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Original Research Article

Breast-shape changes during radiation therapy after breast-conserving surgery

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ABSTRACT

Background & purpose: With the introduction of more conformal techniques for breast cancer radiation therapy (RT), motion management is becoming increasingly important. We studied the breast-shape variability during RT after breast-conserving surgery (BCS).

Materials & Methods: Planning computed tomography (CT) and follow-up cone-beam CT (CBCT) scans were available for 71 fractions of 17 patients undergoing RT after BCS. First, the CT and the CBCT scans were registered on bones. Subsequently, breast-contour data were generated. The CBCT contours were analyzed in 3D in terms of deviations (mean and standard deviation) relative to the contour of the CT scan for the upper medial, lower medial, upper lateral, and lower lateral breast quadrants, and the axilla.

Results: Regional systematic and random standard deviations of the breast quadrants varied between 1.5 and 2.1 mm and 1.0–1.6 mm, respectively, and were larger for the axilla (3.0 mm). An absolute average shape change of ≥ 4.0 mm in at least one region was present in 21/71 fractions (30%), predominantly in breast volumes $>$ 800 cc ($p = \ < 0.01$). Furthermore, seroma was associated with larger shape changes ($p = 0.04$).

Conclusions: Breast-shape variability varies between anatomic locations. Changes in the order of 4 mm are frequently observed during RT, especially for large breasts. This should be taken into account in the development of protocols for partial breast irradiation and boost treatment.

1. Introduction

In recent years, more conformal radiation techniques have been introduced on a large scale in RT for breast cancer after breast-conserving therapy (BCT). Such techniques demand more attention to potential setup errors of the breast soft tissue. With the introduction of cone-beam computed tomography (CBCT) soft tissue evaluation of patient setup has become clinically feasible. At the same time, the delivered imaging dose throughout treatment became an issue of concern because of the nature of image-guidance protocols which often require frequent (up to daily) imaging of potential larger body volumes [1]. A recent study concluded that monitoring soft tissue motion should become the standard of care for patients at risk for large soft tissue variations [2]. However, available data on daily soft tissue motion and its correlation with clinical factors are limited.

RT after BCT typically consists of whole breast irradiation (WBI) combined with an additional boost to the original tumor position [3]. Boost irradiation can be planned and delivered separately from or integrated with WBI [4–5]. Most of the local recurrences (70–80%) found after BCT are at or close to the original tumor position [6–8]. Therefore, in selected low-risk patients, WBI is unnecessary. Consequently, in low-risk patients partial breast irradiation (PBI) is upcoming, focusing on irradiation of the original tumor position only [9,10].

One of the major challenges in RT boosting or PBI is the correct definition of the target volume and its localization during treatment. Geometrical uncertainties can be divided in three major categories: delineation uncertainties, patient setup, and organ motion, or in the case of the breast, shape changes. Accurate delineation of the original tumor position poses a major challenge [11–13]. Even when clips are implanted during surgery, variability in delineated volume is substantial [14]. Variation caused by day-to-day setup variation was found to be considerable, with central lung distance values (defined as the distance between the deep field edge and the interior chest wall at the central axis) ranging from 5.9 mm to 29.4 mm [15]. Little data have been published on inter-fractional shape changes of the breast.

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Significant changes and time trends on post-operative seroma volumes (i.e., fluid build-up in the excision cavity) have been reported prior to RT and during RT [16–18]. Further, breast surface deformation values, based on 3D surface data acquired with a video based surface imaging system, of < 2.0 mm (2SD) were reported [19]. In a previous study, the robustness of dose distributions from three whole-breast RT techniques involving different levels of intensity modulation against patient setup inaccuracies and breast-shape changes was investigated [20]. Plan deterioration due to shape changes of the breast was primarily observed in planning techniques without glancing fields, demanding specific attention in PBI techniques.

If all geometric uncertainties are known, an evidence-based safety margin can be estimated by collating standard deviations of the uncertainties [21]. The purpose of this study was to thoroughly investigate the breast-shape changes during the course of RT after breast-conserving surgery (BCS). For this purpose, breast contours extracted from cone-beam computed tomography (CBCT) scans acquired during the course of treatment were analyzed in 3D in terms of deviations (mean and standard deviation) relative to the contour of the breast on the planning CT scan. Additionally, we divided the contour data in separate regions of interest (four breast quadrants and axilla) and investigated the shape changes for these regions separately. Furthermore, we investigated correlations between breast-shape changes and clinical parameters.

2. Materials and methods

This study included 17 female breast cancer patients who received RT after undergoing microscopically complete tumor excision. No study consent was needed for this retrospective analysis of clinically available data (waived by the Ethics Committee). To also enable investigation of the effect of different arm-support systems on breast-shape changes, we included patients treated in two periods (2006 and 2011). Characteristics are summarized in Table 1.

2.1. Treatment and imaging

The RT planning target volume included the whole breast (and the axilla if indicated by the physician). Prescribed dose and fractionation varied between patients. Six patients received 50 Gy in 25 fractions with a sequential photon boost of 16 Gy in 8 fractions. Two patients received 50 Gy (25 fractions) without a boost. For the other nine patients, different fractionation schedules > 2 Gy/fraction were prescribed (seven patients with an integrated boost): 73.8 Gy in 31 fractions (n = 2), 64.4 Gy in 28 fractions (n = 1), 55.9 Gy in 21 fractions (n = 4), 42.6 Gy in 16 fractions with no boost (n = 2). Delineated organs at risk were the heart (for left-sided breast cancer) and the lungs.

For all but one patient treated in 2006 an in-house-developed arm-support system was used during RT whereas for the patients treated in 2011 an arm-support system developed by CIVCO Medical Solutions (C-Qual Breastboard, CIVCO Medical Solutions, Orange City, IA) was used. In both arm-support systems the positioning of the patients is similar with both arms brought above the shoulders out of the RT field. A difference between these two arm-support systems is that the C-Qual provides a more conformal support, enhancing the reproducibility of the patient arm setup. For one patient, with a limitation in arm function, a support system was used that allowed to position her arm next to the treatment table with the elbow flexed 90 degrees. During RT all patients were positioned on a breast board at a 10 degrees tilt. Further, a knee-support device (CIVCO Medical Solutions, Orange City, IA) was used for the patient's comfort.

Table 1
Baseline characteristics of included female breast cancer patients.

Characteristic (n = 17)	
Age year (median, range)	60 (39–75)
Breast volume cc (median, range)	927 (430–1312)
Tumor volume cc (median, range)	15 (5–42)
Left-sided/right-sided n (%)	6 (35%)/9 (65%)
Arm support + year of treatment (n)	
In-house developed type I (2006)	8
In-house developed type II (2006)	1
C-Qual Breastboard (2011)	8

Free-breathing CT scans (Somatom Sensation Open, Siemens, Forchheim, Germany) made for RT planning were used. Immobilization during acquisition of the planning CT scan was identical to immobilization during treatment. At our institute, CBCT scans (Elekta Synergy, Elekta Oncology Systems, Crawley, West Sussex, UK) are acquired routinely for setup verification. A two-phase shrinking action level protocol was used with daily verification during the first phase and weekly verification during the second phase [22]. We selected for all patients CBCT scans that represented the entire treatment; CBCT scans with at least three days between acquisitions were included.

2.2. Contour extraction

First, the follow-up CBCT scans and planning CT scan were aligned by performing a rigid registration on the bony anatomy using a 3D box-shaped region of interest containing the sternum and ribs on the irradiated side, excluding the arm. A chamfer matching algorithm was used that only considers bony anatomy for registration [22]. Next, the CBCT data were pre-processed by use of a digital filtering technique (median filter with window size 5) to remove noise. After filtering, suitable thresholds, based on the ratio of the grey values of breast tissue and air, for segmentation of the patient contour in the CBCT data were manually assessed for the 2006 and 2011 patient groups separately. Further, a 3D contour was automatically extracted from the planning CT scan by means of thresh-holding and smoothing using in-house developed software [23]. Contours are a collection of 3D points in space that are connected into triangles (contour elements).

2.3. Data analysis

Different regions of interest (ROIs) were defined on the planning CT contour data: the upper lateral breast quadrant (UL), upper medial breast quadrant (UM), lower medial breast quadrant (LM), lower lateral breast quadrant (LL), and the axilla (Fig. 1-left).

For each contour element in the planning CT contour, the nearest neighbor contour element in the CBCT contour was determined and the distance between the two elements was calculated (Fig. 1-right).

For each included CBCT scan, we calculated, per ROI, the weighted mean distance and the standard deviation of the distances found for the contour elements. We also assessed these values for the whole breast by calculating the weighted average of the values found for the four breast quadrants. Further, based on the weighted mean values, group means (M), systematic error (Σ), and random errors (σ) were assessed [21].

Next, for each patient separately, for each contour element in the planning CT the mean and standard deviation of the contour-element distances computed for all included follow-up CBCT scans were assessed (inter-fractional shape changes). Then the proportion of contour area that exhibits a certain distance was assessed for each ROI separately as well as for the whole breast. These findings were averaged over all patients.

2.4. Statistical analysis

Correlations between breast-shape-change parameters and clinical parameters (seroma (y/n), breast volume, arm-support system, number of days from start treatment, tumor size, and original tumor position) were calculated (Spearman correlation). Statistical significance was set at $p < 0.05$. Differences in shape changes between subgroups were