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Toxicity from breast cancer radiation using helical tomotherapy with a simultaneous integrated boost

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Abstract

Purpose: To evaluate two helical tomotherapy treatment planning techniques for breast conserving therapy with regard to acute skin toxicity and dosimetry.

Methods: Thirty-two patients were studied. The original approach was used for sixteen patients and incorporated a directional block of the ipsilateral lung and breast. An additional sixteen were planned using a modified approach which incorporated a full block of the ipsilateral lung exclusive of 4cm around the breast. Dose-volume histograms of targets and critical structures were evaluated. Skin toxicity monitoring was performed throughout treatment and follow-up using the Common Terminology Criteria for Adverse Events.

Results: Treatment was well tolerated with patients receiving a median dose of 59.36 Gy. 8/16 patients in both groups had grade 2 erythema immediately after radiation. On three-week follow-up ten and seven patients in the original and modified groups showed grade 1 erythema. On three and six month follow-up, both groups had minimal erythema, with all patients having either grade 0 or 1 symptoms. No grade 2 or 3 toxicities were reported.

Mean treatment time was 7.5 and 10.4 minutes using the original and modified methods. Adequate dose coverage was achieved using both methods ($V_{95} = 99.5\%$ and 98%). Mean dose to the heart was 10.5 Gy and 1.8 Gy respectively ($p < 0.01$). For right-sided tumors the original and modified plans yielded a mean of 8.8 Gy and 1.1 Gy ($p < 0.01$) versus 11.7 Gy and 2.4 Gy for left-sided tumors ($p < 0.01$). The mean dose to the ipsilateral lung was also significantly lower in the modified plans (11.8 Gy vs. 5.0 Gy, $p < 0.01$).

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Conflict of Interest

All authors certify that this manuscript has not been published in whole or part nor is it being considered for publication elsewhere. The authors have no conflicts of interest to declare.

Conclusions: Tomotherapy is capable of delivering homogeneous treatment plans to the whole breast and lumpectomy cavity using SIB treatment. Using the treatment methods described herein, extremely low doses to critical structures can be achieved without compromising acute skin toxicity.

Keywords

Tomotherapy; breast cancer; toxicity; radiation therapy

Introduction

Breast conserving surgery followed by adjuvant whole breast irradiation lowers the risk of ipsilateral breast tumor recurrence and improves overall survival^{1, 2}. The most common approach is one of conventionally fractionated radiation with a standard dose of 45–50 Gy given at 1.8–2.0 Gy/daily 5 days per week followed by a sequential boost to the tumor bed^{3–6}. More recently, the use of a simultaneous integrated boost (SIB) has increased for early stage breast cancer patients, with the intent of reducing overall treatment time and cost without compromising local control^{7–10}. Studies have shown that, compared to a conventional sequential boost, a SIB delivered through 3D conformal radiotherapy (3D-CRT) or static-field intensity-modulated radiotherapy (IMRT) can improve target dose conformity with better sparing of normal tissues such as the heart and lungs^{7–10}. Furthermore, Tomotherapy (TomoTherapy, Madison, WI) has emerged as a platform for delivering modulated helical treatment for both post-lumpectomy and post-mastectomy patients that were once treated with a combination of electron and static photon beams^{11–14}. A report from our institution first described the use of tomotherapy for breast conserving therapy with SIB¹⁵, followed by a comparative planning study which showed that tomotherapy is capable of delivering a SIB with adequate tumor coverage and superior normal tissue sparing to the lungs and heart in comparison with the 3D-CRT¹⁶. Although the use of helical tomotherapy for whole breast irradiation (WBI) has been well reported, there are few clinical reports of acute and late toxicity using this radiation delivery modality to deliver WBI with a SIB.

In this study we present a dosimetric evaluation and acute skin toxicity resulting from two treatment planning techniques for whole breast irradiation with a SIB to the lumpectomy bed using helical tomotherapy. We compare a technique that we have previously described¹⁵ to a modified treatment planning technique that attempts to further decrease the dose of radiation to normal structures including the heart and lungs.

Methods and Materials

Thirty-two early-stage breast cancer patients treated with breast conserving therapy and recommended to undergo whole-breast radiotherapy without dedicated lymph node coverage were consecutively identified. This study was approved by the University of Wisconsin Institutional Review Boards. Half of the patients (n=16) were treated with the original planning technique, while the other half (n=16) were treated with a modified technique, as described below.

CT simulation scans with a slice thickness of 2.5 mm were acquired for each patient with surgical clips and a radiopaque wire placed on the lumpectomy scar in order to assist in lumpectomy cavity delineation. Superior, inferior, medial, and lateral aspects of the entire breast were also outlined with a radiopaque wire based on clinical exam. CT scans were imported to the ADAC Pinnacle treatment planning system (TPS) (Philips Medical Systems, Cleveland OH) for contouring. The treated breast was contoured with the assistance of the radiopaque wires placed during simulation and based on the radiographic findings of breast tissue with no skin retraction. The lumpectomy bed was contoured as a boost CTV with a 1 cm expansion to the PTV. Critical organs including the ipsilateral and contralateral lung, heart, spinal cord, esophagus, trachea, and contralateral breast tissue were also delineated for dose constraint during optimization. The heart was contoured from its base to the branch point of the pulmonary trunk into the pulmonary arteries. The contralateral breast was defined per the consensus definitions of the anatomical borders from the RTOG Breast Atlas. The supraclavicular, internal mammary, and axillary lymph nodes were not purposefully contoured for treatment purposes. The CT images and related contours were exported to the TomoTherapy TPS (Version 4.2.3) for planning.

Planning parameters included field width, pitch, and modulation factor. Selecting appropriate values for these parameters is crucial to the plan dose distribution and treatment delivery time^{15, 17}. For the studied patients, TomoTherapy planning parameters include a 2.5 cm field width, pitch of 0.287 and modulation factor of 1.8–2.4. For most patients, the prescription dose was 50.4 Gy in twenty-eight fractions to the whole breast with a SIB of 59.36 Gy over 28 fractions to the lumpectomy cavity. The goal of each plan was to deliver 100% of the prescription dose to 95% of the PTV.

Treatment planning for patients planned with the original technique used a complete block of the contralateral lung and breast and a directional block of the ipsilateral lung, heart, and spinal cord. Patients treated using the modified method were planned with a complete block for the contralateral lung, directional block for the heart, and no block for the contralateral breast. In addition, we generated a new complete block that included the ipsilateral lung exclusive of a 4cm expansion around the breast PTV. The goal of this new ROI was to control the dose to the ipsilateral lung and reduce the total lung dose. While dose constraints were met in all cases, this modified treatment planning method was used in later patients in an attempt to further decrease dose to normal structures.

Dose volume histograms (DVH) were computed for the PTV and critical structures. Target dose homogeneity index (HI) was defined as:

$$HI = [(D_{2\%} - D_{98\%}) / D_p] * 100\%$$

Reported doses include the prescription dose (D_p), and the dose received by 2% and 98% of the PTV ($D_{2\%}$ and $D_{98\%}$, respectively). Other dosimetric indices include the percentage of the PTV receiving 107% ($V_{107\%}$) and 95% ($V_{95\%}$) of the prescription dose as well as the ratios of mean, maximum, and minimal doses to the prescription dose (D_{mean}/D_p , D_{max}/D_p , and D_{min}/D_p). In addition, a conformity index, defined as the ratio of the volume covered by the 95% prescription isodose over the volume of the breast planning target volume as per the

RTOG 1005 protocol was calculated. Normal structure dosimetric indices such as mean dose, volume receiving 30 Gy, and volume receiving 5 Gy were acquired for the heart, ipsilateral lung, contralateral lung, total lungs, and contralateral breast.

All patients were treated with helical tomotherapy with daily megavoltage CT (MVCT) guidance for setup verification.

The clinical endpoint of this study was acute skin toxicity immediately following completion of the treatment. Patients' acute skin toxicity monitoring was performed using the Common Terminology Criteria for Adverse Events (CTCAE) (Version 3.0) upon completing treatment and was prospectively recorded for a period of 6 months.

Statistical analysis was performed using STATA version 11.1 (StataCorp, College Station, TX).

Results

Patient Characteristics

Seven patients in each group had right-sided tumors while the remaining nine in each group had left-sided lesions. Patients' ages ranged from 36 to 81 years at time of diagnosis, with a mean of 61.8 years. Patients had a mean BMI of 28.9 in the original planning method group and 28.6 in the modified planning method group ($p = 0.87$). Patients in the first group were more likely to be active smokers (5/16) versus patients in the modified group (2/16). The characteristics of the 32 patients are shown in Table 1.

Treatment Delivery

The mean treatment delivery time using the original planning technique was 7.5 minutes with a range of 5.1–11.6 min. The median dose delivered to the whole breast PTV was 50.4 Gy (range 48.6 – 50.4) with median total dose to the lumpectomy PTV 59.36 Gy (range 58.05 – 63.0) (Table 2a).

The mean treatment delivery time using the modified planning technique was 10.4 minutes with a range of 8.6–12.4 min. The median dose delivered to the whole breast PTV was 50.4 Gy (range 41.4 – 50.4) and the median total dose to the lumpectomy PTV was 59.36 Gy (range 48.99 – 61.6) (Table 2b).

Target volumes

Dosimetric evaluations of target volumes for both planning methods are summarized in Table 2. Target volumes were comparable between the two groups, with a mean breast PTV of 772.4 and 709.1 in the original and modified groups respectively ($p = 0.65$), and mean lumpectomy PTV volumes of 54.1 and 35.4 ($p = 0.13$). For the whole breast PTV, the “cold spot” for the whole breast ($V_{<95\%}$) was slightly higher in modified plans as compared to the originals, 2.1% versus 0.5%. Patients treated with the original planning method had ratios of mean and minimum breast PTV dose to prescription dose average 106.7% and 80.7% with a homogeneity index of 17.5%. The modified plans' ratios averaged 104.3% and 51.8% respectively, with mean homogeneity index of 28.4% of the prescription dose. The

conformity index per the RTOG 1005 protocol was also calculated. The original plans had a mean conformity index of 0.99 for the whole breast PTV, with a standard deviation of 0.01. Modified plans also had a breast PTV mean conformity index of 0.99 and standard deviation of 0.01 ($p = 0.68$).

For the lumpectomy PTV, the mean hot spot ($V_{>107\%}$) volume was low in both the original and modified plans, with a value of 0.7% and 0.2%. All hotspots were confined to the lumpectomy PTV regions. The mean cold spot volume ($V_{<95\%}$) was less than 0.5% in both cases. The ratios of mean, maximum, and minimum lumpectomy PTV dose to prescription dose averaged 102.6%, 106.9%, and 96.9% in the original plans and 101.7%, 105.4%, and 91.9% in modified plans. The mean homogeneity index of the lumpectomy PTV was 5.7% and 6.1% in original and modified plans respectively. Lumpectomy PTVs were also similarly conformal, with a mean conformity index of 0.98 using the original planning method and 1.00 with the modified method ($p = 0.02$).

Organs at Risk

Dose distributions are shown for both right and left-sided patients using both planning techniques (Figure 1). The dose indices for organs at risk are shown in Table 3. The mean dose to the heart was 10.5 Gy using original planning methods and 1.8 Gy using the modified technique ($p < 0.01$). For patients with right-sided tumors, the original and modified plans yielded a mean of 8.8 Gy and 1.1 Gy respectively ($p < 0.01$) and 11.7 Gy and 2.4 Gy for left-sided tumors ($p < 0.01$). Heart V30 was similarly low, with a mean of 1.2% and 0.1% ($p = 0.11$).

The average mean lung dose (MLD) for the ipsilateral lung was also significantly lower in the modified plans, with a mean of 11.8 Gy versus 5.0 Gy ($p < 0.01$). The MLD for the contralateral lung was significantly lower in modified plans, with a mean of 5.6 Gy versus 0.5 Gy for the thirty-two patients ($p < 0.01$). Similarly the percentage of total lung receiving 20 Gy was 6.0% in original plans versus 4.8% in modified plans ($p = 0.02$). The mean dose to the contra-lateral breast was slightly higher in the modified plans, 4.4 versus 5.3 Gy, but the difference was not statistically significant ($p = 0.08$). The maximum dose and the percentage volume receiving 5 Gy were also slightly higher. Maximum spinal cord dose was lower in the modified plans. The absolute volume of the total body (the rest of unspecified normal tissue) receiving >5 Gy was 6700 cc in the original plans and 5200 cc in the modified plans ($p < 0.01$).

Acute skin toxicity

Overall, treatment was extremely well tolerated. Per CTCAE Version 3 definitions, 8/16 (50%) of patients treated using both the original and modified planning methods had grade 2 erythema immediately after treatment (Figure 2). On a three-week follow-up, erythema had largely resolved with ten patients showing grade 1 erythema in the original planning group and seven showing grade 1 erythema in the modified treatment planning group.

On both three and six month follow-up, both groups of patients had minimal residual erythema, with all patients either having grade 0 or grade 1 symptoms. There were no grade 2 or grade 3 toxicities reported at these endpoints.

Discussion

We have demonstrated that simple alterations in treatment planning techniques for breast and lumpectomy cavity radiation for early stage breast cancer can improve dosimetric measures while achieving minimal skin toxicity. This was achieved with a mean treatment delivery time of 7.5 and 10.4 minutes, a savings of 25–50% as compared to published studies^{13, 14, 16}. The slightly increased treatment time using the newer planning techniques highlights the trade off between increasing dosimetric constraints and treatment time. Similarly, our relatively low rates of skin toxicity show that TomoTherapy can be used to effectively treat patients with acceptable acute skin toxicity; however, some care must be taken with planning. If the skin surface is included as an optimization target, inverse planning can result in solutions that favor tangential beam segments near the skin surface¹⁸. While the combination of inverse planning and continuous rotational delivery allows TomoTherapy flexibility in delivering dose to superficial targets, high dose to the skin can result in significant skin desquamation and fibrosis. It is well known that if the “hot-spot” (>10% of prescribed dose) involves the skin surface, significant acute toxicity can develop¹⁹. A recent study of 158 breast cancer patients treated with 3D-CRT has also suggested that lower doses can also correlate with toxicity²⁰. Nevertheless, acute toxicity must be balanced with ensuring adequate tumor coverage. The RTOG 1005 protocol has an additional constraint, the conformity index, defined as the ratio of volume covered by the 95% isodose line divided by the volume of the breast, that serves as an aid in evaluating plans to ensure they are not too “cool” or too “hot.” Conformal plans are one of the strengths of TomoTherapy, with all of our plans having a CI of nearly 1. We were also able to avoid severe skin toxicity with hot spot means of 107% and 105%, respectively. Similarly, Freedman *et al* treated early-stage breast cancer patients with a four-week hypofractionated IMRT course with a simultaneous electron boost and reported acceptable acute skin toxicity and quality of life²¹. Contouring the skin as an organ-at-risk for optimization has become one way to reduce skin dose and avoid toxicity^{18, 22}, however accurately measuring skin dose is difficult. Increasing breast size during treatment due to inflammation may lead to significant underdosing of the skin, while post-surgical changes may lead to contracture and overdosing²³. Issues also exist with patient positioning, as a 5mm shift may introduce dose variation of 3–9%²⁴. Further complicating matters is that the TomoTherapy planning software itself may overestimate skin dose by anywhere between 3–13%^{25–28}. Nevertheless, adequate breast surface dose has been shown to be achievable utilizing TomoTherapy in clinical practice both at our institution²⁹ as well as others^{30, 31}. Special care must be taken however, when treating breast cancer patients with IMRT. The inherent nature of tomotherapy treatment allows for daily MVCT setup imaging, and extra attention must be paid to ensure that patient positioning is accurate. If patient positioning or setup is found to be inaccurate, our institutional practice is to use additional TLD measurements or dose recalculation on daily MVCT imaging to ensure adequate dosing. Although we have found daily patient setup to be satisfactory as reported above, a robust approach has been described for volumetric modulated arc therapy utilizing an expanded optimization plan to mimic possible changes in size due to edema or breath variation³². A similar technique can be applied using tomotherapy.

Nevertheless, skin dose is not the only factor found to be significantly associated with increased skin toxicity. Body mass index, breast size, the use of breast IMRT, beam energy, maximum dose, and sagittal dose gradient have all been associated with increased toxicity¹⁹.

With regards to other critical tissues, the techniques presented here achieve doses at least as good as those presented in previous studies. Our V20 lung doses were comparable to previously published data including those by Goddu et al. (range, 5.8–10.4%), while our total body dose was 33% lower than those achieved in the same study¹³. While our heart doses using our original treatment planning parameters are comparable to previously published studies by Fogliata et al. (range, 8.7–21.1 Gy)³³ as well as Goddu et al. (mean, 12.2 Gy)¹³, the heart doses achievable using our modified treatment planning techniques are significantly lower. This is especially relevant in enrolling patients on protocol. As practitioner experience with IMRT in the treatment of breast cancer improves, protocols have begun to implement more stringent guidelines. Current RTOG protocol 1005 for example, requests that plans have a mean heart dose of less than 3.20 Gy. The original treatment planning methods described above would not meet this constraint while the modified plans do so easily. For both heart and lung our modified treatment planning approach allows us to achieve statistically significant improvements in radiation doses. With some evidence showing the risk of ischemic heart disease increasing linearly with dose delivered³⁴, this may have implications for long-term cardiac morbidity.

We also acknowledge that while our doses to normal tissues achieved with the modified planning technique are significantly lower than that with the original method, they may in some cases be inferior to those that achievable with a tangential beam arrangement. This is especially true in cases of right-sided tumors and mean dose to the heart. Secondly, dose to the contralateral breast will necessarily be higher than with traditional opposed tangential beams, theoretically increasing the risk of secondary malignancy in a patient population with high long-term survival. These risks must be balanced by the realities of treatment delivery and patient convenience. The center where patients were treated in this study is at an academically affiliated TomoTherapy-only community center, where a single treatment machine must serve a wide variety of radiotherapy needs. In this case, the closest standard linear accelerator is located over 60 minutes away. While we acknowledge that a lower heart and contralateral breast dose may be desirable, the availability of treatment closer to home may increase the proportion of patients receiving recommended radiation as a component of their breast conserving therapy. Finally, patients in this study were accrued before newer limited-angle tomotherapy units were available, so this may be less of a factor in the future.

We acknowledge several limitations to our study. First, the limited number of patients limits our power to draw firm conclusions however, our results are comparable to those previously published for breast IMRT²¹. Secondly, there is some heterogeneity in our treatment cohort, with a handful of patients receiving doses that were slightly higher or lower than originally planned. Furthermore, follow-up assessments did not extend beyond 6 months and thus late toxicity and cosmetic outcome were not assessed. Finally, patients treated on this study were treated using traditional helical TomoTherapy and were accrued before newer limited-angle TomoTherapy units were available.

Conclusion

To date there have not been any published clinical evaluations of toxicity on helical TomoTherapy based breast cancer treatment using the simultaneous integrated boost dose regimen. In this study, we have shown that helical TomoTherapy is capable of delivering homogeneous treatment plans using SIB treatment within a reasonable treatment time, acceptable dose to critical organs, and with minimal skin toxicity.

Abbreviations:

3D-CRT	3D-conformal radiation therapy
BMI	Body mass index
CTCAE	Common Terminology Criteria for Adverse Events
CTV	clinical tumor volume
DVH	dose volume histograms
HI	homogeneity index
IMRT	intensity-modulated radiotherapy
MOSFET	metal–oxide–semiconductor field-effect transistor
MLD	mean lung dose
MVCT	megavoltage CT
PTV	planning Tumor Volume
ROI	region of interest
SIB	simultaneous integrated boost
TLD	thermoluminescent dosimeter
TPS	treatment planning system
WBI	whole breast irradiation

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Figure 1:
Sample contours and dose distributions for both left and right sided patients using both the original and modified planning methods

Figure 2A

Figure 2B

Figure 2: Skin toxicity in patients treated using the original (A) and modified (B) treatment planning methods

Table 1:

Patient Characteristics

Characteristics	Old Planning Method		New Planning Method	
Number of Patients	16		16	
Age (y), range	61.5, 36 – 79		62.1, 37 – 81	
BMI mean	28.9		28.6	
Tumor Size				
Tis	5	31%	3	18.7%
T1a	2	12.5%	0	0%
T1b	3	18.8%	5	31.3%
T1c	6	37.5%	6	37.5%
T2	0	0%	2	12.5%
Nodal Status				
N0	15	93.8%	15	93.8%
N1	1	6.2%	1	6.2%
Tumor Side				
Left	9	56.3%	9	56.3%
Right	7	43.7%	7	43.7%
ER Status				
Positive	13	81.3%	15	93.7%
Negative	2	12.5%	1	6.3%
Unknown	1	6.3%	0	0
PR Status				
Positive	9	56.3%	14	87.5%
Negative	4	25%	2	12.5%
Unknown	3	18.8%	0	0
Table 1: Patient Characteristics				

Table 1: Patient Characteristics

Table 2:

Treatment dosimetry for the original (A) and modified (B) planning methods

	Whole breast PTV		Lumpectomy PTV	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Dose	50.2 $\pm$ 0.6	48.6 – 50.4	59.7 $\pm$ 0.9	58.05 – 63.0
Volume (cc)	772.4 $\pm$ 391.2	247.2 – 1782.3	54.1 $\pm$ 43.8	6.57 – 155.9
V _{107%} (%)	39.4 $\pm$ 14.6	9.8–62.4	0.7 $\pm$ 2.3	0.0 – 9.0
V _{95%} (%)	99.5 $\pm$ 0.7	97.9–100.0	100.0 $\pm$ 0.0	99.9 – 100.0
D _{mean} /D _p (%)	106.7 $\pm$ 1.7	103.5–110.0	102.6 $\pm$ 0.7	101.4 – 104.2
D _{max} /D _p (%)	126.1 $\pm$ 3.3	122.1–132.4	106.9 $\pm$ 1.5	105.0 – 110.2
D _{min} /D _p (%)	80.7 $\pm$ 7.9	66.9–95.8	96.9 $\pm$ 1.9	93.7 – 100.6
CI	0.99 $\pm$ 0.01	0.95 – 1.00	0.98 $\pm$ 0.02	0.95 – 1.00
HI (%)	17.5 $\pm$ 2.1	13.7–19.6	5.7 $\pm$ 1.4	4.0 – 9.4
Homogeneity Index (HI) = (D _{2%} - D _{98%}) / D _p * 100%				

Table 2a: Original Planning Dosimetry

	Whole breast PTV		Lumpectomy PTV	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Dose	49.5 $\pm$ 2.2	41.4 – 50.4	58.9 $\pm$ 2.6	49.0 – 61.6
Volume (cc)	709.1 $\pm$ 389.5	276.3 – 1680.02	35.4 $\pm$ 18.5	17.4 – 91.3
V _{107%} (%)	20.4 $\pm$ 11.9	5.2 – 51.7	0.2 $\pm$ 0.8	0.0 – 3.4
V _{95%} (%)	97.9 $\pm$ 1.8	94.0 – 99.9	99.6 $\pm$ 0.9	96.3 – 100.0
D _{mean} /D _p (%)	104.3 $\pm$ 1.4	102.1 – 108.0	101.7 $\pm$ 1.2	98.4 – 104.1
D _{max} /D _p (%)	125.3 $\pm$ 2.8	121.2 – 130.7	105.4 $\pm$ 1.8	101.0 – 108.8
D _{min} /D _p (%)	51.8 $\pm$ 14.5	28.6 – 77.7	91.9 $\pm$ 5.0	78.0 – 97.4
CI	0.99 $\pm$ 0.01	0.95 – 1.00	1.00 $\pm$ 0.01	0.96 – 1.00
HI (%)	28.4 $\pm$ 9.7	14.6 – 56.2	6.1 $\pm$ 2.1	3.0 – 12.3
Homogeneity Index (HI) = (D _{2%} - D _{98%}) / D _p * 100%				

Table 2b: Modified Planning Dosimetry

Table 3:

Dose to organs at risk using the original (A) and modified (B) planning methods

	All Patients		Right-sided (n=7)		Left-sided (n=9)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Treatment time (min)	7.5 $\pm$ 1.5	5.1–11.6	7.6 $\pm$ 0.8	6.7–9.2	7.5 $\pm$ 1.9	5.1–11.6
Heart						
D _{mean} (Gy)	10.5 $\pm$ 4.1	0.9–18.9	8.8 $\pm$ 4.0	0.9–12.4	11.7 $\pm$ 3.7	7.2–18.9
V _{30Gy} (%)	1.2 $\pm$ 2.5	0.0–9.7	0.4 $\pm$ 0.4	0.0–1.2	1.8 $\pm$ 3.2	0.0–9.7
V _{5Gy} (%)	82.1 $\pm$ 26.2	5.3–100.0	71.9 $\pm$ 33.4	5.3–99.6	90.1 $\pm$ 12.0	68.1–100.0
Ipsi-lateral lung						
D _{mean} (Gy)	11.8 $\pm$ 2.3	6.6–16.0	12.8 $\pm$ 1.2	11.4–15.3	11.0 $\pm$ 2.7	6.6–16.0
V _{20Gy} (%)	11.5 $\pm$ 4.9	0.1–19.4	14.0 $\pm$ 3.1	10.0–19.4	9.5 $\pm$ 5.3	0.1–17.0
V _{5Gy} (%)	85.0 $\pm$ 10.6	64.3–98.3	87.0 $\pm$ 6.9	74.1–98.3	83.4 $\pm$ 12.0	64.3–98.3
Contra-lateral lung						
D _{mean} (Gy)	5.6 $\pm$ 1.9	0.6–9.2	5.0 $\pm$ 2.1	0.6–6.6	6.0 $\pm$ 1.6	3.8–9.1
V _{20Gy} (%)	0.5 $\pm$ 1.0	0.0–3.7	0.2 $\pm$ 0.2	0.0–0.5	0.7 $\pm$ 1.3	0.0–3.7
V _{5Gy} (%)	54.2 $\pm$ 24.5	0.0–91.1	50.5 $\pm$ 24.7	0.0–69.4	57.1 $\pm$ 25.4	19.2–91.1
Total lungs						
D _{mean} (Gy)	8.7 $\pm$ 1.5	6.0–10.9	9.3 $\pm$ 1.1	7.3–10.9	8.2 $\pm$ 1.7	5.9–10.6
V _{20Gy} (%)	6.0 $\pm$ 2.8	1.2–10.6	8.0 $\pm$ 1.5	5.7–10.6	4.4 $\pm$ 2.5	1.2–8.3
V _{5Gy} (%)	70.0 $\pm$ 15.6	41.9–92.7	70.6 $\pm$ 14.2	41.9–83.4	69.4 $\pm$ 17.2	46.2–92.7
Contra-lateral breast						
D _{mean} (Gy)	4.4 $\pm$ 1.0	2.4–6.0	4.6 $\pm$ 0.5	3.6–5.0	4.3 $\pm$ 1.2	2.4–6.0
D _{max} (Gy)	18.1 $\pm$ 5.7	9.7–29.6	20.4 $\pm$ 3.5	13.8–23.2	16.4 $\pm$ 5.6	9.7–27.7
V _{5Gy} (%)	28.8 $\pm$ 15.1	6.5–66.6	29.3 $\pm$ 5.9	15.2–32.6	28.3 $\pm$ 19.4	6.5–66.6
Spinal Cord						
D _{max} (Gy)	8.6 $\pm$ 2.9	2.0–13.3	9.0 $\pm$ 3.5	2.0–13.0	8.2 $\pm$ 2.5	4.6–13.3
Total body						
D _{mean} (Gy)	5.7 $\pm$ 1.2	3.6–8.0	5.6 $\pm$ 0.8	4.0–6.4	5.8 $\pm$ 1.6	3.6–8.0
V _{5Gy}	38.4 $\pm$ 13.1	20.5–66.7	41.5 $\pm$ 16.0	22.1–66.7	34.8 $\pm$ 8.5	20.5–42.3
V _{40Gy}	0.3 $\pm$ 0.4	0.0–1.2	0.1 $\pm$ 0.2	0.0–0.4	0.5 $\pm$ 0.5	0.0–1.2

Table 3a: Original Planning Method Normal Structures

	All Patients		Right-sided (n=7)		Left-sided (n=9)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Treatment time (min)	10.4 $\pm$ 1.3	8.6 – 12.4	11.3 $\pm$ 1.1	9.7 – 12.4	9.8 $\pm$ 1.0	8.6 – 11.3
Heart						
D _{mean} (Gy)	1.8 $\pm$ 1.1	0.6 – 4.0	1.1 $\pm$ 0.6	0.6 – 2.3	2.4 $\pm$ 1.1	1.1 – 4.0
V _{30Gy} (%)	0.1 $\pm$ 0.2	0.0 – 0.7	0.0 $\pm$ 0.0	0.0 – 0.0	0.2 $\pm$ 0.3	0.0 – 0.7
V _{5Gy} (%)	6.2 $\pm$ 8.4	0.0 – 30.1	1.7 $\pm$ 3.9	0.0 – 10.6	9.7 $\pm$ 9.4	1.1 – 30.1
Ipsi-lateral lung						

	All Patients		Right-sided (n=7)		Left-sided (n=9)	
D_{mean} (Gy)	5.0 ± 1.6	0.6 – 7.2	5.1 ± 1.5	2.7 – 7.0	4.8 ± 1.8	0.6 – 7.2
$V_{20\text{Gy}}$ (%)	8.4 ± 3.4	1.6 – 13.7	8.1 ± 3.9	1.9 – 12.6	8.6 ± 3.2	1.6 – 13.7
$V_{5\text{Gy}}$ (%)	20.6 ± 4.1	11.0 – 28.5	20.9 ± 5.7	11.0 – 28.5	20.4 ± 2.5	16.2 – 23.8
Contra-lateral lung						
D_{mean} (Gy)	0.5 ± 0.2	0.2 – 0.9	0.5 ± 0.1	0.2 – 0.7	0.6 ± 0.2	0.4 – 0.9
$V_{20\text{Gy}}$ (%)	0.0 ± 0.0	0.0 – 0.0	0.0 ± 0.0	0.0 – 0.0	0.0 ± 0.0	0.0 – 0.0
$V_{5\text{Gy}}$ (%)	0.0 ± 0.0	0.0 – 0.0	0.0 ± 0.0	0.0 – 0.0	0.0 ± 0.0	0.0 – 0.0
Total lungs						
D_{mean} (Gy)	2.9 ± 0.7	1.6 – 4.0	3.0 ± 0.9	1.6 – 4.0	2.7 ± 0.4	2.1 – 3.5
$V_{20\text{Gy}}$ (%)	4.2 ± 1.8	0.7 – 7	4.5 ± 2.1	1.0 – 7.0	3.9 ± 1.5	0.7 – 6.1
$V_{5\text{Gy}}$ (%)	10.3 ± 2.6	5.6 – 15.3	11.5 ± 3.3	5.6 – 15.3	9.3 ± 1.4	6.6 – 10.9
Contra-lateral breast						
D_{mean} (Gy)	5.3 ± 1.7	1.9 – 8.5	5.2 ± 1.8	2.5 – 7.9	5.4 ± 1.8	1.9 – 8.5
D_{max} (Gy)	28.1 ± 10.4	13.1 – 48.5	33.2 ± 12.6	15.0 – 48.5	24.1 ± 6.7	13.1 – 36.8
$V_{5\text{Gy}}$ (%)	38.4 ± 14.6	6.0 – 63.3	32.8 ± 9.8	15.5 – 45.9	42.7 ± 16.7	6.0 – 63.3
Spinal Cord						
D_{max} (Gy)	1.2 ± 1.5	0.3 – 6.5	0.7 ± 0.6	0.3 – 2.1	1.5 ± 1.9	0.3 – 6.5
Total body						
D_{mean} (Gy)	5.2 ± 1.4	3.4 – 8.1	5.0 ± 1.0	3.4 – 6.1	5.3 ± 1.7	3.4 – 8.1
$V_{5\text{Gy}}$	16.6 ± 4.9	10.7 – 26.7	15.9 ± 3.4	10.7 – 20.5	17.1 ± 5.9	10.7 – 26.7
$V_{40\text{Gy}}$	5.4 ± 1.4	3.1 – 8.0	5.3 ± 1.1	3.9 – 6.4	5.5 ± 1.7	3.1 – 8.0
Table 3b: Modified Planning Method Normal Structures						