Scientific Article

Cardiac-sparing radiation therapy using positioning breast shell for patients with left-sided breast cancer who are ineligible for breath-hold techniques

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Abstract

Purpose: Patients with left-sided breast cancer (LSBC) are at increased risk of cardiac morbidity from adjuvant breast radiation therapy (ABRT). Breath-hold (BH) techniques substantially reduce the radiation received by heart during radiation therapy for LSBC. However, a subset of patients with LSBC are ineligible for BH techniques due to an inability to breath-hold or because of other comorbidities. To reduce radiation to the heart, we routinely use a custom-made breast shell for the treatment of patients with LSBC who are ineligible for BH techniques. This study evaluates the dosimetric impact of using a breast shell for patients with LSBC undergoing ABRT.

Methods and materials: Sixteen consecutive patients with LSBC who failed BH and underwent ABRT using a breast shell during the period of 2014 to 2016 were identified. Treatment was planned using field-in-field tangents with a prescribed dose of 42.5 Gy in 16 fractions. Comparisons between

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plans with and without a shell were made for each patient using a paired *t* test to quantify the sparing of organs at risk (OARs) and target coverage.

Results: There was no statistically significant difference in the planning target volume of breast coverage. A statistically significant improvement was observed in sparing the heart, left ventricle (LV), and ipsilateral lung (*P*-value < .001). Plans with the shell spared OARs better than the no-shell plans with a mean dose of 2.15 Gy versus 5.15 Gy (58.2% reduction) to the heart, 3.27 Gy versus 9.00 Gy (63.7% reduction) to the LV, and 5.16 Gy versus 7.95 Gy (35% reduction) to the ipsilateral lung. The irradiated volumes of OARs for plans with and without shell are 13.3 cc versus 59.5 cc (77.6% reduction) for the heart, 6.2 cc versus 33.2 cc (81.2% reduction) for the LV, and 92.8 cc versus 162.5 cc (42.9% reduction) for the ipsilateral lung.

Conclusions: A positioning breast shell offers significant benefit in terms of sparing the heart for patients with LSBC who are ineligible for BH techniques. It also can be used as a simple cardiac-sparing alternative in centers without BH capability.

Introduction

Breast cancer is the most commonly diagnosed cancer (29%) and the second leading cause of cancer-related death (15%) among women in North America.[1] The introduction of mammographic screening programs has increased the incidence of early stage breast cancer and resulted in a 20% relative reduction in breast cancer mortality.[2] The standard treatment for early stage breast cancer includes breast conservation surgery (BCS) or mastectomy and sentinel node biopsy, with or without axillary lymph node dissection. Adjuvant breast radiation therapy (ABRT) is an integral part of adjuvant treatment after BCS because ABRT leads to a significant reduction in locoregional disease recurrence.[3] However, patients with left-sided breast cancer (LSBC) are at an increased risk of cardiac morbidity from ABRT. Darby et al reported that the rate of major coronary events after ABRT was proportional to the mean heart dose received and increased 7.4% per Gy received.[4] Hence, it is important to keep the cardiac dose low. The major risk factors associated with increased risk of cardiovascular morbidity and mortality after ABRT include the volume of heart irradiated and radiation dose received by the heart.[5]

Dosimetric studies have shown that the use of modern, high-precision, conformal techniques such as intensity modulated radiation therapy (IMRT) could limit the risk of cardiovascular morbidity from irradiation. Lohr et al showed that IMRT-based treatment planning significantly reduced the maximal dose to the left ventricle (LV), which may translate into reduced cardiac morbidity and mortality.[6] However, the volume of heart irradiated and the portion of the heart receiving maximum dose depend on a number of factors, including the patient's chest wall anatomy, breast position, breast size, treatment position (eg, prone vs supine, lying flat vs on an angled board, arm position) and the position of the field borders.

IMRT may not always be able to lower the dose to the left anterior descending (LAD) coronary artery or LV when the heart lies near the target volumes or chest wall.[5] Hence, even with IMRT, some patients may still receive doses >50% of the prescribed dose to a significant heart volume (>20%), and approximately 10% of those patients receive higher doses to the LV or cardiac apex.[5] The introduction of breath-hold (BH) techniques has substantially reduced the amount of radiation received by cardiac structures during left-breast radiation therapy.[6,7] However, not all patients with LSBC may be eligible for BH techniques due to pulmonary or other comorbidities or the inability to breath-hold.

A thermoplastic shell is routinely used for head and neck radiation therapy for immobilization and improved treatment reproducibility. Zierhut et al reported for the first time the benefit of using thermoplastic breast shells to immobilize large breasts.[8] The study showed improved dose homogeneity, reproducibility, and sparing of the lung and heart if the left breast is irradiated. To avoid or minimize radiation to the heart, at our institution, we have routinely used custom-made breast shells for the simulation and treatment of patients with LSBC who have a substantial amount of heart within the radiation field but are ineligible for a BH technique.

The purpose of this study is to report the dosimetric advantage and our experience with using a custom-made positioning breast shell for cardiac sparing in patients with LSBC undergoing ABRT.

Methods and materials

The study cohort consisted of 16 consecutive patients with LSBC who were treated with field-in-field tangent field radiation therapy using custom-made breast shells after BCS between 2014 and 2016. Data were retrieved after approval from the institutional research ethics board.

All patients underwent computed tomography (CT) simulation (Brilliance Big Bore, Philips Medical Systems, MA) with 3 mm slices in the supine position with arms extended

overhead, using an Orfit AIO board (Orfit Industries, Wijnegem, Belgium). Images were registered in the treatment planning software (Eclipse v10, Varian Medical Systems, Palo Alto, CA), and contouring was aided by the Radiation Therapy Oncology Group Breast Cancer Atlas.[9] The following structures were defined: CTV_Breast, PTV_Breast, heart, LV, and ipsilateral lung (Lung_ipsi). Treatment was planned and delivered using 2 field-in-field tangent fields to cover the planning target volume (PTV) for a prescription dose of 4250 cGy delivered in 16 fractions over 3.5 weeks). Planning goals were to maximize conformity and minimize dose to critical organs with priority to the heart, LV, and lung doses. Dosimetric goals were PTV_Breast V95 ≥95%; heart V25 ≤10%; and ipsilateral lung V30 ≤20%.

Patients in this cohort had failed to meet institutional heart constraints on the basis of an initial simulation and were subsequently resimulated with a positioning breast shell (6-Points Thorax & Abdomen Mask, Orfit Industries, Wijnegem, Belgium). The typical patient population that fails BH techniques are those who have chronic obstructive pulmonary disease, poor lung reserves, or significant anxiety and those who cannot breath-hold for a minimum of 25 seconds (the approximate time required for the acquisition of planning CT images).

The positioning shell extends from the chin to the lower abdomen and is 3.2 mm thick before heating and moulding. The positioning of the breast for immobilization was decided with the aid of the initial CT simulation scans. Standard breast positioning within the shell was such that the ipsilateral breast was pushed inferiorly below the suprasternal notch and medially/anteriorly to the mid-axilla line to avoid crossing the mid-line (Fig 1).

During the molding of the shell, the breast was lifted at the inframammary border to minimize or eliminate the naturally occurring skin fold in that region. If the contralateral breast extended into the anticipated path of the tangential fields, the shell was used to compress the contralateral breast and position it laterally such that it would be out of the beam path. A hole was cut in the shell at the location of the ipsilateral nipple (Fig 1); this allowed the

radiation therapists to access the breast to position it correctly for treatment. Subsequently, patients underwent resimulation with the custom-made shell in place, and images were transferred to the planning workstation for recontouring followed by generation of a new treatment plan. All patients then underwent radiation therapy with the custom-made shell in position.

A dosimetric comparison was performed between the plans with and without shell for each patient by generating dose-volume histograms for clinically relevant parameters to quantify dose sparing of the heart and other organs at risk (OARs). Dosimetric parameters representing coverage of the PTV_Breast (Breast volume, D_{max}, D_{min}, and D95%) and sparing of the heart (maximum dose to 10 cc, D99%, D1%, V5Gy%, V10Gy%, V20Gy%, V25Gy%, V30Gy%, and V40Gy%), LV (maximum, median, and mean dose received; D1Gy%; and D99Gy%), and ipsilateral lung (mean dose received, V20Gy%, V10Gy%, and V5Gy%) were recorded for the plans generated with and without shell.

Comparisons between the plans with and without shell for the same patient were performed using a paired t test with P-values ≤.05 considered statistically significant. SPSS Version 15 was used to conduct all statistical tests.

Results

Improvement in cardiac sparing when using a positioning shell is illustrated in Figure 2. The positioning of the breast within the shell allows shallower tangent angles to be used for treatment. On average, gantry angles were 6° closer to horizontal with the shell in place. At the center of mass of the heart structure, the entry point for the lateral field with the shell in place was an average of 4.1 cm anterior to that with no shell. The average of the maximum random motion of the shell for the entire treatment period was 1.74 (±0.35) mm, 0.86 (±0.29) mm, and 3.36 (±2.3) mm in the anterior-posterior, mediolateral, and craniocaudal axes, respectively. The random motion was measured using KV orthogonals.

Figure 1   Patient with right breast positiong shell . A hole is cut at the location of the nipple and nipple position aligned with laser and field marks on the shell.
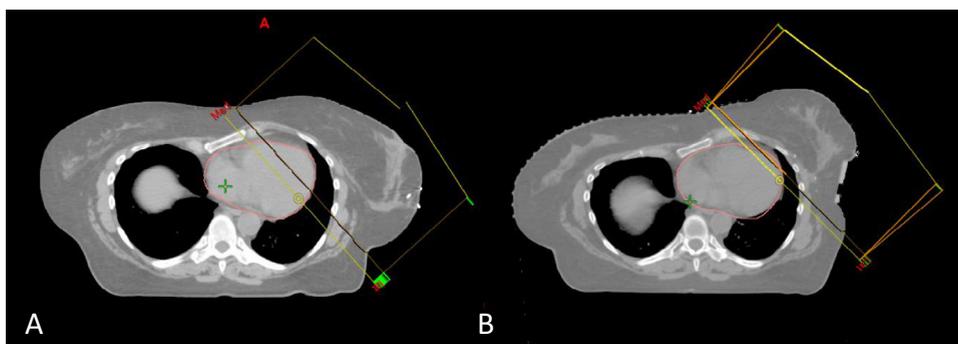
Figure 2 A&B. Representative treatment field arrangements for a patient without (A) and with breast positioning shell (B). The images show improvement in cardiac sparing when using positioning shell.

Table 1 Baseline patient characteristics

Characteristic	
No. of patients	16
Sex	Female
Mean age (range), y	64 (52-78)
Type of cancer	Invasive ductal carcinoma
Tumor stage, n (%)	
I	11 (69)
IIA	2 (12)
IIB	3 (19)
Type of breast surgery	Lumpectomy + SLNB
Adjuvant chemotherapy	3 patients received adjuvant chemotherapy. All patients received adjuvant hormone therapy.

SLNB, sentinel lymply node biopsy.

Details of the baseline patient characteristics are provided in Table 1. Dosimetric comparisons between plans with and without a shell in terms of target coverage and sparing of OARs are shown in Tables 2 and 3 and Figure 3. Both plans showed adequate coverage of the target volume (PTV_Breast) with no statistically significant difference between the plans for target coverage. A comparison of the average dose-volume histograms for heart, LV, and Lung_ipsi for the shell and no-shell plans (Fig 3) illustrates the advantages of the shell for OARs. A summary of the dosimetric analysis (Tables 2 and 3) for the OARS is as follows

For Lung_ipsi, on average, the use of a shell reduces the volume of lung within the treatment field by 43% (162.48 cc vs 92.76 cc; $P < .0001$). The mean lung doses for the shell and no-shell plans were 5.16 Gy versus 7.96 Gy, respectively (35% reduction; $P < .001$). The mean volume

Table 2 Comparison of the PTV and dose-volume parameters of the OARs for the shell versus no-shell plans

PTV/OARs	Characteristics	Shell dose (Gy)	No-shell dose (Gy)	Difference in mean dose (cGy)	% difference in mean dose	P-value[a]
PTV_Breast	D_{min}	30.83	31.42	−0.59	0.69	.669
	D_{max}	44.86	45.12	−0.26	0.57	.426
	D95	35.82	36.45	−0.63	0.72	.495
Lung_ipsi	Mean dose	5.16	7.96	−2.79	35.08	.000
LV	Maximum dose	33.29	40.97	−7.67	18.73	.001
	Median dose	1.71	2.85	−1.14	40.12	.000
	Mean dose	3.27	9.00	−5.73	63.67	.000
	D1	21.19	39.91	−18.72	46.90	.000
	D99	59.31	83.59	−24.28	29.04	.000
Heart	Mean dose	2.15	5.15	−3.00	58.24	.000
	Median dose	0.92	1.31	−3.81	29.11	.000
	Maximum point dose	36.99	41.54	−4.54	10.94	.001
	Maximum point dose (10 cc)	18.12	39.25	−21.13	53.84	.000
	D99	19.62	27.32	−7.70	28.18	.000
	D1	20.62	39.89	−19.27	48.30	.000

D_{max}, dose to 1% of planning target volum; D_{min}, dose to 99% of PTV; LV, left ventricle; LV_$_{max}$, dose to 1% of LV; D1, dose to 1% of target; D99, dose to 99% of target; OAR, organ at risk; PTV, planning target volume.

[a] P-value (paired t) $\leq .05$ is significant.

Table 3 Comparison of the PTV and dose-volume parameters of the OARs for the shell versus no-shell plans

PTV/OARs	Characteristics	Volume receiving specified dose (%) and volume of target within RT field in cc		Mean volume difference (cc)	% difference in Volume	P-value[a]
		Shell (cc)	No-shell (cc)			
PTV_Breast	PTV volume	1190.78	1228.57	−37.79	3.08	.420
	V90%	92.23	92.95	−0.73	0.78	.501
	V95%	85.80	86.75	−0.95	1.09	.517
Lung_ipsi	Total volume	1044.76	1018.53	26.24	2.58	.208
	Volume within RT field	92.76	162.48	69.72	42.91	.000
	V20%	9.19	16.42	−7.23	44.03	.000
	V10%	12.42	20.24	−7.5	38.64	.000
	V5%	19.98	27.86	−7.89	28.28	.000
LV	Total volume	188.41	189.25	−.84	0.44	.917
	Volume within RT field	6.24	33.24	27	81.22	.000
Heart	Total volume	659.74	630.58	29.17	4.62	.337
	Volume within RT field	13.32	59.54	46.22	77.63	.000
	V5Gy%	5.85	15.74	−9.89	62.83	.000
	V10Gy%	3.08	11.53	−8.44	73.29	.000
	V20Gy%	2.14	9.61	−7.47	77.73	.000
	V25Gy%	1.84	1.55	−7.07	18.71	.000
	V30Gy%	1.55	8.19	−6.54	81.07	.000
	V40Gy%	0.13	1.68	−1.56	92.26	.009

LV, left ventricle; OAR, organ at risk; PTV, planning target volume; RT, radiation therapy; VX%, % of the PTV volume receiving X% of the prescribed dose; VXGy%, percentage of the volume of the specific OAR receivign X Gy.

[a] P-value (paired t) ≤ .05 is significant.

of the Lung_ipsi receiving doses ≥20 Gy and 10 Gy were also significantly lower for the shell plans ($P < .0001$).

The shell plans resulted in better sparing of the heart and LV. The mean volumes of heart within the treatment field for shell versus no-shell plans were 13.32 cc versus 59.54 cc, respectively (78% reduction; $P < .0001$). Similarly, the mean LV volumes within the treatment field were reduced to 6.24 cc from 33.24 cc (81% reduction; $P < .0001$). Mean and maximum dose metrics for the heart and LV were also significantly improved with use of the shell. Mean doses for shell versus no-shell plans were 2.15 Gy versus 5.15 Gy (58% reduction; $P < .0001$) for the heart and 3.27 Gy versus 9.00 Gy (64% reduction; $P < .0001$) for the LV. Significant reductions in D1 (Gy) and the maximum point dose (dose to 10 cc) received by the heart were also achieved.

Discussion

The present study was designed to quantify the potential dosimetric benefit of using a thermoplastic positioning shell in patients with LSBC to spare the heart from higher radiation dose and to reduce the volume of irradiated heart exposed during breast radiation therapy. We found that thermoplastic positioning of the breast achieved significant sparing of the heart and LV in both instances.

Smyth et al conducted a systematic review to evaluate the cardiac-sparing benefits of BH techniques.[10] The review reported that BH produced a statistically significant reduction in the mean heart dose when compared with a free-breathing technique. The mean heart dose in their BH plans ranged from 1.3 to 3.9 Gy. Our study showed that the mean heart dose was 2.15 Gy and the mean LV dose was 3.27 Gy with a shell, which suggests a reduction comparable with that of BH techniques. An interesting observation was that most of the study patients had large, pendulous breasts. The mean breast volume in our study was 1209.7 cc, and breast volumes ranged from 671 to 2069.0 cc. However, the primary criterion for consideration for positioning with the breast shell was an inability to breath-hold rather than breast size or tumor stage.

One of the major concerns in using a thermoplastic shell for breast positioning is its ability to effectively stabilize and maintain breast positioning and the level of day-to-day reproducibility because these could have significant dosimetric consequences. Zierhut et al. reported improved dose homogeneity and acceptable reproducibility with the breast shell.[9] The mean ventrodorsal shift was 0.3 ± 0. 29 cm and the craniocaudal shift was 0.41 ± 0. 53 cm with the shell in position.

Strydhorst et al studied the impact of using a thermoplastic shell on setup reproducibility for helical tomotherapy of the breast or chest wall.[11] The authors concluded that the thermoplastic shell effectively reduced intrafraction respiratory motion, but without improvement in interfraction motion, which resulted in systematic errors of up to 10 mm.
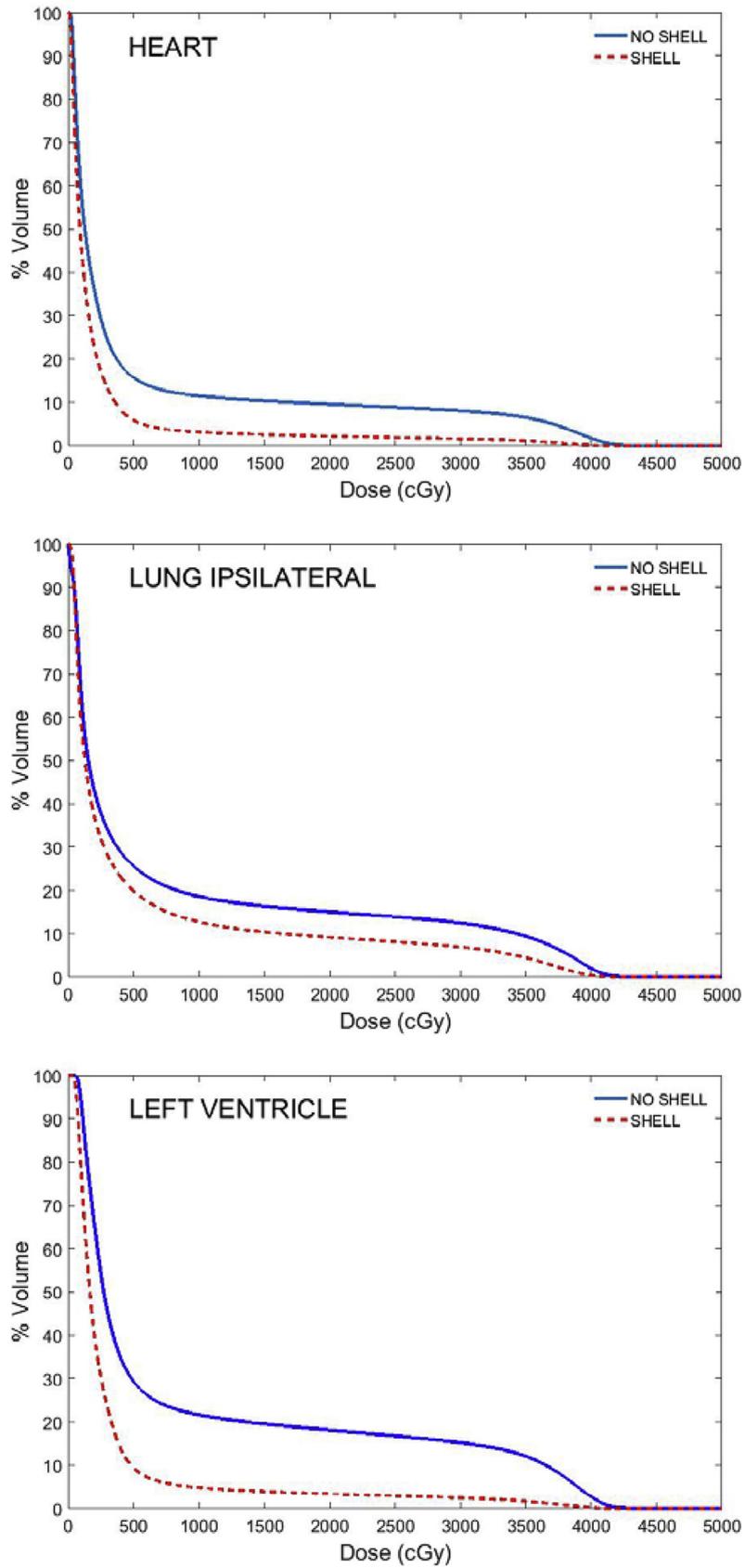
Figure 3 Average dose-volume histograms for ipsilateral lung(Lung_ipsi), heart and left ventricle(LV) for plans with and without shell.

Similarly, Agostinelli et al evaluated the ability of a thermoplastic shell to immobilize the breast/chest wall for helical tomotherapy.[12] Their analysis showed random (σ) and systematic (Σ) errors of $\sigma = 2.6/3.4/4.2$ mm and $\Sigma = 3.0/1.6/2.5$ mm. Our data showed that the average of the maximum random motion of the shell for the entire treatment period was acceptable for standard tangent field ABRT.

A concern with thermoplastic shells is that they can increase skin dose due to the bolus effect with resulting increases in acute skin toxicity. Zierhut et al reported a 17% increase in surface dose (from $47\% \pm 6\%$ to $64\% \pm 12\%$) when using the thermoplastic shell.[9] However, the maximum skin reaction was dry desquamation in 6 patients and moist desquamation in 1 patient. Keller et al investigated the benefit of using a bra to augment breast shape and position in women with large breasts undergoing ABRT.[13] The study endpoint was acute radiation dermatitis, and 90% of patients with a bra developed only grade 2 skin toxicity. None of our patients developed grade ≥ 3 skin toxicity. The practice of cutting a hole in the anterior of the shell around the nipple and using the positioning shells to eliminate skin folds aid in the avoidance of skin toxicity (Fig 1).

Adjuvant left-sided breast radiation therapy has been associated with a higher risk of long-term cardiac morbidity; hence, sparing of the heart and coronary arteries from exposure to higher radiation doses is particularly significant. Gagliardi et al and Mast et al recommended keeping the dose received by the irradiated heart volume, especially in the LAD region, to the minimum achievable dose.[14,15]

Many efforts are underway to minimize cardiac dose for women undergoing left-sided breast radiation therapy. There is increasing evidence that patients who are treated in the prone treatment position could have improved dose inhomogeneity and lung and heart doses.[16] However, prone radiation therapy is limited to treat the breast only or the breast and lower axilla area. A full, regional, nodal irradiation in the prone position is either not possible or leads to inadequate target dose coverage of the supraclavicular, axilla, and internal mammary region.[16-18] In general, patients in a supine-positioning breast shell can undergo 2 to 4 field radiation without compromising adequate target dose coverage. All of our study patients received a hypofractioned dose of 42.5 Gy in 16 fractions on the basis of the study by Whelan et al[19]. Our experience showed that patients with breast shell tolerated hypofractionated radiation well.

Most North American institutions have integrated conformal radiation therapy techniques with BH for left-sided breast radiation therapy to reduce the volume exposed to radiation and the dose delivered to the heart. Mast et al estimated that BH techniques achieved a 20% reduction in irradiated heart volume for V20Gy and an additional 5% reduction in the caudal part of the heart (LAD region) by using IMRT when compared with free breathing.[15] However, there can be significant variation in chest wall anatomy, and in a subset of patients, conformal techniques or IMRT may lead to higher heart doses.

Taunk et al reported that inverse-planned tangent IMRT did not reduce high-dose radiation to the heart compared with 3-dimensional chemoradiation therapy in women with LSBC with unfavorable cardiac anatomy (≥ 1.0 cm heart within the treatment field).[20] There was no significant difference in heart V30 for 3-dimensional chemoradiation therapy and IMRT plans ($P = .8$) for these patients. Similarly, many patients may not be eligible for BH techniques due to pulmonary or other comorbidities or an inability to breath-hold. Globally, many radiation therapy centers do not have the capability for conformal radiation therapy techniques, BH, or other cardiac-sparing programs. Hence, customized breast shells would be a relatively simple alternative for cardiac-sparing ABRT in that situation.

Conclusion

Our study showed that customized breast shells produced a significant reduction in the doses to and volumes of heart, LV, and lung within the radiation field compared with no-shell, free-breathing plans. Hence, customized thermoplastic breast shells could be used as a cardiac-dose-sparing alternative for patients who are ineligible for a BH technique or at cancer centers without a facility for conformal radiation techniques or BH capability.

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