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Original Article

A new method to deliver breast and chest wall radiation in breast radiotherapy for lung and heart sparing

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Abstract: The aim of this study was to assess the efficacy of a modified irradiation technique in breast cancer patients for improving dose distribution to the target and minimizing lung and cardiac doses. Forty-two patients with breast cancer undergoing postoperative radiotherapy were included. Comparative dose planning of two techniques (WBB and CCB-TPM) was performed. Dose Volume Histogam was calculated for the PTV and organs at risk. The lung and heart received a lower dose with the CCB-TPM. The most common symptoms in the CCB-TPM group were pain and tenderness of the skin. The PTV dose coverage was comparable between the groups. CCB-TPM is well accepted and superior for left-sided breast cancer patients with respect to heart dosing and for both sides in terms of pulmonary dosing. This technique improves the dose distribution to the PTV without significantly increasing the dose to organs at risk.

Keywords: Breast cancer, radiotherapy, toxicity

Introduction

The management of primary breast cancer with conservative surgery and radiation therapy is widely recommended as an alternative to mastectomy [1-3]. The addition of locoregional radiotherapy has been proven to improve local control after breast-conserving surgery [4-6]. Radiation therapy modalities used in the primary management of breast cancer are divided into two types: those aimed to irradiate the breast/chest wall alone (local) and those aimed to irradiate the breast/chest wall as well as the regional lymph nodes (loco-regional). Both techniques have side effects on the underlying lung and heart. Radiation pneumonitis is of particular concern and occurs in up to 24% of patients even when advanced techniques are used [7-12]. Another limitation of radiotherapy is long-term cardiac toxicity, a risk that may be increased with the use of radiotherapy in combination with chemotherapy regimens including anthracyclines and taxanes [13-16]. These issues have led to an interest in techniques that optimize maximum locoregional control without increasing late cardiac toxicity.

In our institution, a standard technique is used for tangential breast irradiation [17]. Patients are positioned on a Wedged Breast-Board (WBB) for the purpose of obtaining a precisely matched plane between the tangential fields and the supraclavicular field when multiple field irradiations are used. In the development of an improved technique, we defined a number of key criteria in advance. First, the use of table movements, in order to match close fields, should be avoided to minimize patient movement. Second, the material used for positioning should be easy to set up during treatment, taking no more time than the conventional technique. Finally, the technique should not be restricted by patients' body habitus.

A thermoplastic porous membrane has been used effectively for decades for immobilization of patients undergoing radiotherapy for head and neck tumors [18]. Its use in the thorax and abdomen is also common [19, 20]. However, there has been concern about the increase in skin dose due to the build-up effect of the mask [21].

This study retrospectively compared the conventional use of WBB with CCB-TPM with respect to radiotherapy dosing to organs at risk.

Figure 1. The thermoplastic porous membrane used with the patient in the supine position.

Subjects and methods

Subjects

Consecutive breast cancer patients referred to the Radiotherapy Department of the Fourth Hospital Affiliated to Harbin Medical University for postoperative radiotherapy from September 1, 2013 to December 31, 2013 were included in the study. All patients had undergone breast-conserving surgery. Radiotherapy was started within 6 weeks after surgery. The eligibility criteria included: age >30 years, stage T1N0M0 or stage Tis, and negative surgical margins (≥2 mm). Ethical approval was provided by the Medical Research Ethics Committee of Harbin Medical University.

Devices

A modified radiotherapy immobilization device called a commercial carbonic board fixed by a thermoplastic porous membrane (CCB-TPM) was developed (Xin Hua Factory, Shan Dong Province, China). The cost of this device is about 200 US Dollars. The process of making the CCB-TPM requires two staff members and approximately 30 minutes of time. For the patients treated with WBB, sagittal and transverse alignment marks were made on the skin of the patient, while for the patients treated with CCB-TPM, sagittal and transverse alignment marks were made on the skin and the membrane.

Patient positioning and definition of target volume

Patients treated with WBB were scanned in the conventional treatment position using the WBB. In dose-planning computed tomography (CT), patients lay supine on the WBB and both arms were abducted. The reference points were marked by radiopaque markers in order to serve as registration marks for CT data acquisition (**Figure 1**). Three-millimeter-thick CT scans were obtained with an Aquilion One Vision Low-Dose CT (LDCT) (Toshiba Medical Systems, Tokyo, Japan). Multi-detector-row scanners were used to acquire LDCT scans. The imaging parameters were 120 kVp, ≤50 mAs and ≤2.5 mm in transverse image-reformation thickness. CT scanning was performed from the cranial side of the crico-thyroid membrane to 10 cm caudal from the submammary fold, covering the whole assumed planning target volume (PTV) area and the whole lung volume. The reference slice (origo in CT imaging, z=0) was set up in node-negative cases at the level of the mamilla and in node-positive cases 5 cm caudal to the jugulum. In our treatment planning process volumes were defined according to the ICRU Report 50 [22].

PTV delineation was carried out using the ECLAPSE® radiotherapy planning system (Varian Associates Inc.). We chose the dose levels of 20, 30, 40, and 50 Gy, because 20 and 30 Gy are thought to produce irreversible damage to pulmonary parenchyma [23] and 40 Gy is probably a critical dose in the development of decreased cardiac function up to 15 years after radiotherapy [24]. Fifty Gy is a generally applied dose to the target volume in adjuvant radiotherapy for breast cancer.

The indices for dosimetric analysis were extracted from dose-volume histograms (DVHs) as described previously [25].

Treatment techniques and dose planning

The clinical target volume (CTV) in node-negative patients comprised the entire breast, inclu-

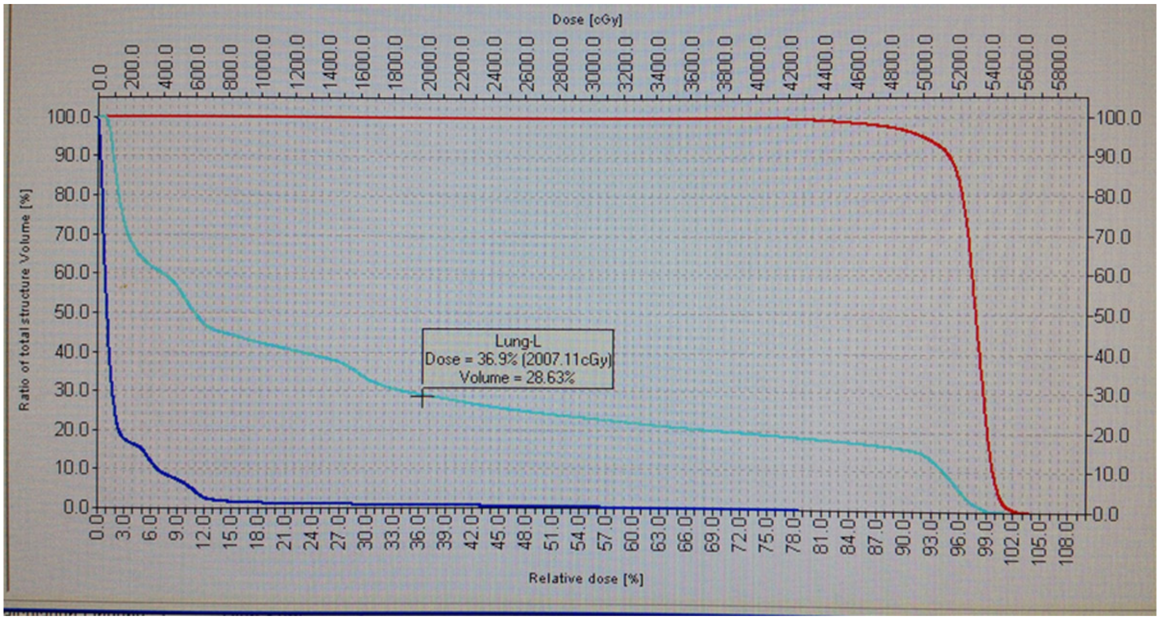

Figure 2. Case 3: Dose-volume histogram and isodose distribution in the target volume in the modified position.

ding fatty tissue and skin. In node-positive patients, the breast and ipsilateral sub and supraclavicular lymph nodes were also included. According to the ICRU Report 50, the PTV comprises the CTV and a margin to account for variations in size, shape, and position relative to the treatment beams. The dose specification was selected according to the ICRU Report 50. A dose of 50 Gy was given as 2-Gy fractions over 5 weeks. Routinely no boost was used.

An intensity-modulated radiotherapy (IMRT) technique using 6 MV photons with a 7-field coplanar beam arrangement was developed. In accordance with our protocol, the CTV contained the chest wall in the operative area and the ipsilateral lymph nodes (sub and supraclavicular). The fields were set up using the ECLAPSE dose-planning system (ECLAPSE, Varian Associates Inc.). The sum dose distribution for all fields was calculated, including the dose volume histograms for the ipsilateral lung and heart. The treatment plans were manually optimized so that more than 95% of the PTV was completely encompassed by the 95% isodose line while maintaining a minimum dose greater than 93% and a maximum dose less than 110%.

Statistical analysis

The paired T test was used for a pair-wise comparison of dose-volume parameters and indices between the CCB-TPM and WBB groups.

Results

The median age of the 50 enrolled patients was 42 years (range, 31-62 years). Thirty patients were diagnosed with invasive ductal carcinoma, and the remaining 20 were diagnosed with invasive lobular carcinoma. The study sample comprised 14 patients with left-sided breast cancer and 36 with right-sided breast cancer. Twenty patients underwent sentinel lymph node biopsy, and 30 patients with invasive carcinoma had axillary node dissection. The primary tumor was located in the upper-outer quadrant in 22 patients, the inner-upper quadrant in 14 patients, and in the central or aerolar region in the remaining 14 patients. Three patients received two cycles of cyclophosphamide, fluorouracil and pirarubicin before radiotherapy, and four patients received one cycle of docetaxel and epirubicin before radiotherapy. All patients received chemotherapy during radiotherapy.

Eight patients were excluded, because two of them did not receive the planned dose of radiotherapy and the other six did not complete the patient questionnaire. Twenty patients were selected to receive treatment with CCB-TPM. The selection of this technique was made on the basis of the dose distributions in the CT slices and the dose-volume Histogram (DVH) by the radiotherapist in charge (**Figures 2-6**).

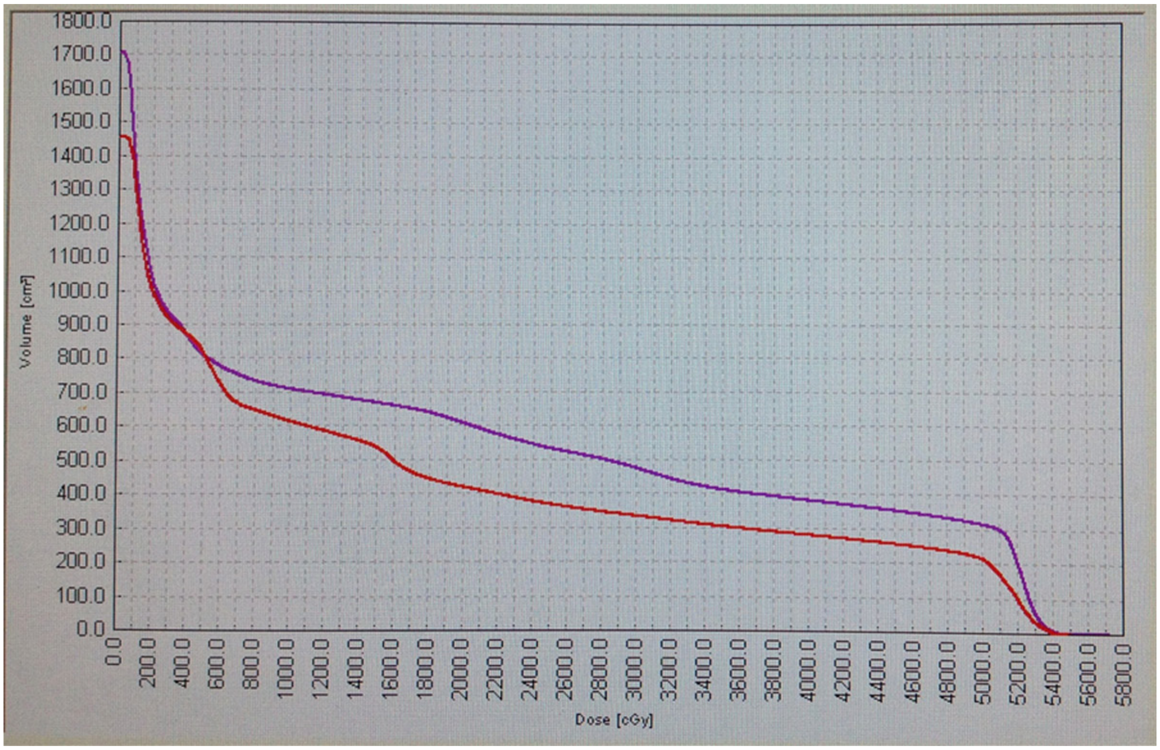

Figure 3. Case 3: Dose-volume histogram and isodose distribution for the ipsilateral lung tissue volume in the conventional position (top) and in the modified position (bottom).

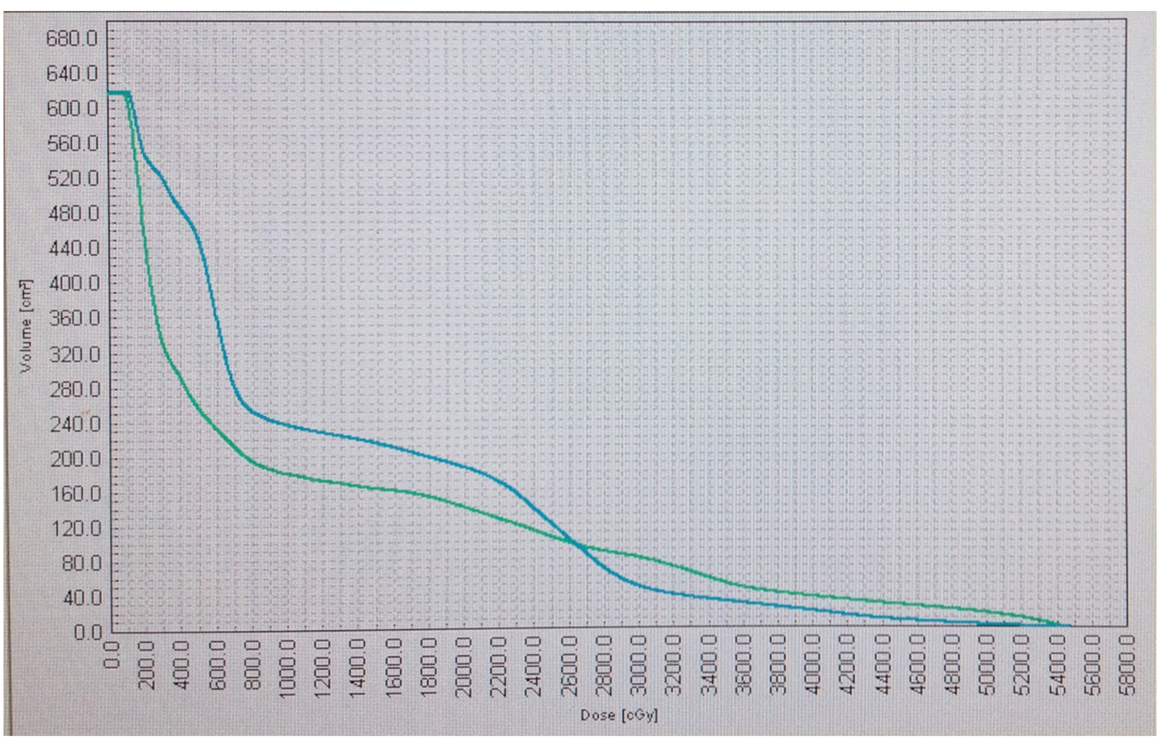

Figure 4. Case 3: Dose-volume histogram and isodose distribution for the heart tissue volume in the conventional position (blue) and in the modified position (green).

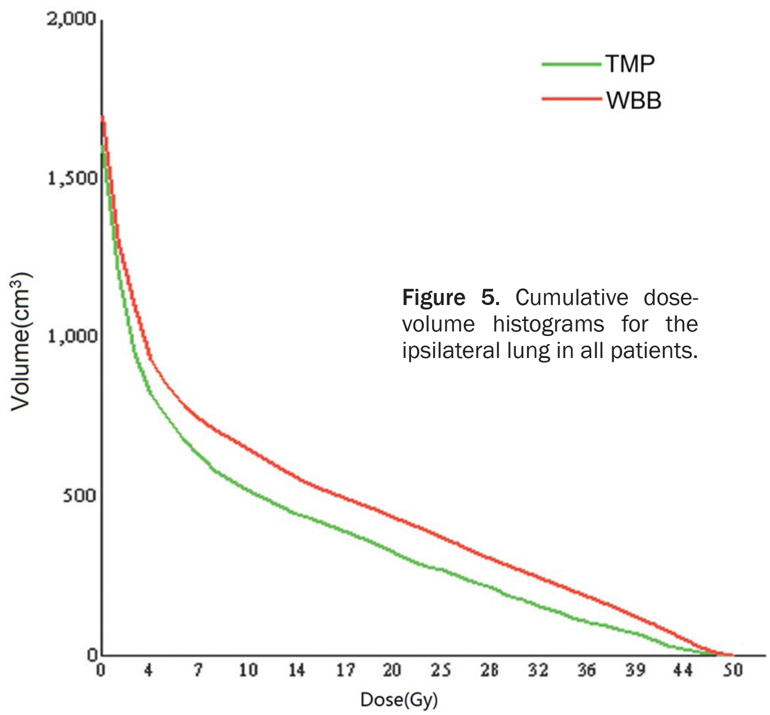

Figure 5. Cumulative dose-volume histograms for the ipsilateral lung in all patients.

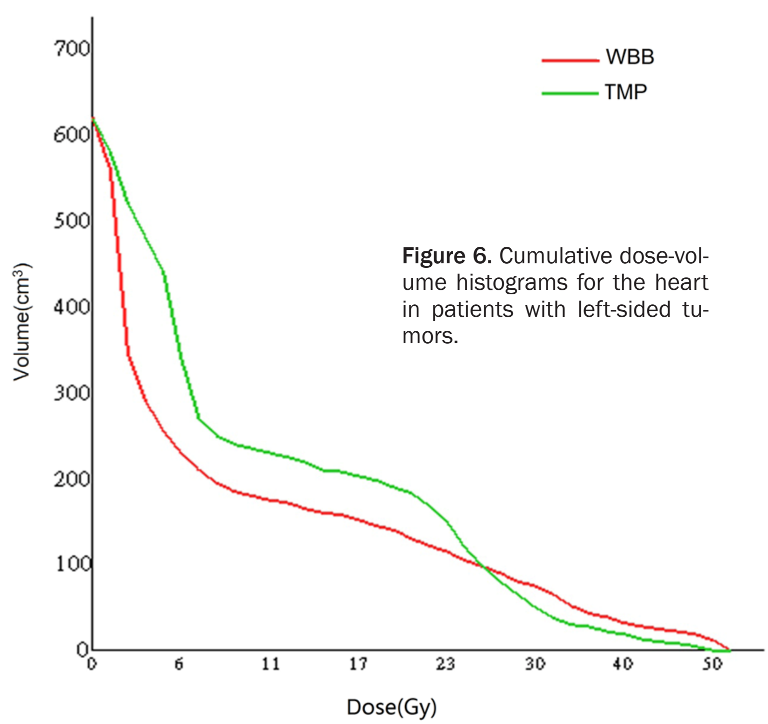

Figure 6. Cumulative dose-volume histograms for the heart in patients with left-sided tumors.

Dose to organs at risk

Utilizing DVHs, we examined the irradiated volumes of each organ at risk, i.e., heart and ipsilateral lung, at the doses of 20, 30, 40, and 50 Gy (**Figures 2-4** and **Tables 1**, **2**). Dose analysis of the ipsilateral lung showed that the average received dose decreased for all patients using the CCB-TPM. There were 5% and 4% reductions in the irradiated lung volume at the therapeutic dose levels of 20 and 30 Gy, respectively. No clinical problems related to irradiation of the lung were observed.

The comparative dose planning showed that the heart volume exposed to irradiation in patients with left-side tumors was lower at doses greater than 30 Gy in patients treated using the CCB-TPM (**Table 2** and **Figure 4**).

Skin reactions

Postoperative pain, tenderness, erythema, and edema were common at baseline. At 3 months after radiotherapy, almost all patients reported skin symptoms. The most common symptom was erythema, with 70% of the CCB-TPM patients suffering from this symptom, which was equal to 9% more than in the WBB group. Seven percent of these patients considered the erythema to be severe (grade 3). The second most common symptom in the CCB-TPM group was pain and tenderness of the skin or breast, which was reported by 80% of patients during the first 3 months, 9% of whom had severe symptoms (grade 3) (**Table 3**).

Dose distributions to target volumes

Twenty patients received treatment with the new technique. The selection of the technique was made on the basis of the dose distributions in the CT slices and DVHs by radiotherapist. Acceptable dose was received by breast parenchyma and axillary and supraclavicular lymph nodes (**Tables 4**, **5** and **Figure 7**).

Table 1. Ipsilateral lung dosage for the two techniques

Technique	Irradiated volume fraction at Gy (%)				
	5	10	20	30	40
WBB	50.03±1.0	38.24±1.2	25.63±0.8	16.77±0.4	5.99±0.2
CCB-TMP	46.73±1.3	32.40±1.2	20.20±0.6	11.84±0.3	3.16±0.3
P value	0.02	0.01	0.04	0.02	0.44

Table 2. Heart dosage for the two techniques in treating tumors in the left breast

Technique	Irradiated volume fraction at Gy (%)				
(12)	5	10	20	30	40
WBB	41.13±0.6	29.03±0.4	20.97±0.6	12.10±0.3	5.16
CCB-TMP	70.96±0.6	37.91±0.5	29.52±0.2	8.10±0.3	3.04
P value	0.03	0.01	0.21	0.02	0.03

Table 3. Frequencies of skin symptoms reported by patients 3 months after RT

Skin reaction (n=42)		Grade in first 3 months after RT (%)			
		0	1	2	3
WBB (n=22)	Pain/tenderness	45	30	19	6
	Erythema	39	31	21	9
CCB-TPM (n=20)	Edema	65	23	8	4
	Pain/tenderness	20	55	16	9
	Erythema	30	40	23	7
	Edema	60	25	11	4

Table 4. Fraction of the target volume (mean value, %) after delivery of 50 Gy or more in all 42 patients (12 left-side and 30 right-side breast cancer)

Target volume	CCB-TPM[36]	WBB[36]
Breast parenchyma	98 (97-100)	95 (93-100)
Axillary lymph nodes	95 (92-100)	94 (90-100)
Supraclavicular lymph nodes	93 (95-100)	94 (91-100)

Discussion

Use of the CCB-TPM technique resulted in the delivery of a lower dose of radiotherapy to the ipsilateral lung. At doses larger than 30 Gy, the volume of myocardium affected also was significantly reduced using the modified technique. Skin reactions and the constitutional symptom of fatigue dominated the early toxicity profile and were similar between patients treated using both techniques. We also noted additional advantages of CCB-TPM technique in that the patient is stationary during horizontal positioning and CT scanning of patients is easier than with the traditional technique.

Radiotherapy after breast-conserving surgery has been demonstrated to significantly reduce the incidence of loco-regional relapse [26]. However, long-term follow-up has demonstrated a significant survival disadvantage due to an increased risk of myocardial infarction after postoperative radiotherapy [27, 28]. Relative risk estimates of fatal cardiovascular disease after left-sided radiotherapy have been as high as 2.2 compared with women who were treated for right-sided breast cancer [29, 30]. Further evaluation has revealed that the increased risk appears to be limited to those who received the highest dose volumes of cardiac radiation.

Irradiation of the breast in the prone position has been shown to decrease radiation doses to the lung and the heart and minimize the effects of respiratory-induced motion, especially for large pendulous breasts [31]. However, prone positioning is more difficult for both the patients and the therapists and is not widely adopted. Thus, there has been intense interest in recent years in the safe delivery of higher doses of irradiation to the breast [32-34]. However, there are a number of significant obstacles to delivering a precise radiotherapy dose to the target in the breast. First, unlike the skull, where the radiation beam can be delivered from many angles, the breast can only be approached from limited angles by external radiation beams generated by a linear accelerator. Second, unlike the skull, which can be firmly immobilized in a coordinate system in order to minimize geometric discrepancy between imaging and treatment, such a degree of immobilization and stereotactic localization has not been able to be achieved with breast irradiation previously. The new technique improves the ability to deliver a precise radiotherapy dose to the breast. Further, patients lying on a WBB are difficult to position inside a CT scanner due to the limited bore of the scanner, and this issue is improved with the new technique. Respiratory control is also improved using our new technique. This finding is consistent with the results

Table 5. Summary of DVH-based analysis for the PTV

Parameters	Plans	Value (Mean ± SD)	*P*-value
$D_{2\%}$ (Gy)	WBB	55.10±0.87	0.051
	CCB-TMP	54.87±0.73	
$D_{98\%}$ (Gy)	WBB	48.81±0.52	0.732
	CCB-TMP	49.99±0.42	
D_{mean} (Gy)	WBB	52.72±1.02	0.102
	CCB-TMP	52.92±0.95	
$V_{95\%}$	WBB	98%±1%	0.073
	CCB-TMP	98%±2%	
$V_{107\%}$	WBB	21%±4%	0.335
	CCB-TMP	30%±5%	
$V_{110\%}$	WBB	2%±2%	0.023
	CCB-TMP	2%±1%	
HI	WBB	0.12±0.03	0.211
	CCB-TMP	0.12±0.01	
CI	WBB	1.34±0.21	0.054
	CCB-TMP	1.44±0.11	

Abbreviations: PTV: planning target volume; $D_{2\%}$: maximum dose; $D_{98\%}$: minimum dose; Dmean: mean dose; CI: conformity index; HI: homogeneity index; Vx%: percent volume of PTV receiving x% of prescription dose.

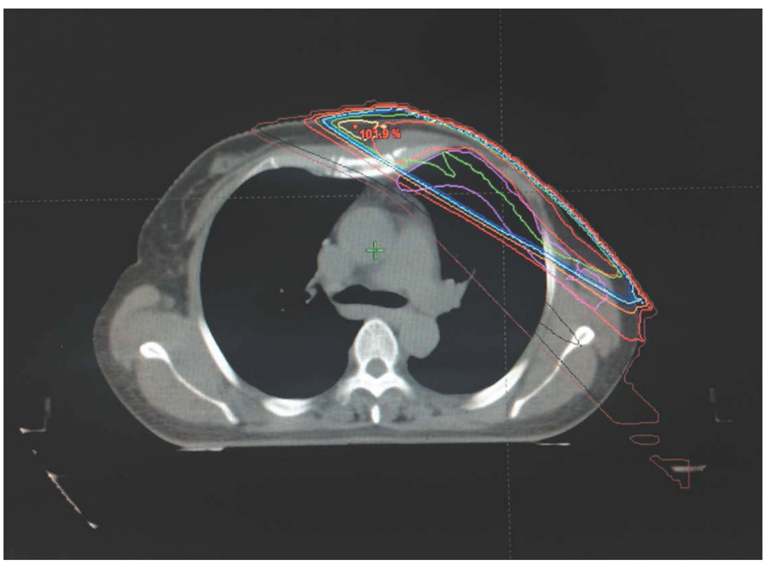

Figure 7. Isodose distributions (in Gy) in a transverse plane in the treatment plan for a patient with a left-sided breast cancer.

of Strydhorst *et al.* [35] who investigated the utilization of thermoplastic immobilization for the breast region and concluded that the addition of a thermoplastic mask can improve respiratory control.

The major limitation of this study is that the volume of total lung exposure during respiration was not calculated and compared between the two techniques, and this should be done in future studies. Furthermore, although encouraging results have been achieved in the short term, long-term follow-up will be required to assess the cardiac and pulmonary effects of decreasing radiation exposure using this technique.

In conclusion, the main purpose of this study was to assess the value of using the CCB-TPM in minimizing the radiation dose to organs at risk, particularly to the lung and the heart. We have clearly demonstrated that this is possible. However, the technique requires further development to optimize the time to achieve registration of targets and reduce motion control. Long-term follow-up will be important to determine whether the observed early dose reductions decrease cardiac and pulmonary complications.

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Disclosure of conflict of interest

None.

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