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DOSIMETRY PREDICTORS OF LATE AND ACUTE TOXICITY AFTER WHOLE BREAST RADIOTHERAPY IN A MONOINSTITUTIONAL LARGE POPULATION

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Abstract

The thesis study aimed to identify dosimetric NTCP models for acute and late skin toxicity after breast cancer radiotherapy. The investigated cohort consisted of 1325 early-stage breast cancer patients treated at San Raffaele Hospital between 2009 and 2017 with a hypofractionated scheme (40 Gy in 15 fractions) without boost delivered to the whole breast. To explore the possible causality between the damage to the cutaneous tissue and the acute and late reactions, we focused on the dose distribution of the skin, defined as the first 5 mm body layers. The study endpoints were: (i) any acute grade 2 or plus skin toxicity; (ii) oedema and hyperpigmentation development; (iii) late moderate/severe grade of fibrosis, atrophy, telangiectasia and pain; and (iv) liponecrosis. For the first time in these endpoints, the considered Organ at Risk for the dosimetry was the first 5 mm of the breast skin. The PTV volume was confirmed as one of the most impacting factors in developing any sequela (except liponecrosis). The volume receiving 20 Gy, the 50% of the prescription dose, was applied as a dosimetric descriptor in models for (i), (ii), (iii) and was able to replace PTV giving, at the same time, the possibility to better interpret the damage in terms of irradiated skin as well as being more generalizable, being independent on the contouring phase; in addition, V42 Gy was entered in the model for describing late toxicity (iii). Among the treatment and patient factors, lymph node dissection was the most impacting factor for three of the four endpoints (i-ii-iii), and it was included as a covariate in the model together with the dosimetric descriptor. Obesity was identified as a risk factor for early skin reaction, while aromatase inhibitor and hormone therapy and age were found as protective factors in a multivariate model for late toxicity and liponecrosis, respectively. The cosmetic status after surgery was found to be associated with the development of late fibrosis and was included in that multivariable model to account for the damage to the breast parenchymal tissue caused by the conservative surgery.