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Partial breast irradiation

Target volume delineation in external beam partial breast irradiation: Less inter-observer variation with preoperative- compared to postoperative delineation ☆

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ABSTRACT

The challenge of adequate target volume definition in external beam partial breast irradiation (PBI) could be overcome with preoperative irradiation, due to less inter-observer variation. We compared the target volume delineation for external beam PBI on preoperative versus postoperative CT scans of twenty-four breast cancer patients.

Accuracy of target volume delineation is of great importance in external beam partial breast irradiation (PBI) in breast conserving therapy in early breast cancer because whole breast irradiation is omitted. PBI should provide similar local control rates as the standard whole breast irradiation. Whole breast irradiation after local excision of the tumor is associated with a tumor control probability of more than 90% after 10 years. An additional boost dose after whole breast irradiation increases the local control rate, with a local recurrence rate of 6% at 10 years [1]. In order to result in similar local control rates, PBI should accurately irradiate the proper target volume. However, delineation studies defining the postoperative clinical target volume (CTV) for boost irradiation or PBI after lumpectomy have shown a large inter-observer variability [2–4]. Intra-operative (brachy) therapy, as PBI method, does not have this disadvantage. The absence of pathology information during treatment may however lead to over- or under treatment of the target area [5]. 3D-external beam conformal radiotherapy (RT) has advantages in terms of dose homogeneity and it is wide available, making it accessible to large groups of patients. By delivering external beam PBI preoperatively, less inter-observer variation in target volume delineation is expected. Therefore preoperative irradiation might prove to be a more effective way of delivering PBI.

Preoperative RT for other tumors such as sarcomas and rectal carcinomas has led to smaller treatment volumes and to less toxicity of the normal tissue compared to the postoperative setting [6,7]. Breast cancer studies suggests the same for preoperative PBI [8,9]. By reducing target volumes in PBI, smaller volumes of normal breast tissue will be irradiated, probably leading to less adverse effects and an improved cosmetic outcome. The aim of this study was to compare target volume delineation for preoperative external beam PBI with that for postoperative external beam PBI, with respect to inter-observer variation and difference in size of the delineated volumes.

Material and methods

Patient characteristics

For this study we used the dataset of 24 of the 26 patients from our previous study [10], where we investigated the influence of the use of a preoperative CT scan on the inter-observer variation for delineation of the boost CTV. Patients were scanned in RT position prior to and after surgery, as described earlier [10]. That study was approved by the Medical Ethics Committee of the Maastricht

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University Medical Centre, according to the Dutch law and regulations. Written informed consent to undergo an additional CT scan was given by all patients. Two patients were excluded from the present study, since the tumor appeared to be multifocal. We excluded these patients to make sure that patient selection was comparable with patient selection for PBI. In all 24 patients a mammography and ultrasound was available to guide delineation. Preoperative magnetic resonance imaging (MRI) was available in 6 out of 24 patients. The radiological mean tumor size was 12.6 mm (range, 6–23 mm), and the mean pathological tumor size was 10.4 mm (range, 3–17 mm). In the present study we used the postoperative delineated boost volumes as a surrogate for postoperative PBI and compared these to preoperative target volume delineation.

Delineation

Five observers delineated the tumor bed on the postoperative scan, and expanded this delineation with 15 mm minus the minimum histological free margin (CTV-post). At the time of delineation, they did not have the information of the preoperative CT scan. Hereafter, the same observers delineated the gross tumor volume (GTV) on the preoperative scan; this delineation was expanded with 15 mm (CTV-pre). Both CTV-post and CTV-pre were, if required, adjusted to exclude the chest wall and the first 5 mm underneath the surface of the skin. One observer delineated the whole breast on the pre- and postoperative scans of all patients. All observers were experienced radiation oncologists (5–20 years experience), specialized in radiation treatment of breast carcinoma.

Delineation was performed using strict guidelines as described previously [10]. In short, the CTV-post was defined as the 15 mm rim of tissue that surrounded the primary tumor. To reconstruct this rim of tissue on the planning CT scan, guidelines were developed for three postoperative situations based on the presence of seroma; clear seroma cavity visible, no seroma cavity visible or a partial seroma cavity present. Surgical clips were placed at the deepest resection border and used for guidance [10]. The mean number of surgical clips placed during surgery was 5.1 (range, 4–6).

Observation parameters

We tested the inter-observer variation by calculating the conformity index (CI = common volume divided by encompassing volume; CI = 1 indicates perfect agreement) and the distance between the centers of mass of the target (ComD) for each patient, for each observer pair and for both volumes. We also calculated the standard deviation (sd) of all target volume delineations with respect to the median delineation (in cm), defined per patient as an artificial median structure on which at least half the observers agreed [11]. The mean sd of the delineations of all observers with respect to this median delineation is a measure of the inter-observer variation. Further, we compared the mean volumes of the GTV and the tumor bed, the volumes of CTV-pre and CTV-post and the CTV-pre-versus the CTV-post/whole breast volume ratio. We estimated the mean GTV/tumor bed to CTV-pre/CTV-post expansion for each patient, by assuming that all delineations are perfectly spherical but limited to the glandular tissue.

Statistical parameters

Statistical significance was determined using a Wilcoxon test, with a significance level of $\alpha = 0.05$. Correlations were studied using the Spearman rank correlation. All statistical tests were performed using the SPSS for windows software (version 19).

Results

The mean CI, the mean ComD and the mean sd all show considerably less inter-observer variation in the preoperative setting compared to the postoperative setting (all parameters: $p < 0.001$). The mean CI was preoperative 0.78 and 0.38 postoperative. The mean ComDs pre- and postoperatively were 0.36 cm and 1.02 cm; the mean sds pre-and postoperatively were 0.30 cm and 0.57 cm, respectively. Fig. 1 shows examples of delineation of the CTV-post and the CTV-pre for two patients with a clearly superior conformity in the preoperative situation.

The mean volumes of the GTV and the postoperative tumor bed were 0.97 cc (sd = 0.83 cc, range 0.01–4.40 cc) and 8.68 cc (sd = 9.16 cc, range 0.27–52.61 cc), respectively ($p < 0.001$). The volume of the CTV-pre was on average 36.8 cc (sd = 12.1 cc) compared to CTV-post 41.0 cc (sd = 34.6 cc) ($p = 0.789$). CTV-pre- and CTV-post/whole breast volume ratio were similar as well ($p = 0.289$).

The estimated average expansion of the mean GTV/tumor bed to the CTV was in the preoperative situation 14.7 mm (SD), while in the postoperative situation the average expansion was only 8.4 mm (SD) ($p < 0.001$).

Discussion

We showed that preoperative external beam PBI leads to considerably less inter-observer variation in target volume delineation compared to postoperative external beam PBI. While most other studies focusing on target volume delineation investigated boost volumes, the clinical impact of accurate target delineation is of even higher importance when using PBI. Tumor bed delineation in boost studies has a wide range of CI values depending on seroma size, clarity, delineated volume size and target definition. The mean CI values reported in the literature are ranging from 0.36 to 0.73 [2–4,10,12]. The mean CI, in our present study focusing on PBI, improved from 0.38 in the postoperative situation to 0.78 in the preoperative situation. This finding can provide an argument in favor of treating patients with PBI preoperatively.

While in our study the delineated postoperative tumor bed volume was significantly larger than the preoperative GTV, the CTV-pre and CTV-post volumes were comparable. This seemingly contradictory finding can be explained by the fact that in postoperative CTV delineation, the knowledge on histological margins was used, by subtracting the histological free margin from the prescribed CTV margin extension of 15 mm, as shown by the estimated expansion. We performed this procedure in analogy to our clinical practice for boost delineation and this procedure results in principle in the smallest acceptable CTV-post delineation. Other studies did not incorporate the knowledge on the histological free margin in their postoperative CTV, and applied the full 15 mm as postoperative CTV margin [13–15], thus leading to an overestimate of the minimal CTV-post volume.

Stroom et al. [16] support our approach of subtracting the histological free margins in the postoperative setting; they showed that CTVs can frequently be reduced when using excision margins. Kirby et al. [14,17] also concluded that an anisotropic CTV margin should be applied in the postoperative setting, but they reasoned that the total margin around a tumor should be 30 mm, i.e. 15 mm to be removed by the surgeon, and 15 mm to be included in the CTV. Oncoplastic breast conserving surgery techniques, with parenchymal rearrangement, causes challenges to the localization and therefore delineation of the tumor bed. Due to more uncertainty a larger area will be delineated or a larger CTV margin will be added. This problem will be avoided in pre-operative RT.