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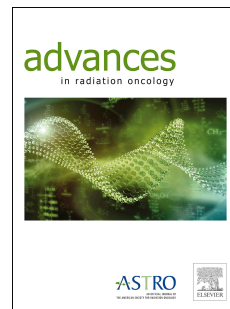
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Adapting Radiotherapy Treatments for Breast Cancer Patients during the COVID-19 Pandemic: Hypofractionation and Accelerated Partial Breast Irradiation to Address World Health Organization Recommendations

A. Al-Rashdan^{1,2}, M. Roumeliotis^{1,2,3}, S. Quirk^{1,2,3}, P. Grendarova^{1,4}, T. Phan^{1,2}, J. Cao^{1,2}, N. Logie^{1,2}, W. Smith^{1,2,3}, L. Barbera^{1,2}

1 Department of Oncology, University of Calgary, Calgary, Alberta, Canada

2 Tom Baker Cancer Centre, Calgary, Alberta, Canada

3 Department of Physics and Astronomy, University of Calgary, Calgary, Alberta, Canada

4 Grand Prairie Cancer Centre, Grand Prairie, Alberta, Canada

Corresponding author:

Lisa Barbera MD MPA FRCPC

Professor and Chair, Department of Radiation Oncology

Tom Baker Cancer Centre, 1331 29 St NW, Calgary, AB, Canada, T2N 4N2

(p) +1-403-521-3077,

(f) +1-403-283-1651

lisa.barbera@albertahealthservices.ca

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On March 11, 2020, the World Health Organization (WHO) declared the COVID-19 outbreak as a global pandemic. Public health officials have urged communities to minimize transmission by changing our habits, including post-travel self-isolation, increased hygiene vigilance, remote working, and social distancing (1). To accommodate these measures, radiotherapy departments are adapting by limiting on-site staff, patient visits and patient-to-staff interactions, reconciling the goals of minimizing exposure for both patients and health care providers while still maintaining quality cancer care.

During this pandemic, opportunities exist to reduce patients' visits and thus potential exposure to COVID-19 and judiciously allocate radiotherapy operation resources by implementing alternative hypo-fractionated regimens for select, safe treatment sites. Radiotherapy for patients with breast cancer represents a significant proportion of treatment delivery workload in any radiotherapy department. Some centers may consider omission or deferral of radiation therapy in those patients perceived to have a lower risk of adverse outcomes, such as patients with ductal carcinoma in situ (DCIS) or early stage disease with low risk features. However, with an unknown and potentially lengthy timeline for a pandemic, many patients and clinicians are not comfortable with these options. Modeling studies predict that this pandemic may take months to peak and these heightened public health measures may remain in place for many months (1). Therefore, strategies to adapt to this "new normal" are crucial to maintaining access to radiotherapy for cancer patients. Our strategy is based on the appropriate use of hypofractionation and accelerated partial breast irradiation (APBI).

The focus on breast radiotherapy is crucial due to its significant impact on radiotherapy resources. The adoption of hypofractionation for patients, including those requiring locoregional irradiation, and the option of accelerated partial breast irradiation (APBI) for suitable patients based on international consensus guidelines can serve to significantly reduce the number of radiotherapy fractions and, as a result, minimize patient exposure during treatment and counteract increased pressure on the healthcare system.

Hypofractionation regimens, such as 42.5 Gy in 16 fractions or 40 Gy in 15 fractions have demonstrated equivalent local control and cosmetic outcomes in most patients after breast conserving therapy (2). Although less

commonly used in post-mastectomy with regional nodal irradiation, hypofractionation is comparable to standard fractionation with favourable long-term efficacy results and low overall toxicity (3). More recently, one-week 5 fraction regimens have been compared to the 40 Gy in 15 fraction whole breast radiation in the UK FAST Forward trial for treatment of early stage disease with favourable acute toxicity (4). We are now awaiting the local control and survival data outcomes from this trial. Compared to the conventional 5-week fractionation of 50 Gy in 25 fractions, these shortened courses save patients between 9 to 20 visits to the cancer centre.

The evidence to support APBI for early stage breast cancer is also maturing. In 2019, two separate phase III randomized control trials – RAPID and NSABP B39/RTOG 0413 – reported on efficacy of APBI fractionation regimens compared to whole breast irradiation (5,6). The results are favourable, showing no statistical difference in overall survival and comparable local control for patients treated in the APBI arm. The evidence supporting APBI agrees with the American Society of Radiation Oncology (7) patient selection guidelines. Many centres have adopted the use of APBI in a limited capacity, primarily for patients on clinical trials. Publications describing APBI techniques that meet major trial constraints with simple 3D conformal techniques and, more recently, advanced techniques for improved dosimetry are available to support the radiation planning (9). Implementing an APBI fractionation of 27 Gy in 5 fractions can save a further 10, 11, or 20 treatment visits for select patients.

In our tertiary care facility, the majority of patients with breast cancer (all stages; intact breast and post-mastectomy locoregional) are standardly treated with a 3-week regimen of 42.5 Gy in 16 fractions. In consideration of COVID-19 and after a multidisciplinary review, our centre is now offering a 5-fraction APBI option for eligible patients (8). A review of the last three months of patient treatment data was performed at our institution to determine the impact of this change on radiotherapy resources. Across all tumour sites, 770 total patients were treated and, of these, breast cancer patients represent 30% of all delivered fractions. For our patient population, approximately 40% of breast cancer patients are suitable candidates for APBI. Over a 3-month span, a 5-fraction regimen of APBI for these eligible breast cancer patients could reduce the number of daily treatment visits by approximately 500 and 900 for 16- and 25-fraction regimens, respectively. Across all radiotherapy resources, this overall reduction is approximately 5 to 10% of total daily fractions.

This commentary intends to advocate for careful adoption of APBI for centres that are equipped to make the transition. Many centres have implemented the use of APBI in a limited capacity, primarily for patients on clinical trial. Publications describing APBI techniques that meet major trial constraints with simple 3D conformal techniques and, more recently, advanced techniques for improved dosimetry are available to support the radiation planning (9).

Flattening the COVID-19 curve may necessitate careful adoption of measures that decrease the interaction within the radiotherapy departments and minimize treatment interruptions, without compromising their cancer outcomes. At a time when healthcare systems aim to minimize stress on the system's resources, radiotherapy can do its part to adapt. As noted by Achard et al (10), the use of practical measures to ensure the treatment of radiotherapy patients is important to approach with a balance of pragmatism and safety. The utilization of hypofractionated regimens and APBI may be a treatment option that best fits the balance of patient and staff safety while still maintaining access to quality cancer care during a pandemic.

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