

Dosimetric comparison of 3-dimensional conformal and intensity-modulated radiotherapy techniques for whole breast irradiation in the prone and supine positions

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ABSTRACT

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Background: The aim of this study was to compare the differences of the dosimetric parameters between three-dimensional conformal radiotherapy (3D-CRT) and simultaneous-integrated boost intensity-modulated radiotherapy (SIB-IMRT) techniques in the prone and supine positions for breast irradiation. **Materials and Methods:** Ten patients underwent a computed tomography simulation in both the prone and supine positions. For each set-up position, the treatment plans were created with 3D-CRT and SIB-IMRT. The dosimetric parameters were obtained from dose-volume histograms. **Results:** High-dose regions in the whole breast were decreased in IMRT with a simultaneous integrated boost technique. The lung doses were significantly reduced for all patients, and the heart doses were lower in left-sided breast cancer patients in the prone position. The heart doses except mean dose were not significantly lower with SIB-IMRT in the prone position. **Conclusion:** SIB-IMRT allowed a more conformal dose distribution regardless of position. The prone position is superior to the supine treatment regarding doses in the ipsilateral, contralateral lung, and heart. The contralateral breast doses were increased in the prone position. Prone IMRT can be chosen for simultaneous integrated boost treatment in women with pendulous breasts.

Keywords: Breast cancer, prone, supine, IMRT, 3D conformal radiotherapy.

INTRODUCTION

The breast cancer incidence has increased in females worldwide and constituted 25% of the overall cancer cases and 15% of the overall cancer deaths among women in 2012 ⁽¹⁾. Radiotherapy after breast-conserving surgery is an essential component of treatment. Several studies have shown that the survival rate does not change between women with breast cancer who were treated with a total mastectomy and postoperative breast irradiation after lumpectomy. On the other hand, irradiation of

the breast after surgery significantly reduces the incidence of recurrence in the breast ⁽²⁾. In addition, boost treatment-10 Gy delivered to the tumor bed following whole breast irradiation-can improve early local control ⁽³⁾. In addition to these favorable treatment outcomes, cardiac and pulmonary complications may develop due to the large irradiated volume in the heart and ipsilateral lung, and poor dose homogeneity may lead to worse cosmetic results in patients with pendulous breasts ⁽⁴⁾. Therefore, doses to organs-at-risk (OARs) should be minimized as much as possible while obtaining a

homogeneous dose distribution in the breast.

The three-dimensional conformal radiotherapy (3D-CRT) technique was used as the standard care of irradiation of the breast until 2000. It was frequently performed using two opposing tangential fields. Wedges have been used to compensate for tissue irregularities in which high doses occur. However, high-dose regions located within the target or normal tissues have become unavoidable in women with large breasts ⁽⁵⁾. Various radiotherapy techniques have been developed to obtain better dose distributions in the target and decreasing doses in healthy tissues. The intensity modulated radiotherapy (IMRT) technique has been applied to breast treatment. The optimization algorithm is used to create nonuniform fluence maps that are delivered to the patient from several beamlets in inverse IMRT planning ⁽⁶⁾. Many studies have indicated that the IMRT technique, compared with the 3D-CRT technique, has advantages in terms of dose reduction in OAR and for improving dose homogeneity ^(7,8).

Generally, breast cancer patients receive radiotherapy in the supine position. In the supine position, sparing of the OAR cannot be achieved in concavely shaped pendulous breasts because the irradiated breast is wrapped around the heart and ipsilateral lung. In addition, high-dose regions in the breast lead to late effects, such as fibrosis and telangiectasias. In the prone position, the breast tissue moves away from the chest wall by gravity, diminishing the amount of the heart and lung in the treatment fields. In addition to this benefit, several studies have shown that more homogeneous dose distributions were obtained in the prone position than in the supine position. Prone position breast irradiation has been preferred to reduce doses to the critical structures and prevent high-dose regions in large-breasted women ⁽⁹⁾. There are few trials comparing the 3D-CRT and IMRT techniques in both the prone and supine positions for whole breast irradiation (WBI) without a tumor bed boost. Investigations concerning which patient positioning and treatment technique is better for whole breast irradiation with tumor bed boost

are lacking. We believe that IMRT with a simultaneous integrated boost (SIB-IMRT) technique in the prone position may result in better dose homogeneity and lowering of the doses to the ipsilateral lung and heart. The purpose of this study was to compare the 3D-CRT WBI plus 3D-CRT boost with the SIB-IMRT techniques in terms of dose homogeneity in the target and OAR doses in both the supine and prone set-up positions in women with large and pendulous breasts.

MATERIALS AND METHODS

Ten breast cancer patients (6 left-sided, 4 right-sided) who received radiotherapy after lumpectomy at the Istanbul University Oncology Institute were randomly selected for this study. All patients were treated in the appropriate set-up position using 3D-CRT or IMRT without lymph node irradiation. At the start of the simulation, all patients were informed about the study, and informed consent was obtained.

Patient positioning and CT simulation

Computed tomography (CT) images were obtained with a slice thickness of 3 mm using Phillips Brilliance Big Bore 4D CT (Philips Electronics N.V.) in both the supine and prone positions on the same day for all patients. In the supine position, a patient-specific vacuum air cushion was prepared for immobilization for each patient, and the ipsilateral arm was raised above the head. After supine simulation, patients were repositioned on the MedTec prone breast board. In this set-up position, both arms were placed above the head, and the contralateral breast was laterally turned away from the treated breast on the device. The CT data of ten patients were transferred to the treatment planning system (TPS) for both contouring and planning.

Target and OAR delineation

The target volumes and critical structures were delineated on the CT data by the same radiation oncologist using Varian Eclipse

Version 8.9 TPS. The whole breast tissue was outlined as the planning target volume (PTVbreast). The tumor bed volume was also defined according to the metal surgical clips and clinical details. This volume was enlarged by adding an isotropic 10-mm margin to obtain the

planning target volume (PTVboost). This margin was added for uncertainty in the patient set-up. The ipsilateral lung, heart, contralateral lung and breast were also contoured. In addition, a PTVbreast-boost was generated by excluding the tumor volume from the PTVbreast.

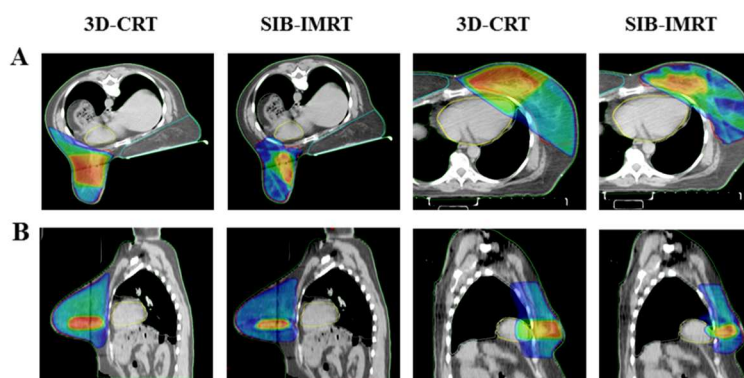


Figure 1. Dose distributions (45 Gy) in the transverse plan (A) and sagittal plan (B) for the prone and supine positions. The heart in yellow, the PTVbreast in red, the PTVboost in pink, the ipsilateral lung in light green, the contralateral lung in dark green, the contralateral breast in cyan.

Treatment planning

All of the treatment plans were performed by the same medical physicist on Varian Eclipse Version 8.9 TPS. The Anisotropic Analytical Algorithm (AAA) photon dose calculation algorithm with tissue inhomogeneity correction was used for the 3D-CRT and SIB-IMRT plans. The dose calculation grid size was 2.5 mm. Next, 6-MV photon beams from Varian Clinac DBX 600 (Varian Medical System, Palo Alto, CA) equipped with a Millennium Multileaf Collimator (MLC) with 120 leaves were used for all of the plans. All of the plans were normalized so that 90% of the PTVbreast received 95% of the prescribed dose and 95% of the PTVboost received 100% of the prescribed dose. The dose-volume constraints

for the OAR are listed in table 1.

3D-CRT plans were created using two parallel opposing tangential beams (medial and lateral tangents) with a 2-cm anterior fall off for the PTVbreast. Appropriate tangential beam angles were used to avoid contralateral breast irradiation and reduce the doses to the OAR. The treatment field aperture was designed using the beam’s eye view (BEV) option of the TPS. Next, the beams were manually shaped considering the beam penumbra with an MLC for blocking normal structures within fields on BEV whilst maintaining satisfactory coverage of the PTVbreast. Virtual wedges were used when needed to reduce the maximum doses and achieve better dose distribution in the target.

Table 1. Dose-volume constraints for the OAR.

OAR	Dose-Volume Constraint	
Ipsilateral Lung	V20<20%	
	V10<40%	
Contralateral Lung	V5<15%	
Contralateral Breast	Dmax<10 Gy	
Heart	Left-Sided	Right-Sided
	V25<5%	V25=0
	V10<35%	V10<15%

OAR: organ at risk, Dmax: maximum dose, Vx: volume (%) receiving x dose

The prescribed dose to the PTVbreast was 50 Gy in 25 fractions. After planning for the whole breast, tumor bed boost plans were conducted using two oblique fields. The boost dose was 12 Gy in 6 fractions.

SIB-IMRT plans were generated using an inverse planning process. Seven beams for the supine position and six beams for the prone position were used to obtain the desired dose distribution. First, the same tangential beam angles as the 3D-CRT were used and then the other beams (five beams for the supine and four beams for the prone position) were placed between these fields at equal intervals. The dose constraints of the PTVbreast-boost, PTVboost and critical organs were described to the optimization engine of TPS to acquire optimal fluence maps. The prescribed dose to the PTVbreast-boost was 50 Gy and the PTVboost was 59.92 Gy in 28 fractions. Following fluence-map optimization, the leaf motion calculation with a sliding-window technique was carried out to create actual fluence maps that were deliverable using an MLC. The optimization was performed until the planning goals were satisfied. At last, a 2-cm anterior fall off was fulfilled to the fields using the skin flash tool.

Analysis

The treatment plans were compared in terms of dose conformity, homogeneity, target coverage, and OAR doses by analyzing the dose-volume histograms (DVH) for both set-up positions. The volume of the PTVbreast receiving 95% of the prescription dose (V95) and the PTVboost receiving 100% of the prescription dose (V100) were compared for target coverage. The mean dose and dose received by 2% volume (D2) of the PTVbreast and PTVboost were also compared. In this study, the conformity index (CI) and homogeneity index (HI) were determined for the PTVbreast and PTVboost utilizing the DVH of the 3D-CRT WBI + 3D-CRT boost and SIB-IMRT plans. The conformity index was calculated using the following equation (1):

$$CI = (VT_{ref}/VT) \times (VT_{ref}/V_{ref}) \quad \text{eq (1)}$$

Where: VT_{ref} represents the target volume covered by the reference isodose (95% of the prescribed dose), VT is the target volume, V_{ref} is the total volume of the reference isodose. The ideal value of CI is 1. The following formula (eq 2) was used for the homogeneity index.

$$HI = D5/D95 \quad \text{eq (2)}$$

In this formula, D5 and D95 represent the doses received by 5% and 95% volumes of the PTVbreast and PTVboost, respectively. The ideal value of HI is 1.

The percentage of the PTVbreast-boost receiving 105% and 110% of the prescribed 50 Gy ($V_{105\%}$, $V_{110\%}$) to the PTVbreast, the ipsilateral lung receiving a dose equal to or more than 5 Gy, 10 Gy, and 20 Gy (V_5 , V_{10} , and V_{20}), the heart receiving a dose equal to or more than 5 Gy, 10 Gy, and 30 Gy (V_5 , V_{10} , and V_{30}), the contralateral lung receiving a dose equal to or more than 5 Gy (V_5), and the contralateral breast receiving a dose equal to or more than 5 Gy (V_5) were compared. The ipsilateral lung, contralateral lung, heart, and contralateral breast mean doses (D_{mean}) were also evaluated. The D2 of the contralateral breast was also collected.

The Statistical Package for Social Sciences (SPSS) version 11.0 was used for statistical analyses. The dosimetric parameters obtained from DVH were compared using a non-parametric Wilcoxon test because the sample number of this study is small. For statistical analysis, a p value less than 0.05 was considered to be statistically significant.

RESULTS

Forty treatment plans were generated using the CT data of ten patients obtained in the supine and prone positions. The 3D-CRT and SIB-IMRT techniques were applied for each CT data set. The dose distributions and dose-volume histograms for one patient are shown in figures 2, 3, and 4.

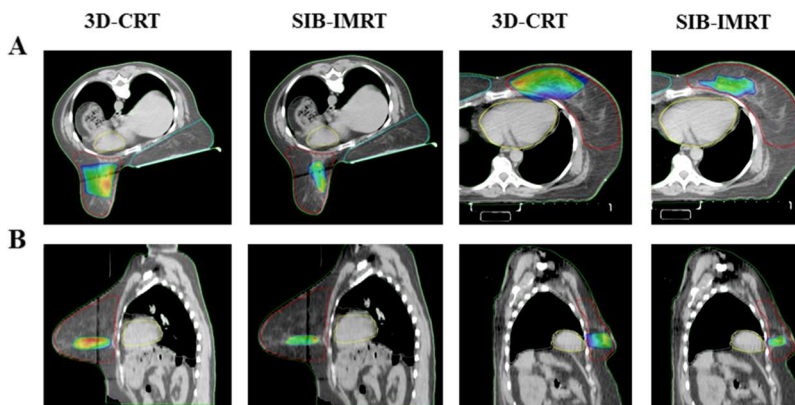


Figure 2. Dose distributions (60 Gy) in the transverse plan (A) and sagittal plan (B) for the prone and supine positions. The heart in yellow, the PTVbreast in red, the PTVboost in pink, the ipsilateral lung in light green, the contralateral lung in dark green, the contralateral breast in cyan.

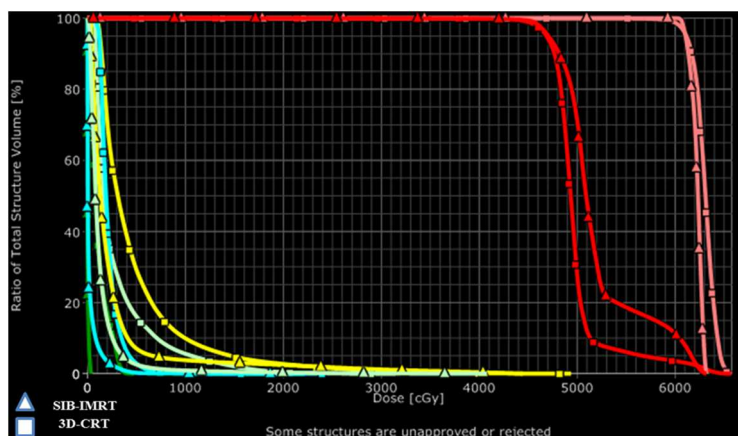


Figure 3. DVHs for the prone position. The heart in yellow, the PTVbreast in red, the PTVboost in pink, the ipsilateral lung in light green, the contralateral lung in dark green, the contralateral breast in cyan.

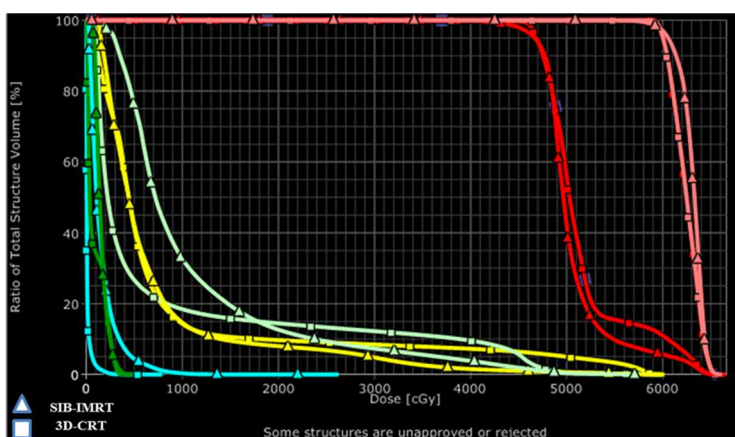


Figure 4. DVHs for the supine position. The heart in yellow, the PTVbreast in red, the PTVboost in pink, the ipsilateral lung in light green, the contralateral lung in dark green, the contralateral breast in cyan.

Dose Parameters for the Target

The mean volume of the PTVbreast and

PTVboost are 1070.0 (range 617.9-1344.1 cc) and 39.6 (range 10.8-91.4 cc) cc in supine

position, respectively. The CI, HI, target coverage, Dmean and D2 for the PTVbreast and PTVboost and the percent of volume of the

high-dose regions in PTVbreast-boost are summarized in table 2.

Table 2. Dose parameters for the PTVbreast and PTVboost

n=10	Supine	Prone		Supine	Prone		Prone	Supine
	3D-CRT	3D-CRT		SIB-IMRT	SIB-IMRT		3D-CRT vs SIB-IMRT	3D-CRT vs SIB-IMRT
	Mean±SD	Mean±SD	p*	Mean±SD	Mean±SD	p*	p*	p*
PTVbreast								
CI	0.59±0.08	0.74±0.08	0.007	0.81±0.03	0.86±0.03	0.009	0.005	0.005
HI	1.31±0.02	1.32±0.02	0.210	1.23±0.07	1.23±0.76	0.812	0.008	0.012
V95%(%)	90.72±2.51	92.77±1.46	0.074	91.59±2.95	92.10±1.18	0.799	0.314	0.285
Dmean (cGy)	5206.25±98.61	5233.79±76.44	0.333	5047.41±74.44	5051.91±52.17	0.959	0.005	0.007
D2(cGy)	6258.14±112.65	6282.10±107.60	0.285	6169.23±174.02	6142.62±225.53	0.445	0.022	0.203
PTVboost								
CI	0.28±0.08	0.19±0.05	0.022	0.79±0.10	0.68±0.08	0.041	0.005	0.005
HI	1.05±0.02	1.05±0.02	0.888	1.06±0.01	1.06±0.01	0.608	0.147	0.150
V100%(%)	95.99±2.87	97.45±2.26	0.051	96.99±1.19	97.02±1.14	0.799	0.169	0.314
Dmean (cGy)	6167.25±76.82	6201.02±78.59	0.333	6246.87±46.65	6256.25±44.85	0.575	0.037	0.047
D2(cGy)	6347.81±45.23	6353.82±106.81	0.959	6415.29±73.45	6401.83±65.76	0.575	0.051	0.139
PTVbreast-boost								
V105% (%)	27.88±8.76	29.29±7.31	0.712	9.07±5.12	6.60±4.54	0.203	0.005	0.005
V110% (%)	17.29±7.39	18.44±7.52	0.508	1.90±1.45	2.57±2.11	0.445	0.005	0.005

SD: standard deviation, CI: conformity index, HI: homogeneity index, Dmean: mean dose, D2: dose received by 2% volume of the PTV, PTV: planning target volume, 3D-CRT: three-dimensional conformal radiotherapy, SIB-IMRT: simultaneous-integrated boost intensity-modulated radiotherapy, V95%: percentage of the PTVbreast volume receiving 4750 cGy, V100%: percentage of the PTVboost volume receiving 6000 cGy, V105%, 110%: percentage of the PTVbreast-boost volume receiving 5250cGy, 5500 cGy, * Significance tested using non-parametric Wilcoxon test.

The CI of the PTVbreast was significantly better in the prone position for both treatment techniques (p=0.007 for 3D-CRT, p=0.009 for SIB-IMRT). Compared with 3D-CRT, the SIB-IMRT plans significantly improved the CI of the PTVbreast in the same position. (p=0.005 for both positions). The HI of the PTVbreast was not significant difference between supine and prone position for both treatment techniques (p=0.210 for 3D-CRT, p=0.812 for SIB-IMRT). However, the HI of the PTVbreast was significantly better with SIB-IMRT plans in the same position (p=0.008 for the prone position, p=0.012 for the supine position). The results show no significant difference in terms of V95 between supine and prone position for both treatment techniques (p=0.074 for 3D-CRT, p=0.779 for SIB-IMRT). There was also no significant difference in the V95 between 3D-CRT and SIB-IMRT in the same position (p=0.314 for the prone position, p=0.285 for the supine position). The Dmean

and D2 to the PTVbreast were not significantly different between the two positions for both 3D-CRT and SIB-IMRT. Compared with 3D-CRT, the SIB-IMRT reduced the Dmean to the PTVbreast in the same position (p=0.005 for the prone position, p=0.007 for the supine position). The D2 to the PTVbreast was significantly lower with SIB-IMRT in the prone position (p=0.022).

The CI of the PTVboost was significantly better in the supine position for both treatment techniques (p=0.022 for 3D-CRT, p=0.041 for SIB-IMRT). Compared with 3D-CRT, the SIB-IMRT plans significantly improved the CI of the PTVboost in the same position. (p=0.005 for both positions). The HI of the PTVboost was not significant difference between both set-up positions and treatment techniques (p=0.888 for 3D-CRT, p=0.608 for SIB-IMRT; p=0.147 for the prone position, p=0.150 for the supine position). The results show no significant difference in terms of V100 between both set-up positions

and treatment techniques ($p > 0.05$). The Dmean to the PTVboost were not significantly different between the two positions for both 3D-CRT and SIB-IMRT ($p > 0.005$). Compared with 3D-CRT, the SIB-IMRT increased the Dmean to the PTVboost in the same position ($p = 0.037$ for the prone position, $p = 0.047$ for the supine position). The D2 to the PTVboost was not significant difference between both set-up positions and

treatment techniques ($p > 0.05$).

In addition, SIB-IMRT reduced the percentage of the high-dose regions in the PTVbreast-boost in both positions.

Doses to OARs

The ipsilateral lung, contralateral lung, contralateral breast and heart mean doses are shown in Table 3 and 4.

Table 3. Dose parameters for the ipsilateral lung, contralateral lung and contralateral breast.

n=10	Supine	Prone	p*	Supine	Prone	p*	Prone	Supine
	3D-CRT	3D-CRT		SIB-IMRT	SIB-IMRT		3D-CRT vs SIB-IMRT	3D-CRT vs SIB-IMRT
	Mean±SD	Mean±SD		Mean±SD	Mean±SD		p*	p*
Ipsilateral Lung								
Mean dose (cGy)	925.39±169.14	119.56±90.60	0.005	1070.82±98.51	343.77±108.75	0.005	0.007	0.022
V20(%)	15.78±3.60	0.83±1.64	0.005	13.48±2.83	2.11±1.87	0.005	0.047	0.028
V10(%)	20.01±4.02	1.43±2.23	0.005	30.84±4.12	8.09±3.74	0.005	0.007	0.005
V5(%)	29.57±6.62	2.71±3.17	0.005	72.15±9.93	19.30±6.40	0.005	0.005	0.005
Contralateral Lung								
Mean dose (cGy)	18.86±27.33	4.23±2.27	0.005	189.15±53.05	130.01±59.55	0.037	0.005	0.005
V5(%)	0	0	1.000	2.44±4.08	3.83±4.21	0.374	0.012	0.012
Contralateral Breast								
Mean dose (cGy)	7.70±5.44	23.40±11.33	0.005	152.17±45.42	175.04±52.24	0.241	0.005	0.005
D2(cGy)	64.28±35.60	154.46±79.84	0.005	495.02±128.36	503.83±208.33	0.721	0.007	0.005
V5(%)	0.01±0.03	0.18±0.47	0.109	2.51±2.17	2.70±2.97	0.575	0.008	0.008

SD: standard deviation, Vx: volume (%) receiving x dose, D2: dose received by 2% volume of the contralateral breast, 3D-CRT: three-dimensional conformal radiotherapy, SIB-IMRT: simultaneous-integrated boost intensity-modulated radiotherapy, * Significance tested using non-parametric Wilcoxon test.

Table 4. Dose parameters for the heart.

n =6(L) n=4(R)	Supine	Prone	p*	Supine	Prone	Prone		Supine
	3D-CRT	3D-CRT		SIB-IMRT	SIB-IMRT	3D-CRT vs SIB-IMRT	3D-CRT vs SIB-IMRT	
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	p*	p*	p*
LBI								
Mean dose (cGy)	412.87±241.54	208.25±80.61	0.028	542.63±92.13	401.05±71.62	0.028	0.028	0.116
V30(%)	3.77±2.70	0.58±0.69	0.028	1.02±1.81	0.38±0.36	0.752	0.416	0.028
V10(%)	6.77±4.38	2.58±2.53	0.027	6.60±3.86	4.97±2.63	0.173	0.116	0.686
V5(%)	14.10±13.72	5.33±3.50	0.027	38.80±4.84	24.67±8.43	0.046	0.028	0.028
RBI								
Mean dose (cGy)	56.58±16.74	47.05±9.63	0.144	278.80±45.69	228.80±47.36	0.273	0.068	0.068
V30(%)	0	0	1.000	0	0	1.000	1.000	1.000
V10(%)	0	0	1.000	0.05±0.10	0.03±0.05	0.655	0.317	0.317
V5(%)	0	0	1.000	7.68±3.30	7.30±3.58	1.000	0.066	0.068

L: left, R: right, LBI: left breast irradiation, RBI: right breast irradiation, SD: standard deviation, Vx: volume (%) receiving x dose, 3D-CRT: three-dimensional conformal radiotherapy, SIB-IMRT: simultaneous-integrated boost intensity-modulated radiotherapy, * Significance tested using non-parametric Wilcoxon test.

The ipsilateral lung mean dose, V20, V10 and V5 were significantly lower for the prone position ($p=0.005$). For both set-up positions, 3D-CRT, compared with SIB-IMRT, reduced the ipsilateral lung mean dose, V10 and V5 ($p<0.05$). Ipsilateral lung V20 was also significantly lower with 3D-CRT in the prone position ($p=0.047$). However, ipsilateral lung V20 was significantly lower with SIB-IMRT in the supine position ($p=0.028$). The mean dose of the contralateral lung diminished in the prone position ($p=0.005$ for 3D-CRT, $p=0.037$ for SIB-IMRT), but SIB-IMRT increased the contralateral lung mean doses ($p=0.005$ for both set-up positions).

The mean dose and D2 of the contralateral breast were greater in the prone position than in the supine position for 3D-CRT ($p=0.005$), but they were similar to SIB-IMRT for both set-up positions ($p=0.241$ for the mean dose, $p=0.721$ for the D2). The results show no significant difference in terms of V5 of the contralateral breast between supine and prone position for both treatment techniques ($p>0.05$ for all). Compared with 3D-CRT, SIB-IMRT increased the contralateral breast mean dose, D2, V5 in both set-up positions ($p<0.005$).

The mean dose, V30, V10, and V5 of the heart were found significantly to be lower in the prone position for left breast irradiation (LBI) with 3D-CRT ($p<0.05$). In the prone position, compared with the supine position, the heart V30 and V10 did not differ with SIB-IMRT for LBI ($p>0.005$). However, the heart mean dose and V5 were found significantly to be lower in the prone position with SIB-IMRT for LBI. There were no significant difference in terms of V30 and V10 of the heart between 3D-CRT and SIB-IMRT in the prone position for LBI. Compared with 3D-CRT, SIB-IMRT increased the mean dose and V5 of the heart in the prone position for LBI ($p=0.028$). The heart mean dose and V10 were not statistically significant between 3D-CRT and SIB-IMRT in the supine position for LBI. The heart V30 was lower and V5 was higher with SIB-IMRT in the supine position for LBI ($p<0.05$). None of the dose parameters of the heart significantly changed with either technique or position for right breast irradiation (RBI), but the heart doses increased

with SIB-IMRT for RBI.

DISCUSSION

Various treatment options have been developed, resulting in better sparing of the critical structures, particularly the ipsilateral lung and heart, for whole breast irradiation. IMRT is one of the options that can reduce the high-dose areas within the heart and lung. However, the mean dose and volume of the low-dose of healthy organs can increase because of the sophisticated multifield arrangement^(5,10). Darby *et al.*⁽¹¹⁾ reported that the incidence frequency of the perfusion deficits and microvascular disease are related to the volume of the heart in the radiation field. Irradiation of the breast in the prone set-up position is an alternative option to reduce the volume of healthy organs in the field. In this study, we investigated which treatment position and technique was better for the critical structure doses and homogeneity of the target including additional boost treatment.

In our study, the target coverage (V95 for the PTVbreast and V100 for the PTVboost) was similar in the four plans. Our study showed that SIB-IMRT provided more conformal dose distributions than 3D-CRT in both positions. In addition, the results show that more conformal dose distributions for the PTVbreast obtained in the prone position. D2 of the PTVbreast was reduced with the SIB-IMRT technique in the prone position. Mulliez *et al.*⁽¹²⁾ compared wedged tangential fields (W-TF), tangential field intensity-modulated radiotherapy (TF-IMRT) and multi-beam IMRT (MB-IMRT) in the prone and supine positions for 18 breast cancer patients. They reported that D2 was lowered with MB-IMRT in the prone position. Yavas *et al.*⁽¹³⁾ compared field-in-field technique (FIF) with conformal tangential field radiotherapy for whole breast irradiation and indicated that the maximum dose of the PTV was significantly lower in the FIF technique. High-dose regions in the target led to worse cosmetic results⁽¹⁴⁾. The percentages of the high-dose areas in the PTVbreast-boost (V105 and V110) were

significantly lower for SIB-IMRT than for 3D-CRT in both positions. Goodman *et al.* ⁽¹⁵⁾ applied the 3D-CRT and IMRT planning techniques for 20 patients in the prone position, and the dosimetric outcomes showed that IMRT improved the dose homogeneity in women with larger, pendulous breasts.

The doses to the ipsilateral lung were found to be significantly lower in the prone position with the 3D-CRT or SIB-MRT techniques. Chen *et al.* ⁽¹⁶⁾ generated four plans using forward intensity-modulated radiotherapy (fIMRT) and conventional wedged tangents for each of the 21 patients in the supine and prone positions. Their results showed that the mean dose and V20 of the ipsilateral lung were diminished in the prone fIMRT and conventional wedged tangents plans. Another study demonstrated that V20 of the lung was dramatically lower in the prone position ⁽¹⁷⁾. The mean dose, V10 and V5 were greater in SIB-IMRT than in 3D-CRT for the supine position. V20 of ipsilateral lung was lower with SIB-IMRT in the supine position. The mean dose, V20, V10 and V5 were greater in SIB-IMRT than in 3D-CRT for the prone position. It was not surprising that IMRT increased the volume of the low dose in the critical structures. The prone position is useful for sparing the lung doses; therefore, the risk of radiation-related toxicities in the lung may be minimized.

We found that the heart doses were lower in the prone position for left-sided breast irradiation with 3D-CRT. In the literature, there are different results concerning the dose of the heart in the prone position compared with the supine position. Buijsen *et al.* ⁽¹⁴⁾ reported that the V30 of the heart was $2.4 \pm 3.0\%$ for the prone position and $7.3 \pm 4.6\%$ for the supine position using tangential fields (without boost fields) in 7 left-sided breast patients, and the difference was not statistically significant. Krenqli *et al.* ⁽¹⁸⁾ showed that there are no differences between the prone and supine positions in terms of V20, V10, V5 and Dmean for the heart in 41 patients with left breast cancer. Varga *et al.* ⁽¹⁹⁾ found the mean dose of heart was 2.89 ± 0.19 Gy in the supine position and 2.18 ± 0.15 Gy in the prone position with 3D-CRT (significant difference)

and the V25 of the heart was significantly lower in the prone position. In addition, Lymberis *et al.* ⁽²⁰⁾ indicated that the mean heart dose was lower in 46 left-sided patients (the total patients: 53) in the prone position. Kirby *et al.* ⁽²¹⁾ also demonstrated that prone positioning reduced the heart doses in 19/30 whole breast irradiation cases. There are conflicting results concerning the heart doses among studies, possibly due to different set-up devices and patient anatomy. It is also known that the heart may move anteriorly by gravity in the prone set-up position.

The threshold dose is not known for radiation carcinogenesis, which is a stochastic process in the contralateral breast ⁽²²⁾. In our study, the contralateral breast doses were significantly higher in the prone position than in the supine position with 3D-CRT, but it was lower with 3D-CRT than with IMRT in the prone position. Mulliez *et al.* ⁽¹²⁾ reported that there was no significant difference in the contralateral breast doses between the set-up positions or irradiation techniques. A mean dose <1.5 Gy was achieved in all of the plans in their study. In our study, the contralateral breast mean dose was 23.40 ± 11.33 cGy for the prone position with 3D-CRT, and we satisfied this dose constraint. The contralateral breast doses, like other healthy tissues, should be reduced as much as possible. The literature suggested that skin dosimeters could be used for the determination of the contralateral breast dose during irradiation ⁽¹⁷⁾.

In conclusion, prone breast irradiation decreases lung doses for all patients regardless of the treatment technique. The prone position also allows for the reduction of heart doses in left-sided breast cancer with 3D-CRT compared with SIB-IMRT. The high-dose regions in the PTVbreast-boost were significantly smaller in SIB-IMRT compared with that in 3D-CRT whole breast irradiation+3D-CRT boost irradiation. Prone IMRT can be chosen for simultaneous integrated boost treatment in women with pendulous breasts.

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REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A (2015) Global cancer istatistics, 2012. *Ca Cancer J Clin*, **65**: 87-108.
2. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER *et al.* (2002) Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*, **347**: 1223-1241.
3. Romenstaing P, Lehingue Y, Carrie C, Coquard R, Montbarbon X, Ardiet JM, *et al.* (1997) Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. *J Clin Oncol*, **15**: 963-8.
4. Fernández-Lizarbe E, Montero A, Polo A, Hernanz R, Morís R, Formenti S, *et al.* (2013) Pilot study of feasibility and dosimetric comparison of prone versus supine breast radiotherapy. *Clin Transl Oncol*, **15**: 450-9.
5. Schubert LK, Gondi V, Sengbusch E, Westerly DC, Soisson ET, Paliwal BR, *et al.* (2011) Dosimetric comparison of left-sided whole breast irradiation with 3DCRT, forward-planned IMRT, inverse planned IMRT, helical tomotherapy, and topotherapy. *Radiother Oncol*, **100**: 241-6.
6. Khan FM (2010) *The Physics of radiation therapy*. Lippincott Williams & Wilkins, Philadelphia, USA.
7. White JR and Meyer JL (2011) Intensity modulated radiotherapy for breast cancer: advances in whole and partial breast treatment. *Front Radiat Ther Oncol*, **43**: 292-314.
8. Lin Y and Wang B (2015) Dosimetric absorption of intensity-modulated radiotherapy compared with conventional radiotherapy in breast-conserving surgery. *Oncol Lett*, **9**: 9-14.
9. Huppert N, Jozsef G, DeWyngaert K, Formenti SC (2011) The role of a prone setup in breast radiation therapy. *Front Oncol*, **1**: 1-8.
10. Taylor CW and Kirby AM (2015) Cardiac side-effects from breast cancer radiotherapy. *Clin Oncol*, **27**: 621-9.
11. Darby SC, Cutter DJ, Boerma M, Constine LS, Fajardo LF, Kodama K, *et al.* (2010) Radiation related heart disease: current knowledge and future prospects. *Int. J Radiat Oncol Biol Phys*, **76**: 656-65.
12. Mulliez T, Speleers B, Madani I, De Gerssem W, Veldeman L, De Neve W (2013) Whole breast radiotherapy in prone and supine position: is there a place for multi-beam IMRT? *Radiat Oncol*, **8**: 1-7.
13. Yavas G, Yavas C, Acar H (2012) Dosimetric comparison of whole breast radiotherapy using field in field and conformal radiotherapy techniques in early stage breast cancer. *Int. J Radiat Res*, **10**: 131-138.
14. Buijsen J, Jager JJ, Bovendeerd J, Voncken R, Borger JH, Boersma LJ, *et al* (2007) Prone breast irradiation for pendulous breasts. *Radiother Oncol*, **82**: 337-40.
15. Goodman KA, Hong L, Wagman R, Hunt MA, McCormick B (2004) Dosimetric analysis of a simplified intensity modulation technique for prone breast radiotherapy. *Int J Radiat Oncol Biol Phys*, **60**: 95-102.
16. Chen JL, Cheng JC, Kuo SH, Chan HM, Huang YS, Chen YH (2013) Prone breast forward intensity-modulated radiotherapy for Asian women with early left breast cancer: factors for cardiac sparing and clinical outcomes. *J Radiat Res*, **54**: 899-908.
17. Griem KL, Fetherston P, Kuznetsova M, Foster GS, Shott S, Chu J (2003) Three dimensional photon dosimetry: a comparison of treatment of the intact breast in the supine and prone position. *Int J Radiat Oncol Biol Phys*, **57**: 891-9.
18. Krengli M, Masini L, Caltavuturo T, Pisani C, Apicella G, Negri E, *et al.* (2013) Prone versus supine position for adjuvant breast radiotherapy: a prospective study in patients with pendulous breasts. *Radiat Oncol*, **8**: 1-232.
19. Varga Z, Cserhádi A, Ráosi F, Boda K, Gulyás G, Együd Z *et al.* (2014) Individualized positioning for maximum heart protection during breast irradiation. *Acta Oncol*, **53**: 58-64.
20. Lymberis SC, DeWyngaert JK, Parhar P, Chhabra AM, Fenton Kerimian M, Chang J, *et al.* (2012) Prospective assessment of optimal individual position (prone versus supine) for breast radiotherapy: volumetric and dosimetric correlations in 100 patients. *Int J Radiat Oncol Biol Phys*, **84**: 902-9.
21. Kirby AM, Evans PM, Donovan EM, Convery HM, Haviland JS, Yarnold JR (2010) Prone versus supine positioning for whole and partial-breast radiotherapy: a comparison of non-target tissue dosimetry. *Radiother Oncol*, **96**: 178-84.
22. Hall EJ and Giaccia AJ (2006) *Radiobiology for the Radiologist*. Lippincott Williams and Wilkins, Philadelphia, USA.