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A comparative analysis of 3D conformal deep inspiratory–breath hold and free-breathing intensity-modulated radiation therapy for left-sided breast cancer

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Patients undergoing radiation for left-sided breast cancer have increased rates of coronary artery disease. Free-breathing intensity-modulated radiation therapy (FB-IMRT) and 3-dimensional conformal deep inspiratory–breath hold (3D-DIBH) reduce cardiac irradiation. The purpose of this study is to compare the dose to organs at risk in FB-IMRT *vs* 3D-DIBH for patients with left-sided breast cancer. Ten patients with left-sided breast cancer had 2 computed tomography scans: free breathing and voluntary DIBH. Optimization of the IMRT plan was performed on the free-breathing scan using 6 noncoplanar tangential beams. The 3D-DIBH plan was optimized on the DIBH scan and used standard tangents. Mean volumes of the heart, the left anterior descending coronary artery (LAD), the total lung, and the right breast receiving 5% to 95% (5% increments) of the prescription dose were calculated. Mean volumes of the heart and the LAD were lower ($p < 0.05$) in 3D-DIBH for volumes receiving 5% to 80% of the prescription dose for the heart and 5% for the LAD. Mean dose to the LAD and heart were lower in 3D-DIBH ($p \leq 0.01$). Mean volumes of the total lung were lower in FB-IMRT for dose levels 20% to 75% ($p < 0.05$), but mean dose was not different. Mean volumes of the right breast were not different for any dose; however, mean dose was lower for 3D-DIBH ($p = 0.04$). 3D-DIBH is an alternative approach to FB-IMRT that provides a clinically equivalent treatment for patients with left-sided breast cancer while sparing organs at risk with increased ease of implementation.

Introduction

The American Cancer Society estimates approximately 230,000 cases of breast cancer annually in the United States.[1] Approximately 35% of patients undergo mastectomy, and 65% of patients choose breast conservation therapy. Assuming the incidence of right- and left-sided breast cancers are the same, *i.e.*, 150,000 cases of right- and left-sided breast cancer, then, annually, approximately 75,000 patients develop left-sided breast cancer and choose breast conservation therapy requiring radiation therapy as a component of therapy based on current national treatment recommendations for the vast majority of patients.[2]

The clinical benefit of adjuvant radiation therapy in the setting of breast cancer is well established.[3,4] A recent meta-analysis of randomized clinical trials demonstrated that the addition of radiation therapy to surgery alone not only reduced locoregional recurrence but also the risk of death from breast cancer.[4] Further evidence, however, has shown that the aforementioned benefits may be offset by an increase in morbidity and mortality from late cardiovascular damage.[5-9] At 20 years after undergoing radiation therapy for breast cancer, it has been reported that patients with left-sided breast cancer have a cumulative risk of cardiac death of 6.4% compared with 3.6% for patients with right-sided breast cancer.[10] Doses as low as 2.6 to 3.0 Gy to the heart have been shown to increase the risk of coronary heart disease.[11] The left anterior descending coronary artery (LAD) travels in the anterior interventricular groove that separates the right and the left ventricle. This groove is located on the anterior surface of the

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heart, and therefore, the LAD is positioned close to the chest wall and the target area for radiation of patients with left-sided breast cancer.

Based on these findings, and with the advent of computed tomography (CT)-based treatment planning, multiple methods and alterations in radiation technique to reduce cardiac dose for patients with left-sided breast cancer have been developed. Partial-breast irradiation significantly lowered radiation exposure to the heart in multiple studies.[12,13] Lettmaier *et al.* reported that heart doses received in the setting of partial-breast irradiation with multicatheter brachytherapy *vs* whole-breast external-beam radiotherapy differed by a factor of 4.[13] Intensity-modulated radiation therapy (IMRT) used for adjuvant treatment of breast cancer has shown improved target coverage as well as lower doses to cardiac structures.[14,15] The use of deep inspiration–breath hold (DIBH) during tangential breast radiation therapy has also proved to be a high-quality means of reducing the cardiac volume that receives the radiation dose.[16-21] McIntosh *et al.* reported a 7% decrease in the mean heart dose and a 9% decrease in the mean LAD dose when utilizing DIBH compared with free breathing in 3-dimensional (3D) conformal whole-breast irradiation.[16]

Other dosimetric studies have focused investigation on the reduction of dose to organs at risk by comparing IMRT with 3D radiation therapy and 3D free breathing with 3D-DIBH.[14-18] Our goal was to compare a previously reported 6-field tangent IMRT free-breathing technique[14] with a 3D-DIBH technique with standard tangents to quantify the dose to the following organs at risk: the heart, LAD, lungs, and right breast while maintaining comparable target coverage and homogeneity.

Methods and Materials

We clinically implemented a DIBH whole-breast radiation program for patients with left-sided breast cancers in an effort to reduce heart dose. We retrospectively analyzed the first 10 patients treated at our institution with DIBH on an Institutional Review Board–approved institutional study to compare the dosimetric advantages of 3D-DIBH to free-breathing (FB)-IMRT for whole-breast irradiation.

Patient positioning

Patients were positioned on a breast board with both arms raised over the head and a Vac-Lok (Med Tech Inc., Orange City, IA) bag positioned to immobilize the patient's arms during simulation and treatment.

Patient breath-hold monitoring

Prior to simulation, the patient was advised to hold her breath under deep inspiration a few times, allowing her to become familiarized with the procedure. The Varian real-time position management (RPM) system was used during the DIBH scan to initiate imaging and to monitor the length and displacement of breath hold for each patient. The RPM block was positioned 2 cm below the xyphoid, facing the camera perpendicularly, and this position was marked on the patient at simulation for setup during treatment.

For each fractionation, the RPM breath-hold signal obtained at the simulation was used as the baseline for breath-hold reproducibility. An upper and lower limit of 0.5 cm from the baseline displacement was set so that the treatment would occur only when the patient's breath hold was within this displacement gate. Between each image acquisition and between each treatment field, patients were allowed to perform free breathing. If the patient had to perform multiple breath holds, a minimum of 15 seconds was allowed for free breathing between breath holds.

CT simulation and contouring

Patients were scanned with a 16-slice Philips (Philips Healthcare, Andover, MA) large-bore CT scanner during free breathing and DIBH. Scan duration for the DIBH helical CT was approximately 20 seconds. The Pinnacle treatment-planning system (Philips Medical Systems, Fitchburg, WI) was used for planning, contouring, and dosimetric comparisons. A single physician contoured the heart, LAD, lungs, and right and left breast in each data set. The breast clinical target volume (CTV) was defined as the visible left breast parenchyma and the superficial skin seen from the planning CT.

Table 1
Initial inverse planning optimization constraints for IMRT plans

Organ	Volume (%)	Dose (cGy)	Weight	Type
Left breast CTV	0	5000	90	Max DVH
	100	4500	100	Min DVH
		4500	90	Uniform dose
Lung	5	500	1	Max DVH
	2.5	2000	1	Max DVH
Heart	5	500	1	Max DVH
	0	4500	1	Max DVH

DVH = dose-volume histogram.

Treatment planning

Three-D conformal radiation treatment plans were optimized on DIBH CT data sets. Tangential beams with the inclusion of lung (with < 2-cm central lung distance) in the treatment fields were utilized to treat all of the left breast tissue with 2 cm of flash on the anterior breast skin. Wedges or "field-within-a-field" planning were used to optimize dose homogeneity.

IMRT plans were optimized on free-breathing CT data sets. Six tangential beams (3 medial and 3 lateral) were utilized by using the gantry, collimator, and table angles of a standard plan for conventional radiation therapy of the left breast and then shifting the couch $+\ 10^{\circ}$ and $-\ 10^{\circ}$ on each side, as previously reported.[14] Initial inverse planning constraints used during the optimization procedure are given in Table 1. A prescription of 45 Gy in 1.8-Gy fractions was utilized in both the techniques.

Dosimetric analysis

For the dosimetric comparison between FB-IMRT and 3D-DIBH, the mean volumes of the heart, LAD, total lung, and right breast receiving 5% to 95% (5% increments) and the CTV receiving 90% to 115% of the prescription dose were calculated.

Statistics

A t-test was performed and *p*-values were obtained to evaluate the statistical significance of the dose differences in FB-IMRT *vs* 3D-DIBH for each of the structures of interest. A *p*-value of ≤ 0.05 was considered statistically significant.

Comparative medicine cost analysis

Medicare reimbursement rates for 3D and IMRT treatment planning and delivery were used to compare the financial cost of the 2 treatment techniques, with each delivering a 25-fractions course of radiation.

Results

CTV coverage

Table 2 represents left breast mean volume (%) receiving dose levels from 90% to 115% of the prescription dose. The coverage for the left breast was not significantly different between IMRT and 3D-DIBH. There was more dose heterogeneity with the 3D-DIBH plans with a mean dose to the left breast of 4586 cGy *vs* 4530 cGy for IMRT ($p = 0.0115$). Figure 1 shows a representative isodose

Table 2
CTV mean volume (%) receiving different dose levels in IMRT and 3D-DIBH plans

Dose (%)	Dose (Gy)	Mean volume (%) IMRT	Mean volume (%) 3D-DIBH	Mean difference volume (%)	*p*-Value
90	40.50	98.17	99.76	1.59	0.0010
95	42.75	96.51	98.05	1.54	0.0062
98	44.10	90.23	89.15	− 1.08	0.5663
105	47.25	5.38	10.70	5.33	0.0906
110	49.50	0.29	0.05	− 0.24	0.1403
115	51.75	0.03	0.00	− 0.03	0.2819