

Letter to the Editor

A Call for a Radiation Oncology Model Based on New 4R's During the COVID-19 Pandemic



Shrinivas Rathod, FRCPC,* Arbind Dubey, FRCPC,
Amitava Chowdhury, RCSI, Bashir Bashir, FRCPC, and
Rashmi Koul, FRCPC

CancerCare Manitoba and University of Manitoba, Winnipeg, Manitoba, Canada

We are in the midst of an unprecedented crisis worldwide. Since the first reports in China on December 31, 2019, coronavirus disease 2019 (COVID-19) infections have spread extensively across the globe. As of April 4, 2020, >1,100,000 cases and >60,000 deaths have been reported worldwide.¹ These numbers continue to increase exponentially and the health care system is strained to the maximum. Immunocompromised and elderly individuals are susceptible to COVID-19 with a higher risk of mortality.² Data show an aggressive course of COVID-19 and >3 times a higher risk of death in patients with cancer.³ The health care system is under enormous pressure to deal with this constantly changing and ever-evolving crisis. Several countries and provinces are reallocating resources and prioritizing available options in this emergency. Radiation oncology is an integral part of cancer care and expected to face significant challenges in the coming weeks as COVID-19 continues to impact our lives.⁴⁻⁶

Classic radiation oncology is based on the 4 classic R's: repair, reassortment, repopulation, and reoxygenation. During the COVID-19 pandemic and global emergency, we suggested a radiation oncology model based on 4 new R's to mitigate the impact of the current pandemic on patients and cancer centers.⁷ The new 4R's are remote/virtual care (ie, reduce in-person consultation/follow up/treatment visits), ration radiation (ie, offer radiation wisely and avoid radiation therapy with minimal benefit), rational deferring of radiation (as appropriate),

and reduce fractions/hypofractionated radiation (where applicable).

Significant emphasis is placed on minimizing in-person visits for patients, and several Canadian provinces have adopted remote/virtual care as a standard model during the current emergency.⁸ Remote/virtual care helps minimize patient visits to the hospital and thus the risk of infection.

Radiation oncologists should wisely ration radiation and avoid radiation in cases where there is minimal or questionable benefit. Favorable ductal carcinoma in situ⁹ (ie, mammographically detected, <2.5 cm in size, low-intermediate grade, and adequate resection margins), favorable low-grade invasive breast carcinoma¹⁰ (age ≥ 70 years, primary ≤ 3 cm with negative resection margins, estrogen receptor positive, node negative, and eligible to receive hormone therapy), and low-volume favorable intermediate-risk prostate carcinoma¹¹ may be appropriate for active surveillance. There are several potential scenarios where avoiding radiation should be strongly considered.

We should also diligently assess options of rational deferring of radiation as appropriate based on the clinical scenario. Ductal carcinoma in situ and invasive breast carcinoma could be safely delayed up to 12 weeks.¹²⁻¹⁴ Favorable intermediate-risk prostate cancer and unfavorable intermediate-risk prostate cancer could defer radiation for 3 to 4 months or longer. Androgen deprivation therapy could be used as a temporizing measure for radiation deferral in appropriate cases, such as unfavorable intermediate-risk and high-risk prostate cancer.^{15,16}

In these unusual times, the use of reduced fractions/hypofractionation regimens is strongly recommended.

Sources of support: None.

Disclosures: None.

* Corresponding author. Shrinivas Rathod, FRCPC; E-mail: srathod@cancercare.mb.ca

<https://doi.org/10.1016/j.adro.2020.04.013>

2452-1094/© 2020 The Author(s). 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/>).

Before COVID-19, the use of hypofractionated radiation was highly variable across the world for various reasons despite supportive data. There are enough data to practice this regimen safely for common cancer sites, such as the prostate, breast, rectum, lung, and even palliative situations.^{7,17–22} The use of hypofractionated and ultra-hypofractionated radiation could save potentially 10 to 20 visits and thus lower the risk of infection and even mitigate the risk of treatment breaks and allow for radiation facilities with reduced manpower. With the expected resource and manpower constraints, this model is gaining popularity.²³ A clinical scenario where boost radiation adds minimal benefits to the outcomes is also another potential opportunity to reduce the number of fractions.^{24,25} Judicious resource allocation is paramount and hypofractionation regimens serve a vital purpose.

We used this model and proposed thoracic cancer-specific provincial consensus.⁷ Prostate and breast cancer-specific radiation guidelines were recently proposed.^{16,23} The new 4Rs-based model framework could help several other disease site group designs and use site-specific policies. The framework would also help the global radiation oncology community use constrained resources efficiently, function and fight better, and ultimately flatten the curve of the COVID-19 pandemic. May we all emerge victoriously.

References

- World Health Organization. Coronavirus disease (COVID-19) pandemic. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed April 4, 2020.
- Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708-1720.
- 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.
- Filippi AR, Russi E, Magrini SM, Corvò R. Letter from Italy: First practical indications for radiation therapy departments during COVID-19 outbreak [Epub ahead of print]. *Int J Radiat Oncol Biol Phys*. 2020. <https://doi.org/10.1016/j.ijrobp.2020.03.007>. Accessed April 4, 2020.
- Rivera AON, Thomas E, Miller R, Knoll MA. The impact of COVID-19 on radiation oncology clinics and cancer patients in the U.S. *Adv Radiat Oncol*. 2020;5:538-543.
- Krengli M, Ferrara E, Mastroleo F, Brambilla M, Ricardi U. Running a radiation oncology department at the time of coronavirus: An Italian experience. *Adv Radiat Oncol*. 2020;5:527-530.
- Rathod S, Dubey A, Bashir B, et al. Bracing for impact with new 4R's in the COVID-19 pandemic- a provincial thoracic radiation oncology consensus [Epub ahead of print]. *Radiother Oncol*. 2020. <https://doi.org/10.1016/j.radonc.2020.03.045>. Accessed April 4, 2020.
- Canadian Medical Association. Virtual care in Canada. Available at: https://www.cma.ca/sites/default/files/pdf/News/Virtual_Care_discussionpaper_v2EN.pdf. Accessed April 4, 2020.
- McCormick B, Winter K, Hudis C, et al. RTOG 9804: A prospective randomized trial for good-risk ductal carcinoma in situ comparing radiotherapy with observation. *J Clin Oncol*. 2015;33:709-715.
- Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: Long-term follow-up of CALGB 9343. *J Clin Oncol*. 2013;31:2382-2387.
- Mohler JL, Antonarakis ES, Armstrong AJ, et al. Prostate cancer, version 2.2019, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2019;17:479-505.
- Shurell E, Olcese C, Patil S, McCormick B, Zee KJV, Pilewskie ML. Delay in radiotherapy is associated with an increased risk of disease recurrence in women with ductal carcinoma in situ: Risk of IBTR With RT Delay in DCIS. *Cancer*. 2017;124:46-54.
- Olivetto IA, Lesperance ML, Truong PT, et al. Intervals longer than 20 weeks from breast-conserving surgery to radiation therapy are associated with inferior outcome for women with early-stage breast cancer who are not receiving chemotherapy. *J Clin Oncol*. 2008;27:16-23.
- Karlsson P, Cole BF, Colleoni M, et al. Timing of radiotherapy and outcome in patients receiving adjuvant endocrine therapy. *Int J Radiat Oncol Biol Phys*. 2010;80:398-402.
- Pisansky TM, Hunt D, Gomella LG, et al. Duration of androgen suppression before radiotherapy for localized prostate cancer: Radiation therapy oncology group randomized clinical trial 9910. *J Clin Oncol*. 2015;33:332-339.
- Zaorsky N, Yu J, McBride S, et al. Prostate cancer radiotherapy recommendations in response to COVID-19. *Adv Radiat Oncol*. 2020;5:659-665.
- Dearnaley D, Syndikus I, Mossop H, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, noninferiority, phase 3 CHHiP trial. *Lancet Oncol*. 2016;17:1047-1060.
- Widmark A, Gunnlaugsson A, Beckman L, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RTPC randomised, non-inferiority, phase 3 trial. *Lancet*. 2019;394:385-395.
- Brunt A, Wheatley D, Yarnold J, et al. Acute skin toxicity associated with a 1-week schedule of whole breast radiotherapy compared with a standard 3-week regimen delivered in the UK FAST-Forward Trial. *Radiother Oncol*. 2016;120:114-118.
- Whelan TJ, Julian JA, Berrang TS, et al. External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): A randomised controlled trial. *Lancet*. 2019;394:2165-2172.
- Vicini FA, Cecchini RS, White JR, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. *Lancet*. 2019;394:2155-2164.
- Rathod SJB, Fidarova E, et al. Quality of life outcomes in a phase 3 randomized trial of optimization of treatment of advanced non-small cell lung cancer using radiation therapy and chemotherapy: IAEA multicentric randomized phase 3 study (NCT00864331). *Int J Radiat Oncol Biol Phys*. 2017;99:S103.
- Al-Rashdan A, Roumeliotis M, Quirk S, et al. Adapting radiotherapy treatments for breast cancer patients during the COVID-19 pandemic: Hypofractionation and accelerated partial breast irradiation to address World Health Organization recommendations. *Adv Radiat Oncol*. 2020;5:575-576.
- Moran MS, Zhao Y, Ma S, et al. Association of radiotherapy boost for ductal carcinoma in situ with local control after whole-breast radiotherapy. *JAMA Oncol*. 2017;3:1060.
- Bartelink H, Maingon P, Poortmans P, et al. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. *Lancet Oncol*. 2015;16:47-56.