective for particles as small as 0.1 μm in size.[9] Currently, we do not have information regarding filtration efficiency for particles <0.1 μm, and it has been noted that COVID-19 particles may vary in size from 0.06 to 0.14 μm.[5] Although it may be assumed that the actual transmitting respiratory droplet size may be larger—and thus more effectively filtered—than individual viral particles themselves, the specific filtration efficiency across the range of COVID-19 particle size remains somewhat unclear.

In addition to this potential uncertainty, ABC is thought to be a higher-risk procedure for staff owing to possible exposure to saliva and respiratory droplets that may be spread during ABC procedures. Furthermore, it requires increased machine time and coordination between treatment machines when ABC systems are shared.

Given the information currently available, our procedure for ABC is as follows:

1. In general, no ABC use for COVID+, PUI, or those who screen positive for new respiratory symptoms. Treating physician can evaluate whether they believe that the respiratory symptoms are low risk for being due to COVID and make an individualized decision to proceed with ABC at physician discretion if so.
2. Future patients: Limit ABC use to patients (1) without COVID+/PUI status or new respiratory symptoms, and (2) for whom there is clear clinical necessity of ABC use. "Clinical necessity" should be determined at the discretion of the treating physician and based on consensus from disease site-specific providers (Table 3 summarizes the approved indications for the use of ABC by disease site).
3. Patients currently on treatment: Can continue with ABC as long as the patients does not have COVID+/PUI status or new respiratory symptoms. Current patients whose new respiratory symptoms cannot be attributed to another low-risk cause should be replanned without ABC if at all possible. If current patients fall into this category and clinically require treatment with ABC, use of ABC will be reviewed with site clinical director on an individual basis.
4. If on-treatment patients using ABC convert to COVID+ or PUI status, the ABC system should be removed from use in the general population. It will not be returned to use until cleared by HEIC. When shared between treatment machines, ABC system use should be tracked to permit for identification of potentially exposed patients in the setting of an

on-treatment patient converting to PUI/COVID+ status (if required per HEIC).
5. If there are PUI/COVID+ patients who clinically require treatment with ABC and cannot be put on a treatment break, they will be treated on a separate ABC system designated for COVID+ use. This may require transfer of care to a site with multiple ABC systems.
6. A new single-use mouth piece and filter kit must be used per treatment per patient. No reuse of these parts is permitted at this time.

Clinical trials and laboratory research

Clinical trials will stop all new enrollments. The sole exceptions are prioritized trials where the trial is the only treatment option for the patient. Follow-up visits for trials will be conducted by phone whenever possible. Research specimens will not be collected unless there is a clear need, for patient safety. All laboratory research has been discontinued, and research staff are working and meeting remotely.

Conclusions

During this period of pandemic, additional considerations are necessary for prioritization of radiation treatment and equipment, as well as for additional infection control measures. The preceding represents selected considerations that we hope will be of value to the radiation oncology community as we navigate these unprecedented conditions.

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Supplementary materials

Supplementary material for this article can be found at https://doi.org/10.1016/j.adro.2020.03.014.

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