Cancer in the context of COVID-19: Summary of emerging evidence (3)

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The CRI presents a selection of emerging research articles and clinical practice guidelines related to cancer and COVID-19, with a summary of their key findings/recommendations (links to the articles are embedded as hyperlinks in the titles). This is the thrid of our weekly compilation, which we plan to update and disseminate as the pandemic evolves globally and nationally.

For this week, we will be focusing on some of the currently available journal articles related to the management of cancer in COVID-19 outbreak settings, some of which had been shared in the past week via the **CRI Twitter page (@UctCri)**. We hope that insights from these pieces of evidence will help guide how we rethink cancer prevention, treatment and care in the context of the ongoing pandemic, in view of its unprecedented implications for patients, healthcare providers and the community in general. Previous weeks' editions can be found on the **CRI website**.

Filippi et al. COVID19 outbreak in Northern Italy: First pratcical indications for radiotherapy departments. Int J Radiat Oncol Biol Phys. 2020 Mar 18. pii: S0360-3016(20)30930-5. doi: 10.1016/j.ijrobp.2020.03.007.

Country context: Italy

Based on lessons learnt from the outbreak in Northern Italy, this report presents a few practical suggestions to ensure continuity of therapies while protecting patients, health professionals, and the general population. The primary aim was to share information and provide guidance to radiotherapy departments worldwide. The report is mainly focused on how to deal with symptomatic, suspect, or COVID-19 positive patients undergoing radiation therapy. It identifies five key priorities, here described, together with a brief analysis of the problems and the possible solutions. The indications were integrated with the WHO recommendations and with the local health authorities' guidelines

PRIORITY 1: TO ENSURE RADIATION THERAPY DELIVERY TO CANCER PATIENTS

Problem analysis: Radiotherapy is a "life-saving" treatment and should be guaranteed to all cancer patients in which is indicated.

Suggested solutions: Regional and hospital management must ensure the full functioning of radiotherapy facilities, even in emergency conditions.

PRIORITY 2: TO ENSURE SAFETY OF HEALTH PROFESSIONALS, PATIENTS, AND CAREGIVERS

Problem analysis: A widespread infection of the staff working in a radiotherapy facility would

effectively result in the closure of part of the activities. Failure to identify the suspect or infected patients would increase the risk of spreading to operators and patients undergoing treatment.
Suggested solutions:
1. If a triage point at the entrance to the hospital has not been activated, the indication is to carry out a triage at the access of the radiotherapy department, to verify possible contacts with COVID-19 positive patients and evaluate suspect symptoms in all others (patients, caregivers) accessing the radiotherapy areas.
2. To provide a hydroalcoholic solution for hand disinfection at the entrance of the radiotherapy center.
3. To wear surgical masks, as recommended for all health professionals and patients according to WHO indications [5], and in particular in the following cases: 1) if the operator has respiratory symptoms, to protect others; 2) if the operator is in close contact with a person who has respiratory symptoms, to protect herself/himself.
4. To use sterile disposable overalls (tunic and trousers), sterile disposable gown, FFP2 masks, clogs, and overshoes when treating patients with suspect COVID-19 positivity, if they need to continue radiotherapy according to medical indications.

PRIORITY 3: MANAGEMENT OF COVID 19 SUSPECT OR POSITIVE PATIENTS
Problem analysis: We need practical guidelines on the appropriate behavior in case of symptomatic, suspect, or COVID-19 infected patients accessing radiotherapy facilities. The triage evaluation should immediately report to the appropriate internal structures all patients who have symptoms possibly related to COVID-19 infection, according to existing regional regulations.
Suggested solutions:
1. If the patient has a cough or fever or dyspnea due to pre-existing morbidity: the patient should wear a protective mask, and radiotherapy should be continued.
2. If a new patient is COVID-19 positive: do not start treatment.
3. If a patient on treatment is suspect for the onset of COVID-19 typical symptoms (cough and/or fever and/or dyspnea) and is waiting for microbiological diagnosis: stop treatment. *
4. If a patient on treatment results COVID-19 positive and is symptomatic: discontinue treatment *
5. If a patient on treatment results COVID-19 positive but is asymptomatic: discontinue treatment*
6. If a patient resulted COVID-19 positive is declared healed by Infectious Disease Clinic: plan carefully to start or restart treatment according to clinical cancer condition
* Patients may continue treatment only in selected cases if their general medical conditions are not compromised by COVID-19 infection, if the oncological condition requires continuation of radiotherapy, if it is permitted by local health authorities, and with the use of adequate disposable protective equipment. We suggest personalized clinical assessment.
If possible, these patients should be treated at the end of the LINAC shift to limit the chances of infection for other patients. After the treatment of positive patients (or patients waiting for diagnostic confirmation), the waiting and bunker areas should be sanitized at the end of the treatment session.

PRIORITY 4: STAFF RE-ORGANIZATION
Problem analysis: It is necessary to avoid the usual professional behavior that favors the aggregation of the professional figures working in the radiotherapy facility.
Suggested solutions: Medical, technical, nursing, and administrative staff must operate in separate
areas, avoiding meetings that cannot ensure the safety distances required for prevention.
In case of infection of health professionals and therefore in case of a severe shortage of staff:
1. report the current situation to the hospital management, for getting help in solving the problem (e.g., hiring new staff);
2. connect with other radiotherapy centers for the use of external personnel to avoid the interruption of ongoing therapies;
3. call for service of retired personnel following the procedures already defined by the administrations;
4. redistribute patients on available machines, and a variation of fractionation, when feasible, is advised.

PRIORITY 5: REDUCTION OF PATIENTS' ACCESS TO RADIOTHERAPY FACILITIES
Problem analysis:
It is advisable to limit patient access to radiotherapy facilities while maintaining optimal care conditions.
Suggested solutions:
1. To adopt hypo-fractionated regimens when possible;
2. To postpone follow-up visits;
3. To use palliative medical treatments at home, instead of radiotherapy, when deemed to be of similar efficacy;
4. To delay non-urgent and deferrable radiotherapy treatments for patients with a better prognosis (e.g., adjuvant radiotherapy of breast cancer patients, radical radiotherapy of patients with low-intermediate risk prostate disease, others);
5. To postpone therapies for benign and functional diseases.

Krengli et al. Running a Radiation Oncology Department at the time of coronavirus: an Italian experience. Adv Rad Oncol 2020. DOI: https://doi.org/10.1016/j.adro.2020.03.003
Country context: Italy
This paper highlights the challenges of continuing radiation oncology treatment and patient care in the context of COVID-19 outbreak. It makes the following recommendations:

- Establishment of a coordination unit with representative of all professionals at Hospital and Department levels;
- Unique source for communication to have clear and timely information and avoid redundancy and contrasting messages;
- General rules for prevention and personal behavior with detailed information to all professionals from the very beginning (procedures for disinfection of rooms and machines, optimize pathways and waiting rooms strictly for patients; precise time for

consultation avoiding unnecessary waiting time, washing hands frequently, surgical mask for operators and for patients/accompanying persons);

- Review of organizational procedures: postponement of treatments for low-priority cases (prostate with hormone, benign diseases, etc.), favor short-term therapy (hypofractionation), skip F/U visits (use phone contacts)
- Definition of a priori policy for coronavirus suspected or positive at the beginning and during treatment (recommended not to start Tx and recommended to interrupt treatment);
- Triage procedure at the entrance of the department for all patients and accompanying persons: first access – questionnaire, temperature measurement, check of symptoms; daily treatment – temperature measurement, check of symptoms;
- Check warehouse stocks for masks, coats, gloves, alcoholic cleaning solutions and disposable devices;
- Plan for transportation of patients who could not be supported by family or volunteers;
- Organization of psychological support for patient families and professionals.

Kutikov et al. A War on Two Fronts: Cancer Care in the Time of COVID-19. Ann Intern Med. 2020 Mar 27[Online ahead of print] PMID: 32219410 DOI: 10.7326/M20-1133

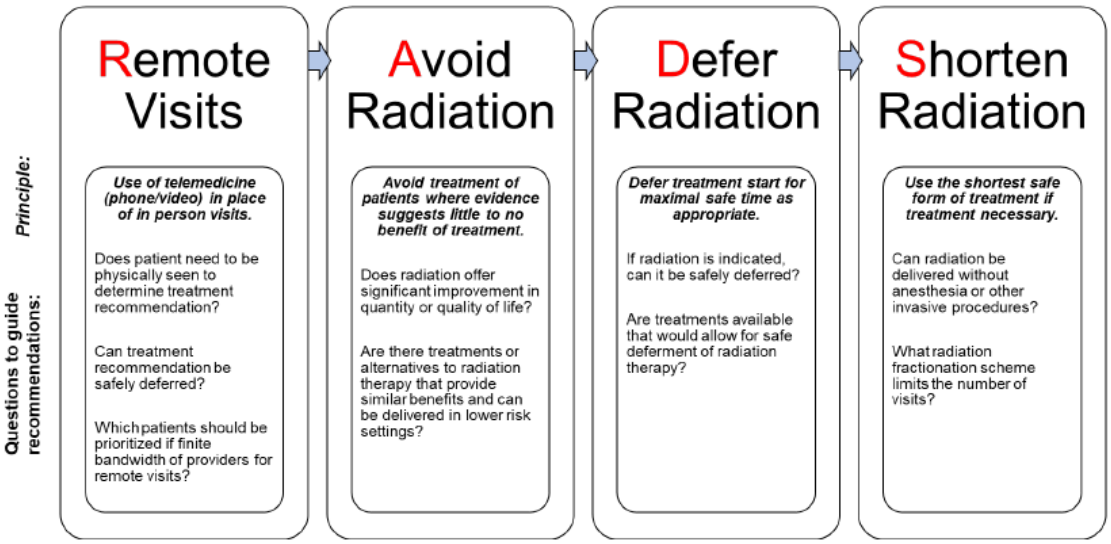
Country context: Global

This commentary article explores the challenges that oncologists face during this extraordinary time. It discusses the need for oncologists as well as other cancer care providers to 1) balance a delay in cancer diagnosis or treatment against the risk for a potential COVID-19 exposure, 2) mitigate the risks for significant care disruptions associated with social distancing behaviors, and 3) manage the appropriate allocation of limited health care resources in this unprecedented time of health care crisis.

Zaorsky et al. Prostate Cancer Radiotherapy Recommendations in Response to COVID-19. Adv Rad Oncol. 2020. DOI: https://doi.org/10.1016/j.adro.2020.03.010

Country context: USA and UK

Radiation Oncologists from the United States and United Kingdom rapidly conducted a systematic review and agreed upon recommendations to safely manage prostate cancer patients during the COVID-19 pandemic. A RADS (Remote visits, and Avoidance, Deferment, and Shortening of radiotherapy) framework was developed based on the findings from litearature. The framework is highlighted in the figure below:



The RADS framework can be applied for all prostate cancer disease states commonly treated with radiotherapy. Though specific to prostate cancer, the framework can be adapted and applied to other disease sites to help with decision making in a global pandemic..

The paper also summarizes the group's recommendations for each disease stage and according to visit type, simulation, fiducial marker and rectal spacer placement, and treatment itself. In all scenarios visits, procedures, and treatment can safely be delayed by variable durations based on stage of disease.

Yu et al. SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. JAMA Oncol 2020 Mar 25. DOI: 10.1001/jamaoncol.2020.0980

Country context: China

This cross-sectional study reviewed the medical records of 1524 patients with cancer treated at a single tertiary care hospital in Wuhan, China to evaluate the characteristics associated with transmission of the SARS-CoV-2 virus. It estimated the infection rate of SARS-CoV-2 in patients with cancer from our single institution at 0.79% (12 of 1524 patients). This was higher than the cumulative incidence of all diagnosed COVID-19 cases that was reported in the city of Wuhan over the same time period (0.37%; 41 152 of 11 081 000 cases; data cutoff on February 17, 2020). The median age of infected patients was 66 years (range, 48 to 78 years); 8 of 12 patients (66.7%) were older than 60 years. Seven of 12 (58.3%) patients had non–small cell lung carcinoma (NSCLC). Five (41.7%) were being treated with either chemotherapy with or without immunotherapy (n = 3) or radiotherapy (n = 2). Three patients (25.0%) developed SARS; 1 patient required intensive-level care. As of March 10, six patients (50.0%) had been discharged, whereas 3 deaths (25.0%) were recorded. Patients with NSCLC and older than 60 years had a higher incidence of COVID-19 than those aged 60 years or younger (4.3% vs 1.8%). The paper concludes that hospital admission and recurrent hospital visits are potential risk factors for SARS-CoV-2 infection. It recommends that aggressive measures be undertaken to reduce frequency of hospital visits of patientswith cancer during a viral epidemic going

forward. For patients who require treatment, proper isolation protocols must be in place to mitigate the risk of SARS-CoV-2 infection.

Simcock. COVID-19: Global Radiation Oncology's Targeted Response for Pandemic Preparedness. Clinical and Translational Radiation Oncology 22 (2020) 55–68 doi.org/10.1016/j.ctro.2020.03.009

Country Context: Global

In March 2020, the radiation oncology (#radonc) community held an urgent online journal club on Twitter, to discuss issues arising from the impact of the COVID-19 pandemic on radiation oncology patient care and to create some consensus on crucial next steps. There were 121 global contributors. This paper summarises these discussions around themes of infection prevention, rationalisation of workload and working practice in the presence of infection. From the discussions, recommendations were made for minimising the risk of COVID transmission during radiotherapy treatment; prioritising treatments; radical treatments; adjuvant treatments, brachytherapy and palliative treatments. Disease-specific recommendations focused on breast, prostate and lung cancers.

Achard et al. Radiotherapy in the time of the Coronavirus pandemic: when less is better. Int J Radiat Oncol Biol Phys. DOI: https://doi.org/10.1016/j.ijrobp.2020.03.008

Country context: Global

This article emphasises that radiation oncologists, as part of health-care workers community, are directly involved in the fight against the viral spread and facing enormous challenges with minimising the epidemic impact on cancer patients' treatment. The authors propose the use of practical measures to mitigate the impact of treatment interruptions, particlularly the wider implementation of hypofractionated schedules for cancer patients. They are of the view that rethinking institutional radiotherapy (RT) fractionations by implementing hypofractionated schedules may represent, when feasible, the essential paradigm to mitiating the impact of the COVID-19 pandemic on radiation therapy and cancer care.

Yang et al. Clinical strategies for treating pediatric cancer during the outbreak of 2019 novel coronavirus infection. Pediatr Blood Cancer, 67 (5), e28248. May 2020

Country context: Global

The letter to the editor aims to provide suggestions on how to choose a reasonable treatment strategy between epidemic prevention and children's anticancer therapy during the COVID-19 pandemic. The authors propose the following:

Pre-admission screening: Before admission, screening for SARS-CoV-2 infection should be carried out in the outpatient and emergency department for every patient and family members or caregivers. Children with fever (temperature > 37.3°C) within three days are advised to be referred to the fever clinic for screening. For suspicious patients, lung CT examination and/or nucleic acid test should be performed. Isolation and corresponding treatment should be given according to the guideline for suspected and confirmed cases.

Patients who are excluded as 2019-nCoV infection can receive anticancer treatment after the isolation is removed.

Preventive measures during hospitalization: Cross infection between medical staff and patients can occur. Strict implementation of these protective measures, including hand hygiene, medical waste management, and other hospital infection control work should be enforced.

Chemotherapy: For children with normal physical status, systematic chemotherapy should be carried out after a detailed assessment of the risk of chemotherapy. For children with stable disease, One can consider moderate reduction of chemotherapy or prolongation of interval between cycles. Chemotherapy at the local hospital is recommended in order to reduce population migration.

Radiotherapy: The effect of radiotherapy on the immune function is relatively less than chemotherapy; thus, it is reasonable to continue radiotherapy according to the overall plan. However, subsequent chemotherapy might be moderately delayed. For children who are ready to start radiotherapy, a moderate delay can be scheduled.

Surgery: For suspicious or confirmed COVID-19, if surgery has to be performed, preoperative preparation should be conducted in an isolation ward, and transportation should be conducted through special channels. Appropriate infection prevention and control measures must be strictly performed during surgery and anesthesia. The operation room should be thoroughly disinfected after the operation.

Follow-up: For patients who require regular follow-up after surgery, it is recommended to delay the review time if there is no special discomfort, or it can be done in the nearest hospital. If the examination results are abnormal, contact the oncologist to discuss a follow-up plan.

Challenges Posed by COVID-19 to Children With Cancer. Lancet Oncol 2020 Mar 25[Online ahead of print] DOI: 10.1016/S1470-2045(20)30205-9

Country context: Global

In this editorial correspondence, the authors highlight the challenges posed by Covid-19 to children with cancer and the implications for their caregivers and families. Notably, the authors argue that, given the high vulnerability of immunosuppressed children to infection and their treatment peculiarities, postponement of therapy may not be an option for chidren on treatment. They recommend that minimising the number of people visiting oncology departments by limiting visitor numbers and postponement of or use of telehealth for non-critical outpatient visits, such as for children in follow-up or survivorship clinics, should be implemented to protect children who require hospital visits.