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Effect of Bra Use during Radiotherapy for Large-Breasted Women: Acute Toxicity and Treated Heart and Lung Volumes

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Abstract

Purpose—Large breast size presents special problems during radiation simulation, planning and patient treatment, including increased skin toxicity, in women undergoing breast-conserving surgery and radiotherapy (BCT). We report our experience using a bra during radiation in large-breasted women and its effect on acute toxicity and heart and lung dosimetry.

Materials and methods—From 2001 to 2006, 246 consecutive large-breasted women (bra size 38 and/or D cup) were treated with BCT using either 3D conformal (3D-CRT) or Intensity Modulated Radiation (IMRT). In 58 cases, at the physicians' discretion, a custom-fit bra was used during simulation and treatment. Endpoints were acute radiation dermatitis, and dosimetric comparison of heart and lung volumes in a subgroup of 12 left-sided breast cancer patients planned with and without a bra.

Results—The majority of acute skin toxicities were grade 2 and were experienced by 90% of patients in a bra compared to 70% of patients not in a bra ($p=0.003$). On multivariate analysis significant predictors of grade 2/3 skin toxicity included 3D-CRT instead of IMRT (OR=3.9, 95% CI:1.8-8.5) and the use of a bra (OR=5.5, 95% CI:1.6-18.8). For left-sided patients, use of a bra was associated with a volume of heart in the treatment fields decreased by 63.4% ($p=0.002$), a volume of left lung decreased by 18.5% ($p=0.25$), and chest wall separation decreased by a mean of 1 cm ($p=0.03$).

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Conclusions—The use of a bra to augment breast shape and position in large-breasted women is an alternative to prone positioning and associated with reduced chest wall separation and reduced heart volume within the treatment field.

Keywords

Breast; radiation therapy; support bra

Introduction

Breast-conserving surgery and radiation (BCT) are standard alternatives to mastectomy for eligible patients with Stage 0, I and II invasive breast cancer ¹. Postoperative whole-breast radiation is associated with long-term local control on the order of 85-95% with equivalent survival outcomes as mastectomy ²⁻³. One problem with conventional tangential whole-breast postoperative radiation is that it is often associated with greater than 10% dose heterogeneity across the target volume, which may increase the incidence of acute side effects and negatively impact upon long-term cosmesis from treatment ⁴⁻⁷. Larger breast size is often associated with increased skin toxicity in women undergoing BCT due to increased dose heterogeneity and auto-bolusing effects at the inframammary fold ^{6, 8}. Acute dermatitis, including moist desquamation of the skin during or within 6 weeks of radiation, is seen in 30-50% of women treated with conventional radiation and more common in large-breasted women ⁹⁻¹⁰. Additionally, a large pendulous breast often displaces laterally which may result in a larger chest wall separation when positioned in the supine position thus increasing incidental dose delivered to the lung and heart ⁶.

At our institution, we have used a commercially available bra or corset for the simulation and treatment of large-breasted women. The bra is custom-fitted for the patient based upon their chest size and cup size. Initially, the bra was used in the era of fluoroscopic simulation in order to reduce the central lung distance of the patients by minimizing the lateral displacement of the large or pendulous breast. Lifting and minimizing the inframammary fold helped to reduce self-bolus. In the CT simulation era, the effects of the bra could be better measured for the reduction of heart or lung in the treatment field during 3D planning.

The purpose of this study is to report our experience using a bra in the supine position for large-breasted women and present data on its effects on acute toxicity and dosimetry including chest wall separation of tangential fields, lung and heart dose.

Methods and Materials

The study population consists of 246 women with early stage breast cancer treated with BCT with or without systemic and/or endocrine therapy from 2001 - 2006. Inclusion criteria were American Joint Committee on Cancer stages 0, I or II breast cancer who completed adjuvant radiation at XXX XXXXX XXXXXX XXXXXX. All patients had a large breast size defined by a bra size 38 and/or D cup. Exclusion criteria for the study included male breast cancer, T3-T4 disease, stage III-IV disease, mastectomy, or patients treated without radiation. Patient demographics, tumor characteristics, and treatment-related information were prospectively entered into a database, and maintained and updated by a single data manager. The collection, storage and data retrieval are under compliance with the hospital Institutional Review Board and Health Insurance Privacy and Portability Act regulations.

Patients underwent CT simulation with an alpha-cradle cast on a 10-20% angled breast board. Radio-opaque markers were placed at the time of simulation around the palpable breast tissue and at clinical estimates of the borders of the tangential fields. The clinical

target volume (CTV) was defined as the palpable breast tissue, glandular breast tissue identified on the CT simulation, and inclusion of the lumpectomy CTV. The breast CTV was trimmed 5 mm from the skin and excluded chest wall musculature. A margin of 7 mm posteriorly and 1.5 cm superiorly and inferiorly were added to the CTV to create a planning treatment volume (PTV). A strapless bustier with plastic stays was custom fitted to ensure that the breast tissue was contained entirely within the bra cup, by the simulation therapists (Figure 1). Use of a bra was at the physician discretion during whole breast RT in 58 cases from the study population.

All patients were treated with whole breast radiation to a median dose of 46 Gy in daily fractions of 2 Gy, with or without regional nodal radiation. A boost to the tumor bed was routinely delivered, and the total dose was determined by the extent of surgery and final margin ¹¹. This total dose ranged from 60 Gy for a negative margin (≥ 2 mm), to 64 Gy with a close margin (< 2 mm), to 66 Gy for a positive final margin. The primary tumor bed was boosted in 99% of patients, and the median total dose delivered was 60 Gy. The bustier was typically removed for the boost, requiring patients to undergo an additional simulation to address the lumpectomy cavity.

Early in the study period, whole breast radiation was conventional wedged photon tangents or 3D conformal radiation (3D-CRT) (n= 145), while the majority of patients in later years received photon IMRT (n=105). Details of the conventional radiation treatment policy during this study period have been previously described ¹¹. Our IMRT technique has previously been published in detail. Briefly this technique used a combination of open and segmented tangential fields using volume-based inverse dose planning with step and shoot beam delivery ¹². Treatment energy was ultimately dependent upon patient chest wall separation, which is the distance through the thorax between the lateral beam entry point and the medial beam entry point, measured in centimeters. A variety of photon energies were utilized for treatment with 22% of patients treated with 6 MV, 50% treated with 10 MV, and 28% treated with 18 MV photons. A beam spoiler was typically incorporated to increase the superficial dose when using photon energies > 6 MV.

The primary endpoint was the rate of acute dermatitis. Acute dermatitis was graded weekly during treatment by the treating physician using the Common Terminology Criteria for Adverse Events, version 3. A second aspect of the study was a dosimetric comparison of left ventricular and lung volumes within the tangential radiation fields on a subset of 12 patients treated for left sided breast cancer and planned with and without a bra. The volume of normal tissue present within the treatment fields was calculated by subtracting the volume present within the tangential fields from the volume of the normal tissue contour. Figure 2 demonstrates a patient simulated with and without a bra.

Univariate and multivariate analyses ¹³ were performed to evaluate potential predictors of acute skin toxicity. Covariates investigated included: use of a bra, bra size, cup size, age, use of IMRT, chest wall separation, beam energy, mean whole breast dose, and smoking history. Univariate analyses were done via Chi-square test for categorical variables and Wilcoxon's test for continuous ones. MVA was performed by using multiple logistic regression.

Results

Table 1 details the patient and treatment characteristics. Significant differences between patients treated in a bra versus those treated without a bra include cup size (bra users: median D, range C-EEE vs. Non-users: median D, range B-EE, $p<0.0001$) and use of a higher beam energy (Bra users: 22% 6 MV, 33% 10 MV, 45% 18 MV vs. Non-users: 21% 6 MV, 55% 10 MV, 23% 18 MV, $p=0.002$). Notably, there were no significant differences

between bra users and non-users based on bra size ($p=0.07$) or chest wall separation ($p=0.55$).

Most acute skin toxicities observed were grade 2, experienced by 90% of patients treated in a bra, as compared to 70% of patients treated without a bra ($p = 0.003$). Grade 3 toxicity was noted in 5.2% of patients treated in a bra as compared to 2.1% of patients treated without a bra ($p = .22$) and there were no instances of grade 4 dermatitis. Grade 1 maximum toxicity was observed in 6% of patients treated in a bra and 28% of patients treated without a bra ($p < 0.001$). The use of IMRT was associated with a reduced rate of grade 2/3 skin toxicity from 91% to 68% ($p<0.0001$) in the study population as a whole. For patients treated without a bra, the rate of grade 2/3 dermatitis was 86% for patients without IMRT and 64% for patients with IMRT ($p = 0.0011$). Every patient treated with a bra but without IMRT experienced at least grade 2/3 dermatitis, but for those patients treated with a bra and IMRT this incidence of grade 2/3 dermatitis was 87% ($p = 0.057$). Table 2 details the rate of grade 2/3 dermatitis by use of a bra and treatment delivery modality.

On univariate analysis, an increased incidence of grade 2/3 dermatitis was significantly associated with use of a bra ($p=0.0003$), use of 3D-CRT ($p<0.0001$), and use of a higher radiation dose ($p=0.001$). On MVA, use of 3D-CRT (OR=3.9, 95% CI:1.8-8.5, $p = 0.0008$) and use of a bra (OR=5.5, 95% CI:1.6-18.8, $p = 0.006$) remained significant predictors of grade 2/3 skin toxicity.

A subgroup of 12 patients was used to compare dosimetry with and without a bra. The use of a bra significantly decreased the volume of heart in the treatment fields by 63.4% ($p=0.002$), as well as decreased chest wall separation by a mean of 1.1 cm (range -4.07 to +0.85, $p=0.03$), as compared to treatment without a bra. The use of a bra also reduced the amount of left lung within the treatment field by 19% ($p=0.25$) that did not reach statistical significance. Table 3 details the effects of a bra on treated heart and lung volumes and chest wall separation within in simulated tangential fields.

Discussion

In the current study, we found an increased incidence of grade 2/3 dermatitis in women treated in a bra as compared to those treated without a bra; this factor remained significant in the multivariate analysis. This may be multifactorial. There was a significant selection bias, with larger-breasted women selected for the use of a bra. Larger breast size itself is associated with increased dose inhomogeneity and acute dermatitis. Positioning the breast within the bra may not have eliminated all skin folds in the inframammary or axillary region. The bra itself is of a thin fabric material, with thin plastic rather than metal stays, so unlikely to cause bolus effect. However, reduction in the degree of breast ptosis and lateral displacement with the use of a bra did have dosimetric advantages in reducing chest wall separation and lung and heart dose. There also may have been reduction in the degree of inframammary self-bolus and therefore less severe toxicity than otherwise would have been observed without the bra. For each patient, the relative pros and cons of a bra need to be considered.

We observed that the use of IMRT rather than 3D-CRT mitigated the risk of dermatitis associated with bra use. Initial experiences with IMRT for breast cancer have shown clinical feasibility, improved dose distributions in the treated breast, lower heart and lung dose, and reduced acute toxicity compared with standard tangents¹⁴⁻¹⁶. We previously have published our IMRT experience, which showed a reduction in the observed incidence and duration of acute grade 2/3 radiation dermatitis, as compared to conventional radiation¹². The maximum toxicity by technique was 48% grade 0/1 and 52% grade 2/3 observed in those

treated with IMRT vs 25% grade 0/1 and 75% grade 2/3 75% observed in those treated with conventional radiation ($p<0.0001$). With the use of IMRT, patients experienced grade 0/1 acute dermatitis during 82% of their total treatment while the remaining 18% of their time on treatment with grade 2/3 dermatitis. The use of conventional radiation nearly reversed this phenomena, with patients experiencing grade 0/1 for 29% of their total treatment time and grade 2/3 for the remaining 71% of the time ($p<0.0001$). IMRT has shown benefits in randomized studies as well. In a randomized trial from the United Kingdom of standard radiotherapy versus IMRT in early-stage breast cancer, a negative change in breast appearance was observed in 58% of patients randomized to 2D conventional treatment as compared to 40% randomized to IMRT¹⁷. An additional randomized trial comparing standard wedge compensated radiation therapy to IMRT found that IMRT was associated with improved dose homogeneity and reduced incidence of moist desquamation (31% vs. 48%, $p=0.0019$)¹⁸. Recently, Barnett et al reported the interim results of their randomized controlled trial of forward planned whole breast IMRT, which revealed that those treated with standard radiotherapy were more likely to develop telangiectasia at two years when compared to patients in the IMRT group (odds ratio, 1.68; 95% confidence interval 1.13-2.40; $p = .009$)¹⁹.

In the current study of large-breasted women, use of a bra during radiation therapy allowed for repositioning of the breast in the supine position in efforts to reduce breast ptosis, which significantly reduced the chest wall separation and thus resulted in a smaller volume of heart to be present within the treatment field. McGale et al. published on the incidence of heart disease in nearly 35,000 women who received RT for breast cancer, based on interrogation of two national population-based disease registries. While no mortality differences were shown when patients with right-sided breast cancer were compared to women with left-sided breast cancer, left sided radiation was associated with an increased incidence of acute myocardial infarction, angina, pericarditis and valvular heart disease²⁰. There was a >50% decrease in mean whole heart dose when treatments for left sided breast cancer were compared to right sided cases (6.3 Gy vs 2.7 Gy). The recently published QUANTEC (Quantitative Analysis of Normal Tissue Effects in the Clinic) consensus recommends reducing the irradiated heart volume as much as possible without compromising the target coverage to limit the risk of potential late effects²¹.

The potential benefit from a reduction in lung dose with a bra is more difficult quantify. We were able to demonstrate a nonsignificant reduction in the volume of the ipsilateral lung treated with use of a bra as compared to treatment plans not utilizing a bra. However, results from this portion of the study focused on women with left-sided breast cancer planned with and without a bra. Perhaps results would indeed prove significant if women with right-sided breast cancer, where a larger volume of lung is likely present within the treatment field, and if a larger population was investigated. However, the incidence is symptomatic radiation pneumonitis is so low that it would be difficult to show clinical change in the incidence with or without a bra.

Prone positioning for breast radiation therapy has been advocated for large breasted women to reduce the volume of normal tissues irradiated and to improve dose homogeneity within the breast²². This technique is not without its challenges, as it requires customized equipment such as prone breast boards and specialized staff training. Bras are relatively inexpensive compared with the cost of prone breast boards. In addition, this approach may not be tolerated by all women, especially in those with substantial medical co-morbidities which may impair a patient's ability to tolerate the prone position. While multiple reports have shown an improvement in the dose distribution, there is some concern that prone positioning may increase dose to normal tissues. Chino and Marks reported a dosimetric comparison of 16 patients treated in the supine position to an investigative treatment plan

developed on a diagnostic breast MRI performed in the supine position. They found that the prone position actually brings the heart closer to the chest wall, increasing the amount of dose delivered to the anterior aspect of the heart²³. In their dosimetric comparison, they revealed that the majority of the rotation occurs in the superolateral direction, with a mean displacement of the superolateral heart 19 mm closer to the chest wall. Indeed, it is the anterior surface of the heart that demonstrates late fibrosis, coronary artery disease, and perfusion related defects after exposure to radiation therapy²⁴⁻²⁶. Additionally the treatment of regional lymphatics in the prone position is difficult and not routinely done. This consideration is especially relevant given the recent results of the MA-20 trial and Oxford meta-analysis, so that more patients with 1-3 nodes are candidates for regional node irradiation. Also, with the Z0011 results, coverage of the low axilla may be more important with high tangents in patients with 1-2 positive sentinel nodes²⁷. The technique of supine position with a bra allows high tangents and regional node treatment that could be an advantage compared to prone positioning.

The use of a customized bra offers a relatively simple alternative to improve the dose distribution of whole breast irradiation. In our experience the use of a bra for large-breasted women improves simulation and positioning in the supine position. As demonstrated in Figure 2 the use of a bra often reduces the amount of loose soft tissue lateral to the breast, thereby improving daily reproducibility. An improvement in homogeneity and reduced acute toxicity, as compared to treatment without a bra for these large breasted women, could improve long term cosmetic outcomes with longer follow-up. Importantly this technique also reduces the left ventricular volume with tangential radiation. We feel that this technique is a reasonable alternative to the prone treatment position, and allows for significant clinical gains in large breasted women.

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Figure 1.
Treatment position photographs of a patient simulated and treated in a bra.

Figure 2.

Treatment fields for a patient simulated with (a) and without (b) a bra, demonstrating a reduced chest wall separation and decreased volume of heart and lung within the tangential fields. Notably use of the bra eliminated the positional variability of a large lateral soft tissue bulge leading to improved reproducibility of daily set-up.

Table 1

Patient demographics of the 246 large breasted women treated with whole breast radiation either with or without a bra after breast-conserving surgery.

	With a Bra	Without a Bra
Number Pts	58	188
Median age (yrs)	64	59
Median Follow-up (mos)*	44	32
Median Dose		
Tangent Fields	46	46
Total	60	60
Beam energy*		
6MV	22%	21%
10MV	33%	55%
18MV	45%	23%
Beam spoiler used		
No	28%	24%
Yes	72%	76%
T stage		
Tis	16%	20%
T1	71%	63%
T2	12%	17%
T3	2%	1%
Bra Cup Size*		
AA/A	0%	0%
B/C	17%	43%
D/E	52%	45%
DD/DDD	29%	12%
EE/EEE	2%	0%
Chest wall separation		
<18 cm	3%	3%
18-23 cm	40%	32%
24-29 cm	33%	42%
30-35 cm	7%	2%
Unknown	17%	21%
Smoking		
Current	9%	12%
History	33%	32%
Never	59%	55%

	With a Bra	Without a Bra
Systemic therapy		
None	35%	26%
Chemotherapy alone	10%	10%
Chemotherapy & Endocrine therapy	17%	25%
Endocrine therapy alone	38%	40%

Note: statistically significant differences are denoted with an asterisk

Table 2

Rates of Grade 2/3 dermatitis as a function of bra use and treatment delivery.

	All Patients	Bra	No Bra	p-value *
IMRT	68%	87%	64%	0.025
3DCRT	91%	100%	86%	0.031
p-value [†]	< 0.0001	0.057	0.0011	

[†]
p-value corresponding to each column

*
p-value corresponding to each row: Bra vs No Bra.

Table 3

Mean heart and lung volumes and mean chest wall separation in the 12 women planned with and without a bra.

	Bra	No Bra	Difference	p-value
% Left ventricle	2.6	7.1	63%	0.002
% Left Lung	10.1	12.4	19%	0.25
Chest wall Separation (cm)	21.8	22.9	1.1 cm	0.03