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FIVE-YEAR RESULTS OF ADJUVANT RADIOTHER

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Abstract

Purpose/Objective—A technique of prone breast radiotherapy delivered by a regimen of accelerated intensity modulated radiation therapy (IMRT) with a concurrent boost to the tumor bed, was developed at our institution. We report the five year results of this approach.

Methods and Materials—Between 2003–2006, 404 patients with Stage I–II breast cancer were prospectively enrolled into two consecutive protocols, institutional trials 03–30 and 05–181, that used the same regimen of 40.5Gy/15 fractions delivered to the index breast over 3 weeks, with a concomitant daily boost to the tumor bed of 0.5Gy (total dose=48Gy). All patients were treated after segmental mastectomy, had negative margins, and nodal assessment. Patients were set up prone: only if lung or heart volumes were in the field was a supine set-up attempted, and chosen if found to better spare these organs.

Results—92% of patients were treated prone, 8% supine. 72% had stage I, 28% stage II invasive breast cancer. In-field lung volume ranged from 0 –228.27cc, mean: 19.65cc. In-field heart volume for left breast cancer patients ranged from 0–21.24cc, mean: 1.59cc. There was no heart in the field for right breast cancer patients. At a median follow-up of five years, the five-year cumulative incidence of isolated ipsilateral breast tumor recurrence was 0.82% (95% CI: 0.65–1.04). The five-year cumulative incidence of regional recurrence was 0.53% (95% CI:0.41–0.69) and the five-year overall cumulative death rate was 1.28% (95% CI: 0.48–3.38). 82% (95% CI: 77–85) of patients judged their final cosmetic result as excellent/good.

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CONFLICTS OF INTEREST

Etin-Osa Osa, MD: None.
Keith DeWyngaert, PhD: None.
Daniel Roses, MD: None.
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Silvia C. Formenti, MD: None.

Meeting Presentation: The four-year results of this series were presented as an oral presentation at ASTRO Annual Meeting, 2011.

Conclusions—Prone accelerated IMRT with a concomitant boost results in excellent local control, optimal sparing of heart and lung, with good cosmesis. RTOG 10–05, a phase III, multi-institutional, randomized trial is ongoing and is evaluating the equivalence of a similar dose and fractionation approach to standard six weeks radiotherapy with a sequential boost.

INTRODUCTION

Adjuvant radiotherapy (RT) has an established role after breast conservation for early breast cancer. [1–2] A meta-analysis by the Early Breast Cancer Trialists Cooperative Group has also linked optimal local control with survival, by demonstrating that at 15 years of follow up, for every four local recurrences prevented, one breast cancer associated death is avoided. [3]

Despite this evidence, breast conserving therapy (BCT), remains underutilized. [4] In a study of Medicaid insured patients treated with BCT, 65% did not receive adjuvant RT, resulting in a statistically significant increase in cancer specific mortality. [5] Reasons for poor compliance to adjuvant RT include poor access to health care, geographic location, and the inconvenience of six to seven weeks of daily attendance required for standard adjuvant breast RT. [4, 6–7] Shortening the overall treatment time, by reducing the number of radiation visits, is likely to increase both compliance to adjuvant breast RT and utilization of BCT.

A Canadian multicenter, prospective, randomized trial of early stage, node-negative, breast cancer patients demonstrated equivalence of a RT regimen of 16 fractions (hypo-fractionated RT) to a standard regimen of 25 fractions. [8] This trial did not include a boost to the tumor bed. However, even among early breast cancer patients the addition of a boost to the tumor bed following whole breast radiotherapy can significantly enhances local control. [9–10]

Over the past ten years, we have developed a technique that combines hypo-fractionation with a concomitant boost to the tumor bed. [11–14] We chose the prone position to treat most patients to best exclude heart and lung from the radiation fields. After demonstrating feasibility of this approach[11], we questioned whether prone positioning was optimal for all breast radiotherapy candidates, by prospectively comparing prone and supine setups in 400 patients.[14–15] In most of the 400 patients studied, the prone setup proved to better spare heart and lung, independently of breast size.[15–16]

Our technique has the combined advantages of reducing the overall treatment length to three weeks and reducing normal organs exposure to radiation. We report the five-year results in terms of local control, overall survival, and late toxicity of 404 patients prospectively treated with this regimen.

PATIENTS AND METHODS

Patient eligibility

This analysis includes women enrolled in two consecutive, prospective institutional trials, 03–30 and 05–181. Institutional Protocol 03–30 was a phase I/II feasibility study of prone breast radiotherapy with a concomitant boost to the tumor bed. It was offered to pre or post menopausal women with stage I–II, biopsy proven, invasive breast cancer who had

undergone segmental mastectomy, excised with negative margins of at least 1mm. With the exception of tumors less than 5mm that did not require nodal assessment, all patients had sentinel node and/or axillary staging. For patients undergoing adjuvant chemotherapy, a minimum of two weeks had to have elapsed prior to starting RT. A maximum interval of eight weeks from previous cancer therapy (surgery or chemotherapy) was allowed.

Similar eligibility criteria were adopted for institutional Protocol 05–181, a trial designed to determine the optimal treatment positioning (prone vs. supine) based on a volume assessment of in-field heart and lung. This trial was also open to women with ductal carcinoma in situ (DCIS). Nodal assessment was not required for DCIS carriers. Women with DCIS are excluded in the analyses presented in this report, as their outcome was already reported.[17]

For both protocols, women with more than three axillary lymph nodes involved by cancer were excluded. Women were also excluded if they had received previous RT to the ipsilateral breast, had active connective tissue disorders, or a prior or concurrent malignancy (with the exception of squamous or basal cell skin cancer) unless disease free for more than five years. There were no restrictions regarding patient body mass index (BMI) or breast size.

Systemic therapy

Patients received systemic therapy at the discretion of the medical oncologist.

Radiobiological rationale for dose selection

A linear quadratic model was used to assure that the proposed accelerated intensity modulated radiation therapy regimen would result in equivalent probability of tumor control as a regimen of 50Gy in 25 fractions to the whole breast followed by a boost of 10Gy in five fractions to the tumor bed, without increasing the probability of early or late normal tissue toxicity. By estimating a tumor α/β ratio of 4, and taking into account the little tumor proliferation expected to occur during the 18 days of accelerated IMRT, the biologically effective doses, BED, for tumor control and acute and late toxicities were found to be comparable to those of standard fractionation RT. [11]

Radiotherapy methods

Computed tomography (CT) simulation was used: coverage of the index breast regardless of position was ensured by placing the posterior edge of the field on a plane connecting the midline to the anterior extent of the latissimus dorsi muscle, visualized at CT.[11–14]

In both protocols, the planning target volume for the breast (PTV1), was derived from the contoured ipsilateral whole breast defined at simulation and reduced by 5mm in all directions to account for the build-up region at the skin interface and penumbra effects along the posterior, superior, and inferior borders. The boost volume (PTV2) corresponded to the contour of the visualized surgical cavity with a 1cm uniform expansion. The surgical cavity was derived from all available clinical and radiographic information including preoperative imaging, the seroma cavity on the planning CT, surgical clips placed at the time of surgery,

and the lumpectomy scar. Multi-beam arrangements were used to treat the index breast, to 40.5Gy in 15 fractions at 2.7Gy per fraction, daily, Monday-Friday over a three week interval. During each treatment, a concomitant boost of 0.5Gy was delivered to the tumor bed (total dose to PTV2=48Gy). The boost was integrated directly into the IMRT optimization and treatment to intentionally deliver a heterogeneous dose pattern within the breast to achieve a supplemental dose to the PTV2. The optimization and calculations were performed using Helios/Eclipse software (Varian Medical Systems, Palo Alto, CA). Normal tissue constraints required that no more than 5% of the heart volume receive >18Gy and no more than 10% of the ipsilateral lung receive >20Gy.

Follow up and outcome measures

Toxicity was assessed by Radiation Therapy Oncology Group Toxicity Criteria for acute effects and Late Effects on Normal Tissues (LENT)/Subjective, Objective, Management and Analytic (SOMA) criteria for late effects. In both studies, patients were seen after completion of treatment at one, three, six, and 12 months, then yearly to assess long term sequelae. Late toxicities were scored by the treating breast radiation oncologist or the breast nurse practitioner. Patients were asked to assess their overall cosmesis as excellent, good, fair or poor at each yearly visit. Eclipse treatment planning system was used to measure the volume of heart and lung included in the field of treatment.

Statistical methods

Study Designs—Protocol 03–30 was a Phase I–II study designed to enroll 90 patients to estimate the 3-year local recurrence rate in the index breast (DCIS or invasive carcinoma). Protocol 05–181 was designed to assess the optimal set up based on the comparison of the volume of heart and lung in the field from two sets of spiral CT images, obtained in the supine and in the prone positions, for each individual patient. Local recurrence (DCIS or invasive carcinoma) in the index breast was also a key endpoint. The study was initially designed to enroll 200 patients, however, after a planned preliminary analysis of the first 168 patients, the prone position was found to be superior in a greater than expected number of patients. The protocol was therefore amended to enroll an additional 200 patients (400 total) to accrue a sufficient number of patient in whom the supine set up would be optimal and to estimate the false negative rate for the supine group classified as prone and vice versa with 95% confidence intervals. In both studies, assessment of late effects (fibrosis, telangiectasia etc.) was a secondary endpoint. Patients were followed similarly for late effects, systemic progression, and survival.

Statistical analysis—Patient and disease characteristics are presented by study and the distributions in the two studies were tested using chi-square tests for qualitative variables and 2-sided t-tests for quantitative variables.

In this paper, we present five-year overall survival and event free survival based on Kaplan Meier estimates along with 95% confidence intervals. To examine the multiple competing outcomes, multiple decrement methods were used to estimate the cumulative incidence rates of local recurrence, regional recurrence, contralateral breast cancer and distant metastasis. These analyses were carried out using the R V3.0.1 package cmprsk. Gray's test was used to

compare the results for the two studies. Mortality incidence rates were also estimated in this framework.

RESULTS

Study accrual and follow-up

Between September 2003 and August 2005, 90 patients accrued to protocol 03–30; between November 2005 and August 2009, 314 patients with invasive disease accrued to protocol 05–181 for a total of 404 patients evaluable for this analysis with a median follow up time of 60 months (for protocol 03–30 range is 4–103 months, median of 84 months; for protocol 05–181 range is 7–92 months, median of 52 months). In both studies, the same technique and dose-fractionation regimen were used to deliver whole breast radiotherapy with a concomitant boost to the tumor bed and the same follow up schedule was used.

Patient characteristics

Baseline patient and tumor characteristics are provided by study in Table 1. The mean age for all women was 56.6 (SD=11.4) with no significant difference in age distribution between studies. The mean tumor size for the invasive tumors was 1.3cm (SD =0.74). 15% (62/404) had node positive disease, and 37% (148/404) received adjuvant chemotherapy. 39% patients (159/404) received adjuvant anti-hormonal therapy. 373(92%) were treated in the prone position, 31(8%) were treated in the supine position. There were no significant differences in baseline patient and tumor characteristic between the studies with the exception of treatment position based on optimal sparing of organs at risk with more patients being treated supine on protocol 05–181. The data were reanalyzed for the prone patients only, and there were no differences in any of the results.

In each protocol the dose constraints for normal tissue were readily achieved.[11, 15] For all patients, the volumes of heart and lung included in the field were calculated from CT simulation planning images (Eclipse) and are presented in Table 5 for patients treated in the prone position and Table 6 for patients treated in the supine position. In-field lung volume ranged from 0–228.27cc, mean: 19.65cc for all patients. In-field heart volume for left breast cancer patients ranged from 0–21.24 cc, mean: 1.59cc. There was no heart in the field for right breast cancer patients.

Treatment efficacy

Frequency of events and the cumulative incidence rates are presented in Table 2 for all patients. The numbers of events were small in each study. We note that there were no statistically significant differences between studies for any of the outcomes reported (Gray's test, all p values >0.25). Therefore, we present the overall rates for the two studies combined.

At an overall landmark time of 60 months, eight patients developed an in breast failure with three occurring by five-years follow-up, resulting in a five-year cumulative incidence rate of isolated ipsilateral breast tumor recurrence of 0.82% (95% CI:0.65–1.04).

The five-year cumulative incidence rate of regional recurrence was 0.53% (95% CI: 0.41–0.69, Table 2). Two of the three patients experienced regional recurrence by five years of follow-up. One of these patients progressed systemically and died after regional recurrence.

The five-year cumulative incidence rate of contralateral breast cancer was 0.55 (95% CI: 0.42–0.72). There were four cases, one DCIS and three invasive breast cancers with two cases occurring by five years of follow-up.

Five patients developed distant failures with four failures occurring by five years of follow-up resulting in a five-year cumulative incidence rate of distant metastases of 1.07% (95% CI: 0.86– 1.32): four patients had stage IIA and one had stage IA invasive ductal carcinoma. Three of these patients initially presented with ER−/PR−/Her2− carcinoma, one with ER −/PR−/Her2+, and 1 with ER+/PR+/Her2+ carcinoma. Four of these patients have expired and one is currently alive with disease.

15 patients expired, corresponding to a five-year cumulative incidence of death of 2.37% (95% CI: 1.96–2.84) and an overall five-year cumulative survival rate of 98.72% (95% CI: 96.62–99.52) without considering competing risks. Five patients died of breast cancer while ten patients died from other causes.

Treatment-related toxicities

A detailed analysis of treatment related late toxicities developed at or greater than six months following completion of RT is presented in Table 3. Late RT toxicities were limited to grade 1 or 2 in most patients. The most frequent grade 3 toxicity was telangiectasia which occurred in 1% (6/404) of patients. Less than 1% of patients experienced grade 3 breast fibrosis, breast retraction, breast edema, or arm lymphedema.

Cosmetic results

Of the 377 patients who agreed to self-assess their cosmetic result 82% (95% CI: 77%–85) judged their final result as excellent-good cosmesis (Table 4). There were no differences in patient and tumor characteristics between studies (Table 1) when we compared the characteristics of patients who provided self-assessments of cosmesis.

DISCUSSION

The current series consists of 404 women with stage I and II breast cancer accrued to two consecutive trials of an identical regimen that includes a concurrent boost to the tumor bed. By delivering the boost concurrently, we were able to limit the overall treatment time to three weeks, compared to previous trials which deliver the boost sequentially thus lengthening the overall treatment time.[8, 18–19]

With a median follow-up time of five years, hypo-fractionated breast RT with concurrent boost results in a five year cumulative incidence rate of ipsilateral breast tumor recurrence of 0.82% (95%CI: 0.65–1.04). The majority of the patients were satisfied with the cosmetic results of this approach.

The recurrence rate reported is comparable to that of several randomized trials comparing hypo-fractionated breast RT to standard fractionation radiotherapy to the breast (25–30 fractions). [8, 18–20] The five year IBTR in the hypo-fractionation arm of the Canadian study was 2.8%, and 2.2–5.2% for the START A/B trials, respectively.[18–19, 21]

Currently available evidence supports the equivalence of hypo-fractionated breast RT to standard fractionation breast RT in patients with T1-2N0 disease, and in patients who do not require treatment with chemotherapy.[22] In contrast to ASTRO guidelines for hypo-fractionated breast RT, that reserve hypo-fractionated RT to T1-2N0 carriers,[22] 15% of the patients in this series were node positive (one-three nodes). While the preliminary results reported suggest that these patient may also be safely treated with this hypo-fractionation technique, it is important to notice that all patients with a positive sentinel node in this series underwent subsequent completion axillary dissection, a practice that is rapidly changing.[23]

Yarnold et al. recently expressed concerns regarding the effect of hypo-fractionated breast RT on the heart and lungs.[24] Similarly, the ASTRO task force recommends reserving hypo-fractionated radiation to patients whose heart and lungs can be excluded from the treatment field.[22] This precaution may be of special importance in a modern patient population, likely to receive adjuvant agents that are cardiotoxic such as doxorubicin or trastuzumab.

We overcame this challenge by adopting setup in the prone position from the inception of all hypo-fractionated trials we conducted. The prone setup demonstrated to be an excellent strategy to protect heart and lung in most women, independently from their body mass or breast size.[14–16, 25] With the majority of patients treated in the prone position, we were able to minimize to volumes of heart and lung in the treatment field, a strategy that reduces the cardiovascular risk and may reveal crucial in preventing cardiovascular events and death in left breast cancer carriers at high risk for cardiovascular disease.[26]

In the setting of rising health care costs, it is becoming more critical to consider the cost effectiveness of treatment. Hypo-fractionated breast RT over 13–16 fraction reduces the cost of breast RT by about 30%.[27] In addition, by shortening the treatment time, hypo-fractionated breast RT is more convenient for the patient, resulting in less time lost from work and other activities. However, intensity modulated radiotherapy was used in this study, which is a more costly approach. We have since described similar feasibility of a conformal approach when the breast is the target, without a concomitant boost[28] and we have recently reported comparability of a daily IMRT boost to a weekly boost.[29] The latter approach is currently being tested in a large prospective randomized trial that compares prone breast radiotherapy with either type of boost by IMRT or conformal radiotherapy. These consecutive studies aim at generating evidence for equivalence of a conformal approach of prone breast radiotherapy to the IMRT technique of this report. If demonstrated equivalent, a conformal RT regimen of prone hypofractionated breast radiotherapy will result in a significant reduction of the cost of breast radiotherapy.

The non-randomized nature of either of the trials reported is a main limitation of this report. The current RTOG 10–05 trial is a phase III, multi-institutional, randomized trial to test the non-inferiority of accelerated whole breast irradiation with hypo-fractionation plus

concurrent boost to standard whole breast irradiation plus sequential boost in early stage breast cancer, with a dose and technique almost identical to the one we used.

Results of this trial will provide conclusive information about breast hypo-fractionation.

Finally, in breast cancer, five-year outcome data is indicative but certainly inadequate to prove equivalence to standard regimens that have much longer follow-up information.

CONCLUSION

In conclusion, with a median follow up time of five years, hypo-fractionated breast RT with a simultaneous integrated boost in the prone position resulted in excellent cosmesis and normal tissue sparing, with a five-year cumulative incidence rate of 0.82% in-breast local recurrence and 98.72% five-year cumulative survival rate. Longer follow-up is needed to confirm the efficacy and safety of this approach.

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Summary

The manuscript reports the 5 year outcome of 490 breast cancer patients prospectively accrued to two IRB-approved trials that tested the same regimen of hypo-fractionated breast radiotherapy with a concomitant boost to the tumor bed. This report is timely and relevant as the dose and fractionation used are almost identical to those required for the hypo-fractionation arm of the currently accruing RTOG 10–05 trial.

Table 1

Baseline Patient and Tumor Characteristics (n=404)

		03–30 (N=90)	05–181 (N=314)	All patients (N=404)	P-Value*
Age	mean +/− SD	56.83 +/− 12.33	56.48 +/− 11.14	56.56 +/− 11.40	0.80
Tumor size (mm)	mean +/− SD	13.64 +/− 12.09	12.76 +/− 13.58	12.96 +/− 7.41	0.32
Stage	I	67 (74%)	223 (71%)	290 (72%)	0.51
	IIA	19 (21%)	82 (26%)	101 (25%)	
	IIB	4 (4%)	9 (3%)	13 (3%)	
Tumor Stage	T1	77 (86%)	260 (83%)	337 (83%)	0.54
	T2	13 (14%)	54 (17%)	67 (17%)	
Histology	Invasive Ductal	72 (80%)	265 (84%)	337 (83%)	0.57
	Invasive Lobular	9 (10%)	27 (9%)	36 (9%)	
	Other	9 (10%)	22 (7%)	31 (8%)	
Nodal Status	Negative	75 (83%)	267 (85%)	342 (85%)	0.69
	Positive	15 (17%)	47 (15%)	62 (15%)	
	Negative	15 (17%)	57 (18%)	72 (18%)	0.75
Tumor estrogen receptor status	Positive	75 (83%)	257 (82%)	332 (82%)	
	Negative	36 (40%)	123 (39%)	159 (39%)	0.89
Tumor progesterone receptor status	Positive	54 (60%)	191 (61%)	245 (61%)	
Tumor Her2/Neu Status	Negative	85 (94%)	273 (90%)	358 (89%)	0.18
	Positive	5 (6%)	31 (10%)	36 (9%)	
	Not Performed		10	10 (2%)	
Breast Laterality	Left	50 (56%)	157 (50%)	207 (51%)	0.35
	Right	40 (44%)	157 (50%)	197 (49%)	
	Prone	90 (100%)	283 (90%)	373 (92%)	0.002
Treatment position, based on optimal sparing of OAR	Supine	0	31 (10%)	31 (8%)	

		03–30 (N=90)	05–181 (N=314)	All patients (N=404)	P-Value*
Chemotherapy	Yes	30 (33%)	118 (38%)	148 (37%)	0.46
	No	60 (67%)	196 (62%)	256 (63%)	
Antihormonal Therapy	Yes	41 (46%)	118 (38%)	159 (39%)	0.17
	No	49 (54%)	196 (62%)	245 (61%)	

*2-sample t-tests (2-sided) for continuous variables; chi-square tests for categorical variables.

Table 2

Competing Risk Model of Cumulative Incidence Rate at Five Years for Specified Outcomes (N=404)

Event	Total Number of Events	Events in 03–30 (N=90)	Events in 05–181 (N=314)	Number of Events by 5 year follow-up 03–30	Number of Events by 5 year follow-up 05–181	5-year Cumulative Incidence Rate Combined (95% CI)*
In breast local recurrence drrecurrecurecurrence	8	4	4	1	2	0.82 (0.65–1.04)
Regional recurrence	3	1	2	1	1	0.53 (0.41–0.69)
Contralateral breast cancer	4	3	1	1	1	0.55 (0.42–0.72)
Distant Metastases	5	1	4	0	4	1.07 (0.86– 1.32)
All Death	15	6	9	4	8	2.37(1.96–2.85) 1.28 (0.48–3.38)**

* There is no difference in cumulative incidence rates between the 2 studies so only the combined rate is provided.

** Overall 5 year cumulative rate of death based on Kaplan-Meier analysis

Table 3

Maximum Grade Late Radiation Toxicity (N=404)

		03–30 (N=90)	05–181 (N=314)	All Patients (N=404)
Pigmentation Change	Grade 1	15 (17%)	62 (20%)	77 (19%)
	Grade 2	0	2 (1%)	2 (1%)
	Grade 3	0	0	0
Breast Fibrosis	Grade 1	19 (21%)	59 (19%)	78 (19%)
	Grade 2	6 (7%)	13 (4%)	19 (5%)
	Grade 3	0	1 (0.3%)	1 (0.3%)
Breast Retraction	Grade 1	14 (16%)	46 (15%)	60 (15%)
	Grade 2	5 (6%)	17 (5%)	22 (5%)
	Grade 3	0	2 (1%)	2 (1%)
Breast Telangiectasia	Grade 1	10 (11%)	47 (15%)	57 (14%)
	Grade 2	4 (4%)	19 (6%)	23 (6%)
	Grade 3	2 (2%)	4 (1%)	6 (1%)
Breast Edema	Grade 1	0	10 (3%)	10 (2%)
	Grade 2	0	0	0
	Grade 3	0	1 (0.3%)	1 (0.3%)
Breast Pain	Grade 1	8 (9%)	28 (9%)	36 (9%)
	Grade 2	1 (1%)	2 (1%)	3 (1%)
	Grade 3	0	0	0
Arm Lymphedema	Grade 1	1 (1%)	1 (0.3%)	2 (1%)
	Grade 2	0	0	0
	Grade 3	0	1 (0.3%)	1 (0.3%)

Table 4

Patient's Self Assessment of Cosmesis By Protocol* (N=377 reported self-assessments)

Patient's Self- Assessment of Cosmesis	03–30 (N=74)	05–181 (N=303)	All patients (N=377)
Excellent/Good	57 (77%)	251 (83%)	308 (82%)
Fair	16 (22%)	45 (15%)	61 (16%)
Poor	1 (1%)	7 (2%)	8 (2%)

* There is no difference in patient's self-assessment of cosmesis between the 2 protocols (chi-square p-value >0.05)

Table 5

Volumes of Heart and Lung for Patients Treated Prone

	Right Breast		Left Breast		
Breast Volume cm^3	**No.**	**In-Field Lung Volume Mean (95% CI), cm^3**	**No.**	**In-Field Lung Volume Mean (95% CI), cm^3**	**In-Field Heart Volume Mean (95% CI), cm^3**
< 750	81	26.19 (19.78 to 30.35)	68	16.62 (9.18 to 24.07)	3.00 (1.74 to 4.26)
750–1500	85	18.68 (12.52 to 24.84)	72	2.92 (1.48 to 4.35)	1.29 (0.40 to 2.17)
> 1500	29	8.24 (1.63 to 14.86)	38	2.27 (−0.98 to 5.52)	0.57 (−0.20 to 1.34)
Total	195	20.25 (16.25 to 24.25)	178	8.01 (4.87 to 11.16)	1.79 (1.15 to 2.43)

Table 6

Volumes of Heart and Lung for Patients Treated Supine

	Right Breast		Left Breast		
Breast Volume cm^3	**No.**	**In-Field Lung Volume Mean (95% CI), cm^3**	**No.**	**In-Field Lung Volume Mean (95% CI), cm^3**	**In-Field Heart Volume Mean (95% CI), cm^3**
<750	1	56.80	22	90.26 (75.14 to 105.39)	0.50 (−0.21 to 1.20)
750–1500	0	NA	6	82.07 (45.48 to 118.66)	0.04 (−0.01 to 0.09)
>1500	1	0	1	27.16	0
Total	2	28.40	29	27.79 (18.72 to 36.85)	0.38 (−0.15 to 0.92)