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Commentary

Commentary on: The actual benefit of intraoperative radiation therapy using 50 kV x-rays in early breast cancer: A retrospective study of 676 patients

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Abbreviations: IORT: Intraoperative Radiation Therapy; PBI: Partial Breast Irradiation; COVID-19: Coronavirus Disease 2019

We recently published the results of a retrospective multicenter study of 676 early breast cancer patients with favorable prognostic factors, treated by breast-conservative surgery and intraoperative radiation therapy (IORT) [1]. This study confirmed that partial breast irradiation (PBI) using IORT via a 50 kV photon device is safe and well-tolerated in select early breast cancer patients. These results, as well as other studies and the recent update of the TARGIT-A trial, should favor its routine use, particularly within the context of the coronavirus disease 2019 (COVID-19) pandemic [2].

This year was branded by the COVID-19, and many countries had to adapt to the issues coming out of this situation. The COVID-19 infection is known to be contagious, involving droplet and hand contamination. Protective measures were taken, like disinfection and avoiding mixing positive or suspected patients with COVID-19-free patients, and disrupted the usual organization of radiotherapy units [3-5].

The elderly rapidly emerged as the most vulnerable patients. Cancer centers faced a challenging dilemma, needing to remain COVID-19-free structures to be able to continue to take care of frail patients [3,6]. In the early phase of the disease spread, it was recommended to postpone as much in-patient treatment as possible, especially in the elderly, to keep them away from life-threatening contamination [3,7,8]. Hence, elderly patients with early endocrine receptors positive breast cancer were offered neoadjuvant endocrine therapy, and breast-conservative surgery, as well as adjuvant radiation therapy, were both postponed to the time of COVID-19 disease spreading slowing down [7,9]. The postponing time of local treatments was not that much since the acute phase of the COVID-19 disease lasted for two months, thanks to summer coming up. Unfortunately, a second wave emerged by the end of autumn, and radiation oncologists are concerned with several problems as follows. First, the elderly population is well-known to be particularly vulnerable to COVID-19 disease infection, urging for social distancing and, therefore, travel limitation [10,11]. Second, radiation oncologists face the fear of treatment interruption if patients contract the disease, in which case the radiation therapy treatment would be inefficient [12]. Third, if infected patients or cured COVID-19 patients resume the radiation therapy course, we don't know the effects of delivering limited lung irradiation (such as the one observed in breast irradiation) in patients with lungs impaired by the COVID-19 disease. Fourth, patients are themselves reluctant to follow daily radiation therapy in this context.

Considering these points, the use of IORT could be an appealing and convenient option for early-stage breast cancer treatment. This 20 Gy single radiation dose is safe to use as long as the conditions are suitable. It is crucial more than ever during the current COVID-19 pandemic to try to

limit the patients commuting to their medical institution, increasing their risk of getting infected by COVID-19, especially for older patients with comorbidities. Compared to iso- or hypo-fractionated regimens (even five fractions treatments like described in the FAST-forward trial[13]), adjuvant IORT is, in the vast majority of cases, directly completed during the surgery, significantly reducing the course of treatment and, therefore, the risk of COVID-19 infection during radiotherapy treatment, which could, even in the most common asymptomatic form, lead to treatment discontinuation. All the same, patients must be informed of a 15-30% risk of adjuvant external beam radiation therapy when the full pathology report is obtained. Thus, IORT would enhance the safety of the patient herself, of the medical staff, and of the other patients whose disease does not allow such single-dose treatment, not only in radiotherapy centers, but also by reducing the number of medical transports (which in addition suppresses their cost – economic aspects taking a more important place in health systems' sustainability since the beginning of pandemic) [14]. Under the current circumstances, all of these arguments led institutions and savant societies like the Italian association of radiotherapy and clinical oncology (AIRO) to recommend the prioritization of IORT as much as possible [14,15].

As a treatment, radiation therapy alone was not associated with an increased risk of both severe adverse event or short-term mortality in the COVID-19 context, although breast cancer patients, as well as radiation therapy, were both weakly represented in retrospective studies (about 10%) [6,16]. Indeed, authors have reported a high rate of COVID-19-associated lung fibrosis [17,18], which could appear to be irreversible [19]. Therefore, in the case of COVID-19 infection, even asymptomatic, long-term cardiac or pulmonary consequences should be considered and call for caution regarding adjuvant whole-breast irradiation (WBI), which is known to deliver small radiation doses in these organs. In the last case, the use of IORT can protect both of them by decreasing the heart and lung delivered doses [20,21].

Besides, some additional elements about IORT were reported over 2020. First of all, the favorable toxicity profile remains consistent between studies and mimics what we observe in daily practice. The efficacy outcomes such as local recurrence also converge on studies already published like ours [2,20-23]. These updates allow the radiation oncologist to propose IORT with more confidence. Patients should be involved in the choice of adjuvant breast irradiation, with clear information about the different options and their consequences. Alvarado et al. showed that most patients who choose to undergo radiation therapy are willing to accept some degree of uncertain side effects and a slightly higher risk of local recurrence to receive radiation delivered as a single intraoperative dose [24]. For that matter, a French study will soon evaluate patients' preferences in their early-stage breast cancer treatment involving IORT, WBI, or adjuvant radiation omission, and could help us guide clinical decision making in this area.

In conclusion, adjuvant IORT provides both acceptable efficacy and favorable tolerance. Given its advantages as compared to WBI, it should be considered as an option and offered to select early-stage breast cancer patients in centers with experience in it and where it is available, particularly within the context of the COVID-19 pandemic.

Authors Contributions Statement

All authors wrote the comment.

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