

## Clinical relevance of radiation pneumonitis in breast cancers

Presently, it is well established that post-operative radiation therapy (RT) reduces both the risk of local recurrence and extends overall survival in patients with breast cancer (BC).<sup>[1-4]</sup> However, concerns have been raised about the risk of acute and chronic RT-induced side effects as there are number of treated individuals and their expected survival is longer compared to most patients with other malignant diseases. Radiation pneumonitis, cardiac toxicity, arm lymphedema, neuropathy, and skin changes are examples of the wide range of complications that have been associated with adjuvant radiotherapy.<sup>[5,6]</sup> The present article by Bhadra *et al.* in this issue of South Asian Journal of Cancer, focuses on one aspect of the first mentioned RT-related complication, viz. lung density changes measured by computed tomography (CT) and their relation to clinical symptoms.<sup>[7]</sup> Since the data on toxicity after RT in BC in high-risk and advanced BC is lacking from developing countries, this work by Bhadra *et al.* is worth admiring.

Patients with radiation pneumonitis may present with symptoms, i.e., dyspnea, non-productive cough, and/or low-grade fever. Only grade 2 or greater pneumonitis, which requires steroids is considered clinically significant. Radiologic lung injury is more common than symptomatic pneumonitis. On the chest radiograph, this is classically manifested as an area of consolidation confined to the treatment portal, so-called straight-line pneumonia. The use of CT scans for follow-up has permitted a much more detailed description of the changes seen in the acute phase of radiation lung injury. These radiologic features include ground-glass opacities, patchy consolidation, pleural reactions, and lung fibrosis.<sup>[8]</sup> This prospective study by Bhadra *et al.* on 53 patients have reported 28% incidence of radiation pneumonitis, which is comparable to the literature. They have found a positive correlation of symptomatic pneumonitis with increasing CT scores, which has been described in the literature.<sup>[9]</sup> It would have been useful to evaluate the radiological changes in a chest X-ray as well, since it has been found that the incidence of chest X-ray abnormalities were 35% as compared to 15% in CT in a cohort of 87 patients of BC.<sup>[10]</sup> The diagnosis of radiation pneumonitis can be established on a chest X-ray rather than on a CT scan, especially in the context of the developing countries. The addition of a CT exam should be considered in patients with respiratory distress following RT, where the chest X-ray does not reveal the cause for the symptoms, e.g., radiation pneumonitis (structural changes

in agreement with the beam arrangement), infection, or disseminated malignant disease, and pulmonary embolism should be excluded.

Though the authors have mentioned the division of CT thorax into three divisions: Apical-lateral, central-parahilar, and basal-lateral segments, the prevalence of CT scan abnormalities in these segments has not been mentioned. Radiological abnormalities in the central-parahilar and apical-lateral regions have been significantly correlated to pulmonary complications by Lind *et al.*<sup>[9]</sup> The positive correlation of decrease in FVC in patients with CT scores 4-9 have been reported by other authors as well. The time course of pulmonary function test (PFT) changes after locoregional RT for BC follows a biphasic pattern. An early reduction in PFTs at 3-6 months with a partial recovery at 12 months after RT is followed by a late, more important PFT reduction up to 8-10 years after RT. Tamoxifen use may have an impact on this late decline in PFTs. At 8-10 years after RT, mean reductions in Forced expiratory volume at 1 second (FEV1) of 4% and in Vital Capacity, Diffusion lung capacity for carbon monoxide (VC, DLCO), and Total Lung Capacity (TLC) of 5%, 9%, and 11%, respectively, were observed compared with pre-RT values. For FEV1 and DLCO, an early decrease was predictive for a late decrease.<sup>[11]</sup>

Radiation pneumonitis after RT for BC has been reported to be related to the following factors: The amount of lung irradiated within the tangential fields, the use of an additional supraclavicular (SC) field, prior exposure to chemotherapy (anthracyclines, taxanes), high-dose chemotherapy, and concurrent tamoxifen medication and smoking habits. Concurrent use of tamoxifen results in higher incidence of radiation pneumonitis.<sup>[12]</sup> The sequential use of chemotherapy was found to result in an actuarial rate of radiation pneumonitis in the paclitaxel-treated group as 15.4% compared with 0.9% with non-paclitaxel-containing chemotherapy.<sup>[13]</sup> Concurrent paclitaxel increases the incidence of RP to 20%.<sup>[14]</sup> RT to the chest wall results in <1% incidence of radiation pneumonitis, and with locoregional RT this increases to 11%.<sup>[15]</sup> The authors did not find a significant difference in change in FVC with or without inclusion of internal mammary chain (IM) of lymphnodes. Recently European Organisation for Research and Treatment of Cancer (EORTC) reported the incidence of radiation pneumonitis as 4% as compared to 1.3% with or without inclusion of IM in the irradiation field, where IM was treated with a combination of photons and electrons.<sup>[16]</sup>

A correlation between increasing irradiated lung volumes and pulmonary complications needs to be mentioned. A correlation between increasing irradiated lung volumes >20 Gy-level (V20), and pulmonary complications has been found. Other dosimetric factors like V13, V20, V30 and mean lung dose have also been found to correlate with

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radiation pneumonitis.<sup>[17]</sup> Use of CT scans to help beam design can avoid the thickness of lung being irradiated in the tangential fields. Individualized cerrobend blocks designed for each patient to define the deep border of the tangential fields when there is a need of IM irradiation can avoid lung irradiation. Use of partial wide tangential fields (P WTF) designed to selectively irradiate only the superior IMN and block the inferior portion of the field by shaped cerrobend blocks or multi-leaf collimators are used by certain centers to reduce incidental cardiac and lung irradiation. Use of 3D conformal radiotherapy (3D-CRT) can minimize the percent of incidentally irradiated lung volume and only 2% radiation pneumonitis has been reported.<sup>[18]</sup> Even with hypofractionated regimes, the incidence of RP is 1.4%.<sup>[19]</sup>

In conclusion, data on pulmonary toxicity in high-risk and advanced BC after RT from developing countries is lacking. Implementation of 3D-CRT reduces this toxicity significantly.

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