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Prone Whole-Breast Irradiation Using Three-Dimensional Conformal Radiotherapy in Women Undergoing Breast Conservation for Early Disease Yields High Rates of Excellent to Good Cosmetic Outcomes in Patients With Large and/or Pendulous Breasts

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Abstract

Purpose—To report our institution's experience using prone positioning for three-dimensional conformal radiotherapy (3D-CRT) to deliver post-lumpectomy whole breast irradiation (WBI) in a cohort of women with large and/or pendulous breasts, to determine the rate of acute and late toxicities and, more specifically, cosmetic outcomes. We hypothesized that using 3D-CRT for WBI in the prone position would reduce or eliminate patient and breast size as negative prognostic indicators for toxicities associated with WBI.

Methods and Materials—From 1998 to 2006, 110 cases were treated with prone WBI using 3D-CRT. The lumpectomy, breast target volumes, heart, and lung were contoured on all computed tomography scans. A dose of 45–50 Gy was prescribed to the breast volume using standard fractionation schemes. The planning goals were ≥95% of prescription to 95% of the breast volume, and 100% of boost dose to 95% of lumpectomy planning target volume. Toxicities and cosmesis were prospectively scored using the Common Terminology Criteria for Adverse Effects Version 3.0 and the Harvard Scale. The median follow-up was 40 months.

Results—The median body mass index (BMI) was 33.6 kg/m^2, and median breast volume was 1396 cm^3. The worst toxicity encountered during radiation was Grade 3 dermatitis in 5% of our patient population. Moist desquamation occurred in 16% of patients, with only 2% of patients with moist desquamation outside the inframammary/axillary folds. Eleven percent of patients had Grade ≥2 late toxicities, including Grade 3 induration/fibrosis in 2%. Excellent to good cosmesis was achieved in 89%. Higher BMI was associated with moist desquamation and breast pain, but BMI and breast volume did not impact fibrosis or excellent to good cosmesis.

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Conflict of interest: none.

Conclusion—In patients with higher BMI and/or large–pendulous breasts, delivering prone WBI using 3D-CRT results in favorable toxicity profiles and high excellent to good cosmesis rates. Higher BMI was associated with moist desquamation, but prone positioning removed BMI and breast size as factors for poorer cosmetic outcomes. This series adds to the growing literature demonstrating that prone WBI may be advantageous in select patients.

Keywords

Prone; Breast; Radiation; Body mass index; Cosmesis

Introduction

The majority of patients with early-stage breast cancer are candidates for breast-conservation therapy (BCT). Several large randomized control trials comparing BCT with mastectomy have demonstrated no difference in locoregional control, disease-free survival, or overall survival (1). These large studies have all been conducted using whole-breast irradiation (WBI) delivered in the supine position. However, supine breast WBI does have limitations. Irradiation after breast-conserving surgery (BCS) in women with large and/or pendulous breasts can be particularly challenging. Several institutions have shown increased radiation-related toxicities and worse cosmetic outcomes for patients with large, pendulous breasts and/or increased body mass index (BMI) undergoing BCT (2–9). Radiation factors identified as potentially causative include increased dose inhomogeneity from medial to lateral separation of the breast and bolus effect on skin, including the inframammary folds, where there is increased skin-on-skin contact. In addition, patients with large breasts may receive increased doses to critical structures such as the heart or lungs owing to the positioning of the breast on the chest wall when the patient lies supine. Prone breast irradiation aims to improve on some of the technical limitations associated with treating large, pendulous breasts and/or large body habitus, and it may also assist in limiting radiation doses to organs at risk (10–15).

Our institution developed a method for delivering breast three-dimensional conformal radiotherapy (3D-CRT) in the prone position to address the technical challenges associated with irradiation of large and/or pendulous breasts. The goal of this study was to report our institution's experience using prone positioning in a cohort of women receiving postlumpectomy WBI, to determine the rate of acute and late toxicities and, more specifically, cosmetic outcomes. We hypothesized that the use of 3D-CRT for WBI in the prone position would reduce or eliminate patient and breast size as negative prognostic indicators for toxicities associated with WBI.

Methods and Materials

Study population

Between 1998 and 2006, 109 women (110 breasts treated) underwent WBI in the prone position using 3D-CRT. One patient had a history of Hodgkin's disease treated with radiation to the mediastinum. All other patients were treated prone secondary to a large body habitus and/or large–pendulous breasts. The median follow-up was 40.3 months (mean 45.9 months, range 1–127 months) for living patients. One hundred five patients had 1 year or more of clinical follow-up (median 43.1 months, mean 47.4 months). This study was performed under the auspices of an institutional review board protocol.

Radiation

All patients underwent CT planning in the prone position with arms immobilized extended forward with either an Alpha Cradle (Smithers Medical Products, North Canton, OH) or Vac

Fix (S & S Par Scientific, Odense, Denmark). All patients were positioned on an in-house prone breast board that indexes to the treatment table. Computed tomography images were obtained in 2.5-mm slices. At the time of CT simulation, a posterior–anterior setup point was established and leveling tattoos placed. Daily shifts were performed from the posterior–anterior setup point to the isocenter. Minimally, an orthogonal pair and port films were obtained weekly. Computed tomography images were used to contour structure volumes for each case: planning target volumes (PTV) for the breast and lumpectomy cavity, ipsilateral lung, and heart (left-sided). The breast PTV (TBV) reflected the clinical breast tissue wired by the prescribing physician at CT simulation, the breast as seen on CT, and in all cases included the lumpectomy PTV (L-PTV). The TBV excluded the chest musculature (pectoralis and serratus anterior muscles) and 5 mm from the skin surface. Typically the TBV did not extend laterally past the mid-axillary line or medially past the sternal–costal interface. The lumpectomy cavity included postsurgical changes, surgical clips, and seroma. The L-PTV represented a final 1.5-cm cavity expansion excluding chest wall and 5 mm from the skin surface.

For 86% of patients, the whole-breast prescribed dose was 46–50 Gy to isocenter in 2.0-Gy fractions such that a minimum of 95% of the TBV was covered by a minimum of 45 Gy. Five cases (5%) received 1.8-Gy fractions to 45–50.4 Gy to the isocenter such that a minimum of 95% of the TBV was covered by a minimum 45 Gy. Ten cases (9%) were treated with a hypofractionated regimen without boost, receiving 42.56 Gy in 16 fractions such that a minimum of 95% of the TBV was covered by a minimum of 40.4 Gy. Boosts were delivered to 72% of patients. Boosts were an average of 10 Gy over 5 fractions, delivered in the prone position using photons. The cumulative total dose prescribed to the L-PTVin boosted patients was a median of 60 Gy.

Treatment goals were to cover 95% of the TBV with a minimum of 95% of the prescribed breast dose (<90% of prescription deemed unacceptable). When no boost was used, 100% of the breast dose was to cover 95% of the L-PTV. When a boost was used, the dose constraints were such that 100% of the boost dose covers 95% of the L-PTV, with the maximum point dose of ≤110%. When a boost was given, the goal was to limit 60 Gy to no greater than 30% of the TBV and 54 Gy to no greater than 50% of the TBV. The lung and heart were excluded from the fields. A median dose of 50 Gy was prescribed to isocenter using an average of three fields to meet the above treatment goals. Mixed beam energy was used in 67% patients for the whole-breast fields, most commonly 6 MV mixed with 15 MV or 18 MV beams to achieve optimal coverage of targets and to minimize dose heterogeneity.

Toxicity and variable definitions

Toxicities were prospectively scored according to the National Cancer Institute Common Terminology Criteria for Adverse Effects Version 3.0. Acute toxicity reflects worse toxicity occurring during the course of radiation. The following categories were scored for acute toxicity: breast edema, dermatitis (including moist desquamation as an individual factor), breast pain, and fatigue. Special focus was given to the following factors for late toxicity: fibrosis/induration, hyperpigmentation, telangectasias, nipple/areolar deformity, and volume loss/symmetry. Late toxicity reflects the worse toxicity present at last follow-up visit. Cosmetic outcome was physician-assessed prospectively with the Harvard Scale (16). Body mass index is an established measure of patient size and was used for body habitus. Body mass index was calculated as (weight in kilograms)/(height in meters)^2. Similarly, because volume loss from surgery can affect breast appearance, excisional lumpectomy volumes were calculated using the product of the three reported dimensions of the pathologic lumpectomy specimens.

Statistical analysis

All cases (n = 110) were included for acute toxicity analysis. Cases with ≥1-year follow-up (n = 105) were included in the late toxicity and cosmesis analyses. Associations between patient characteristics and toxicities were determined using the Fisher exact test for categoric variables and using the Kruskal-Wallis and Wilcoxon rank sum tests for continuous variables. All analyses were performed using SAS software (SAS Institute, Cary, NC).

Results

Study population

The individual characteristics of the patient population are summarized in Table 1. Median age of the patients (n = 110 cases) was 61.0 years. Seventy-five percent of patients were clinically obese (BMI ≥30 kg/m^2), with a median and mean BMI of 33.6 kg/m^2 and 34.6 kg/m^2, respectively. The majority of patients also had large and/or pendulous breasts, with a median breast volume of 1396 cm^3 and 80% of patients with breast volumes of ≥1000 cm^3.

Tumor and treatment characteristics

Table 1 summarizes the tumor and treatment characteristics for patients treated with WBI in the prone position. The majority of patients (81%) had invasive breast cancer, and 14% had nodal involvement. Estrogen and/or progesterone receptors were positive in 77% of invasive cancers, and 18% were Her-2/neu positive or amplified. In 65% of patients antiendocrine treatment was given, and 38% of patients with invasive cancers received chemotherapy.

Toxicity analysis

Acute toxicity—Acute toxicity profiles are shown in Table 2. As expected, all patients had some degree of dermatitis. The largest group of patients had Grade 2 dermatitis, which includes moderate to brisk erythema, dry desquamation, and/or moist desquamation of the skin folds. Grade 3 acute dermatitis was seen in only 5 patients (4.5%; Table 2). To further define the dermatitis experienced, moist desquamation was scored separately. Moist desquamation in the inframammary folds occurred in 14.5% of cases (n = 16), with only 2 patients (1.8%) experiencing moist desquamation outside the inframammary folds. Breast edema was experienced by 24% of patients during irradiation, with 3.6% having Grade 2 edema. Two-thirds of patients experienced breast pain, with 21% requiring pain medication (Grade 2) and no patient experiencing pain that interfered with activities of daily living (Grade 3). In patients experiencing fatigue, it was overwhelmingly mild (Grade 1, 68%), except for 1 patient with fatigue that interrupted daily functioning (Grade 2). Treatment breaks were required by 3 patients: 1 patient was hospitalized for atypical chest pain of unknown etiology, 1 patient experienced moist desquamation resulting in an approximately 1-week treatment break, and 1 patient required a 2-week break due to an abscess at the lumpectomy site approximately halfway through irradiation.

Late toxicity—Table 3 summarizes the late toxicities present at last follow-up. The rate of any Grade 3 late toxicity was 1.9% (n = 2), and 11.4% (n = 12) experienced any Grade 2 toxicity. Twenty-two percent of patients had slight/localized hyperpigmentation (Grade 1), with only 1 patient having marked (Grade 2) hyper-pigmentation. However, 86% of African Americans (n = 14) had Grade 1 hyperpigmentation, compared with 12% of Caucasians or other races. Less than 8% of patients exhibited telangiectasias at last follow-up. Seven percent exhibited limited nipple/areolar deformity (Grade 1), and 2 patients had asymmetry with slight nipple deviation (Grade 2). Volume loss causing asymmetry was present in 28%,

with most of these patients exhibiting volume loss after lumpectomy before their irradiation. Grade 2 or 3 fibrosis was present in 11% of patients.

Overall cosmesis—On the basis of the Harvard Scale for cosmetic outcomes, the majority of patients (89%) had good or excellent cosmetic outcomes. Nine patients had a fair cosmetic outcome (8.6%), and 3 patients had a poor outcome (2.9%). Sixty percent of our cohort had breast volumes >1200 cm^3, and in this group of patients 86% had good to excellent cosmesis.

Toxicity associations with treatment and patient characteristics—Univariate analysis of factors associated with acute toxicities revealed a statistically significant relationship between patient BMI and moist desquamation (Table 4; $p = 0.025$). The presence of breast pain during treatment was also associated with BMI ($p = 0.008$): 42% of patients with a BMI >36 kg/m^2 had mild to moderate pain, whereas only 11% of patients with BMI <36 kg/m^2 experienced similar pain. Dermatitis of Grade ≥2 was not significantly associated with BMI ($p = 0.152$). Similarly, breast volume was significantly associated with moist desquamation ($p = 0.008$) but not with breast pain ($p = 0.371$) or dermatitis ($p = 0.712$; Table 4), findings consistent with those seen when breast volume was examined as a continuous, rather than grouped, variable (data not shown).

The association of BMI, breast volume, race, chemotherapy, number of lymph nodes excised, use of a breast boost, and excisional lumpectomy volume were examined using univariate analyses for association with fibrosis, asymmetry, and cosmesis (Table 5). A significant relationship between BMI and asymmetry was found, but BMI was not significantly associated with fibrosis or poor to fair cosmesis. Breast volume was not significantly associated with asymmetry, fibrosis, or cosmesis (Table 5). This was consistent with analyses using breast volume as a continuous variable (not shown). The use of chemotherapy was significantly associated with fair to poor cosmesis.

Recurrence data

Four patients have been diagnosed with an ipsilateral breast tumor (5-year actuarial rate of 3.0%), with a mean time to recurrence of 62 months (range 33–125 months). One patient had an axillary recurrence (1.0%), and 6 patients had distant metastasis (5.7%).

Discussion

Breast-conserving treatment has allowed many women to receive appropriate breast cancer management with long-term local control and survival rates equivalent to those with mastectomy, while maintaining a cosmetically acceptable breast appearance. Unfortunately, women with larger breasts can be technically challenging to treat with breast irradiation, resulting in higher rates of severe acute dermatitis and late fibrosis causing unacceptable cosmesis. Our institution has developed prone breast 3D-CRT to improve these toxicities in this patient population. We have previously evaluated patient positioning when prone and demonstrated that minimal anterior–posterior movement occurs (17). The positioning and the use of 3D-CRT planning have allowed us to treat patients without consideration of lumpectomy cavity location. The association of dosimetric parameters with toxicity and cosmetic outcomes is the subject of a separate manuscript. Using prone 3D-CRT for WBI in a population with high BMI and/or large pendulous breasts, we have demonstrated acceptable acute and late toxicities, with cosmesis rates comparable to those observed in supine series that included patients with smaller breast and body size.

Several authors have published data indicating worse cosmetic outcomes and toxicities for those with increased weight (7, 18), higher BMI (9, 19), and larger breast size (2–8, 20, 21).

The cosmetic outcomes of the largest breast volumes in our study (>1200 cm^3, 60% of our patients) are compared with a subset of these studies in Table 6. Clarke *et al.* (7) examined 78 cases of supine two-dimensional radiotherapy (2D-RT) for WBI and found 100% excellent cosmesis in patients with A cup size, as opposed to only 50% of those patients with ≥D cup size (p =0.02). Cosmesis was also associated with patient body weight: 90% of patients weighing <120 lb had excellent outcomes, as opposed to only 46% of patients weighing >120 lb (p =0.001). Ray *et al.* (6) examined the influence of breast size on late radiation effects in 130 patients receiving supine 2D-RT WBI. Those with an A or B cup size had 92% excellent cosmesis, vs. only 64% of those with ≥C cup size. Moody *et al.* (5) monitored late radiation changes in 664 women undergoing supine postlumpectomy WBI. They found moderate or severe late radiation changes in 6% of patients with small breasts, vs. 39% of those with large breasts ($p < 0.001$). Gray *et al.* (4) from Memorial Sloan Kettering Cancer Center (MSKCC) specifically looked at the cosmetic outcome of large breasted or heavy women treated supine. A total of 257 patients were divided into a “large” group if weight ≥80 kg, bra size ≥40 in, ≥D cup size, or if tangent separation ≥23 cm. They found a significant difference in cosmesis at 1 and 3 years and a trend toward improved outcomes with “average” patients at 5 years. Of the factors considered in the cosmesis score, retraction and symmetry were statistically significant at 5 years. In the present study, we report good to excellent cosmetic results in 89% of our patients with large and/or pendulous breasts receiving 3D-CRT in the prone position after BCS. This rate of good to excellent cosmetic outcomes is similar to those reported in patients treated supine (22–26). For example, a Phase III randomized study examining 2D-RT vs. intensity-modulated radiotherapy (IMRT) for supine WBI found that 85–95% of patients in both treatment groups had no or mild changes in the breast appearance at 2 and 5 years. These patients had a median breast volume of 1046 cm^3, much lower than our median breast volume of nearly 1400 cm^3 (26).

There is growing literature regarding the use of prone positioning to improve toxicity profiles from irradiating large– pendulous breasts after BCS. Treated supine, women with larger breasts have increased dose heterogeneity, and excess skin folds can create a bolus effect in the inframammary and axillary areas. Prone breast irradiation minimizes separation of the breast tissue and reduces skin folds. The MSKCC has the largest and longest documented study using the prone position for 2D-RT WBI. Cosmetic outcomes were initially reported for 59 patients after a median follow-up of 38 months (27). The population had a median bra size of 41D. Mean cosmetic outcome for the entire group was quite favorable, with a score of 9.37 (out of a total of 10). This group subsequently reported late toxicity on 245 patients treated in the prone position (28). In that series, late Grade 2, Grade 3, and Grade 4 chronic dermatitis was seen in 27.8%, 2.8%, and 1.6% of patients, respectively, with Grade ≥2 chronic edema in 14% of patients. Similarly, Formenti *et al.* (29) treated 91 patients of all sizes in the prone position using accelerated IMRT as part of a Phase I/II trial, and with 12 months median follow-up reported favorable acute and late toxicities corroborating the prone position’s favorable effect on toxicity.

Our patient population had a high median BMI of 33.6 kg/m^2 and median breast volumes of nearly 1400 cm^3 and yet had favorable acute toxicity profiles (Table 2). Only 4.5% had Grade ≥3 acute dermatitis, with 16% of patients experiencing any moist desquamation and only 2% of patients experiencing moist desquamation outside the inframammary folds. These results seem favorable when compared with a Phase III trial examining acute toxicities from IMRT vs. 2D-RT for supine WBI (30). Those patients had a smaller average size than the patients in our series, with a mean BMI of 27 kg/m^2 and median breast volume of 973 cm^3 receiving 95% of the prescribed dose, yet 27.1% had Grade 3 to 4 skin toxicity, and 31.2% experienced moist desquamation in the IMRT arm. Other studies including all sizes of patients have also demonstrated moist desquamation rates of 14–38% (31–33). In

our series of patients with larger body habitus and/or large– pendulous breasts, the overall rate of Grade ≥2 late toxicity was 11.4%, and Grade ≥3 was 1.9% (Table 3). Grade 1 fibrosis and hyperpigmentation were the most common late toxicities. It is difficult to compare retrospective studies given institutional differences in patients, treatments, analysis methods, physician evaluations, and biases. However, it seems that these rates of late toxicities represent significant reductions compared with what was reported previously for patients with large breast or body habitus receiving breast radiotherapy in the supine position (2–8). Most importantly, in our analysis, as discussed below, our patients with the largest BMI and breast sizes did not experience worse fibrosis or poorer cosmetic outcomes from radiation.

We sought to specifically evaluate the effect of breast size and BMI on the incidence of acute and late toxicities as well as cosmesis from prone breast radiotherapy in this population. Assessing breast size proved challenging because most other series have used patient brassiere cup size (4, 6, 7, 27). There is not an industry standard matching volume of breast to cup size. Bra cup size is relative to the band size, with actual cup volume changing as the band size changes. For example, the brassiere cup volume is the same for 30D, 32C, 34B, and 36A (34). Inconsistency can also occur if a woman wears a bra size too large or too small. Therefore, we elected to use CT-based breast volume as a discriminator for breast size. Examining acute toxicities in our study demonstrated that use of prone 3D-CRT resulted in neither BMI nor breast volume being significantly associated with Grade ≥2 dermatitis. However, larger BMI and breast volume were significantly associated with moist desquamation, and BMI was also associated with breast pain during treatment (Table 4). We now use this information to more aggressively monitor and treat acute side effects in these patient groups during treatment. Additionally, larger breast volume and BMI were not associated with worse late toxicities, specifically fibrosis, nor with lower rates of excellent to good cosmesis (Table 5). This supports our hypothesis that the use of 3D-CRT WBI in the prone position eliminates these factors as predictors of poor outcome. As has been demonstrated by others (16, 19, 23–25, 35), the use of chemotherapy was associated with higher rates of fair to poor cosmetic outcomes.

With a median follow-up of 40 months, we had 4 patients (3.0% 5-year rate) with an ipsilateral cancer recurrence. This is within the expected recurrence rate for BCT for early-stage breast cancer (28). Of note, all of these patients had a BMI greater than the median BMI of 33.6 kg/m^2. Further characterization and follow-up of the recurrence patterns relative to BMI will be reported separately.

This analysis has limitations inherent to retrospective studies, such as the potential for reporting bias. It is possible that those lost to follow-up had different outcomes; however, this accounts for only 4.5% of patients (n =5). Our study uses the well-established combination of the National Cancer Institute Common Terminology Criteria for Adverse Effects Version 3.0 and the Harvard Cosmetic Scale for physician-assessed cosmesis and late toxicities that can affect breast appearance. We recognize that the best evaluator of cosmetic and toxicity outcomes is the patient herself and acknowledge that one of the weaknesses of this study is the lack of patient-rated outcomes. However, our study strengths include that the population is specifically focused, that toxicity and cosmesis were scored prospectively, and that the median follow-up is sufficiently long to take into account the latency of radiation toxicities.

In conclusion, the delivery of whole breast radiotherapy using 3D-CRT in the prone position resulted in excellent acute and late toxicity profiles for a patient population at the highest risk for toxicity from breast irradiation. We also report that 89% of patients had good to excellent cosmetic outcomes. We did not find an association between BMI or breast volume and late fibrosis or cosmetic outcomes, indicating that prone whole-breast 3D-CRT

eliminates BMI and breast volume as factors predicting poorer late toxicity and cosmesis. This gives further evidence that prone positioning for WBI is preferable to supine in this patient population.

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Summary

Studies have shown increased toxicities and worse cosmesis for patients with large breasts undergoing whole-breast irradiation. This study reviewed a cohort of large/pendulous breasted women treated prone with 3-D radiotherapy aiming to improve outcomes. With a median follow-up of 40 months excellent to good cosmesis was achieved in 89%. Prone positioning removed BMI and breast size as factors for poorer cosmetic outcomes.

Table 1

Patient and tumor characteristics

Characteristic	%	Mean	Median	Range
Age at diagnosis (y)		61.8	61.0	(27–91)
BMI (kg/m^2)		34.5	33.6	(19–51)
Weight (pounds)		199	193	(114–325)
Breast volume (cc)		1466	1396	(322–4800)
Gross lumpectomy volume (cc)		225	171	(4–1004)
Menopausal status				
Premenopausal	12.7			
Perimenopausal	10.0			
Postmenopausal	75.5			
Unknown	1.8			
Race				
Caucasian/other	87			
African American	13			
T stage				
T0	19.1			
T1	61.8			
T2	17.3			
T3	1.8			
T4	0			
Nodal status				
N0	86.4			
N1	13.6			
Lymph node surgery				
No sentinel LN biopsy or ALND	17			
Sentinel LN biopsy alone	46			
Sentinel LN biopsy and ALND	19			
ALND alone	18			
Invasive histology *				
Ductal	81.6			
Lobular	9.2			
Mixed	4.6			
Other	4.6			
Final invasive margins				
Negative	86.2			
Close	11.4			
Positive	2.3			
Estrogen receptor positive *	76.7			
Progesterone receptor positive *	72.1			
Her-2/neu positive/amplified *	18.4			

Characteristic	%	Mean	Median	Range
Left-sided cancer	60.9			
Chemotherapy*	38.2			
Antiendocrine therapy	64.5			

Abbreviations: LN = lymph node; ALND = axillary lymph node dissection; BMI = body mass index.

*As a percentage of invasive cancers (n = 89).

Table 2

Acute toxicities, scored prospectively using CTCAE version 3.0

Toxicity	None	Grade 1	Grade 2	Grade 3	Grade 4
Dermatitis	0	28.2	67.3	4.5	0
Breast edema	76.4	20.0	3.6	0	–
Breast pain	33.6	45.5	20.9	0	–
Fatigue	30.9	68.2	0.9	0	–

Abbreviation: CTCAE = Common Terminology Criteria for Adverse Effects.

Values are percentages.

Table 3

Late toxicities and cosmesis at last follow-up in patients with >1 year follow-up (n = 105), scored prospectively using CTCAE version 3.0

Toxicity	None	Grade 1	Grade 2	Grade 3
Any late toxicity	29.5	70.5	11.4	1.9
Hyperpigmentation	77.1	21.9	1.0	0
Telangiectasia	92.4	4.8	1.9	1
Deformity	91.4	6.7	1.9	0.9
Fibrosis	46.7	41.9	9.5	1.9

Abbreviation as in Table 2.

Values are percentages.

Table 4

Association of BMI and breast volume with acute toxicities

Variable	Moist desquamation	Breast pain grade ≥2	Dermatitis grade ≥2
BMI (kg/m^2)			
<32 (n = 37)	3 (8.1)	4 (10.8)	25 (67.6)
32–36 (n = 36)	4 (11.1)	4 (11.1)	23 (63.9)
>36 (n = 36)	11 (30.6)	15 (41.7)	39 (83.3)
p	0.025 *	0.008 *	0.152
Breast volume (cm^3)			
0–1200 (n = 37)	4 (10.8)	7 (18.9)	25 (67.6)
1200–1600 (n = 38)	2 (5.3)	5 (13.1)	29 (76.3)
>1600 (n = 31)	10 (32.3)	9 (29.0)	22 (71.0)
p	0.008 *	0.371	0.712

Abbreviation as in Table 1.

Values are number (percentage) unless otherwise noted.

* Statistically significant in the univariate analysis. The p values were determined using Fisher's exact test.

Table 5

Association of patient and tumor factors with late toxicities and cosmetic outcome at last follow-up

	Grade 2–3 fibrosis		Asymmetry present		Excellent–good cosmesis	
Variable	***n* (%)**	***p***	***n* (%)**	***p***	***n* (%)**	***p***
BMI (kg/m^2)						
<32 (*n* = 35)	3 (8.6)	0.695	2 (5.7)	0.001 *	34 (97.1)	0.125
32–36 (*n* = 34)	5 (14.7)		12 (35.3)		29 (85.3)	
>36 (*n* = 35)	4 (11.4)		14 (40.0)		29 (82.9)	
Race						
Caucasian/other (*n* = 91)	13 (14.3)	0.208	23 (25.3)	0.517	82 (90.1)	0.199
African American (*n* = 14)	0 (0)		5 (35.7)		11 (78.6)	
Chemotherapy						
No (*n* = 71)	6 (8.5)	0.112	16 (22.5)	0.238	67 (94.4)	0.017 *
Yes (*n* = 34)	7 (20.6)		12 (35.3)		26 (76.5)	
Lymph nodes dissected						
None (*n* = 19)	2 (10.5)	1.0	3 (15.8)	0.362	18 (94.7)	0.113
1–5 (*n* = 47)	6 (12.8)		12 (25.5)		44 (93.6)	
≥6 (*n* = 39)	5 (12.8)		13 (33.3)		31 (79.5)	
Lymph nodes dissected						
None (*n* = 19)	2 (10.5)	1.0	3 (15.8)	0.390	18 (94.7)	0.690
≥1 (*n* = 86)	11 (12.8)		25 (29.1)		75 (87.2)	
Boost						
No boost (*n* = 28)	1 (3.6)	0.178	7 (25.0)	1.000	26 (92.9)	0.507
Boost (*n* = 76)	12 (15.8)		21 (27.6)		66 (86.8)	
Excisional volume (cc)						
0–100 (*n* = 32)	3 (9.4)	0.165	6 (18.8)	0.097	30 (93.8)	0.160
100–200 (*n* = 32)	2 (6.3)		6 (18.8)		30 (93.8)	
≥200 (*n* = 38)	8 (21.1)		15 (39.5)		31 (81.6)	
Breast volume (cc)						
0–1200 (*n* = 35)	3 (8.6)	0.655	6 (17.1)	0.223	33 (94.3)	0.347
1200–1600 (*n* = 37)	6 (16.2)		13 (35.1)		33 (89.2)	

Variable	Grade 2–3 fibrosis		Asymmetry present		Excellent–good cosmesis	
	n (%)	*p*	*n* (%)	*p*	*n* (%)	*p*
≥1600 (*n* = 29)	4 (13.8)		8 (27.6)		24 (82.8)	

Abbreviation as in Table 1.

* Statistically significant in the univariate analysis. The *p* values were determined using Fisher's exact test.

Table 6

Physician-assessed cosmetic results from breast-conservation therapy in large and/or pendulous breasts

First author/institution (reference)	Position	*n*	Follow-up (y)	Cosmesis scale	Measurement of large breasts	Larger breast group, *n* (%)	RT method	Good and/or excellent cosmetic outcomes (%)
Clarke/Stanford (7)	Supine	78	3.5	3-point scale	≥D cup	12 (15)	2D-RT	50
Ray/Palo Alto Medical (6)	Supine	130	2.6	4-point scale	≥C cup	45 (35)	2D-RT	64
Gray (4)/Grann (27)	Supine	25	3.0	10-point scale	≥D cup	38 (15)	2D-RT	7.85 *
MSKCC	Prone	59	3.2	10-point scale	≥D cup	57 (97)	2DRT	100
MCW, present study	Prone	110	3.3	4-point scale	CT breast volumes >1200 cm^3	66 (60)	3D-CRT	86

Abbreviations: RT = radiotherapy; 2D-RT = two-dimensional RT; MSKCC = Memorial Sloan-Kettering Cancer Center; MCW = Medical College of Wisconsin; 3D-CRT = three-dimensional conformal RT.

* At 3 years, out of 10-point scale.