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Research Article

Dosimetric Comparison of Dynamic IMRT, Field-in-Field IMRT and 3D-CRT in Left-Sided Breast Cancer after Breast-Conserving Surgery

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Abstract

Introduction: The purpose of this study was to compare three different types treatment planing Standard wedged tangential-beam 3D conformal radiotherapy (3D-CRT), field-in-field (FIF) and dynamic Intensıty Modulated radıotherapy (d-IMRT) in early breast cancer patients who have undergone lumpectomy. Our aim was to improve dose-distribution homogeneity in the breast and decrease the dose to organs at risk (OAR), i.e. heart and vessels, ipsilateral lung, and contralateral breast.

Material and Method: 3D-CRT, FIF and d-IMRT treatment plans were carried out for 18 patients with cancer of the left breast. Plans were compared according to cumulative dose-volume histogram (c-DVH) analysis in terms of planned treatment volume (PTV), homogeneity index (HI), and conformity index (CI), as well as dose and volume parameters of OARs.

Results: When the targeted volumes receiving 105% and 110% of the prescribed dose in the PTV were compared, significant decreases were found with the d-IMRT technique. In low dose regions d-IMRT plans were founded significantly higher values in total heart, left lung, ipsilateral breast and cardiac vessels ($p < 0.01$). Monitor Unit (MU) counts were significantly higher in d-IMRT. Dose homogenity in PTV was determined with homogenıty ındex (HI) and it was founded better with d-IMRT.

Conclusions: d-IMRT enables better dose distribution in the PTV. However, OARs volumes exposed to low doses were increased in d-IMRT. It is important for seconder cancer risk. Especially in patients at high risk of heart disease; in the field of low-dose, dose should be considered in heart.

Keywords: Breast Cancer; Field in Field Dynamic İntensity Modulated Radiotherapy; Volumetric Arc Therapy; 3D Conformal Radiotherapy

Abbreviations

d-IMRT: Dynamic Intensity Modulated Radiotherapy; 3D-CRT: Three Dimensional (3D) Conformal Radiation Therapy; FIF: Field-in-Field; PTV: Planning Target Volume; GTV: Gross Tumor Volume; CI: Conformty Index; OAR: Organs at Risk; HI: Homogeneity Index; MU: Monitor Unit; BCS: Breast Conserving Surgery; LAD: Left Anterior Descending Coronary Artery; MLC: Multi-Leaf Collimator; DVH: Dose-Volume Histogram

Introduction

Breast cancer is the most common cancer type seen in women worldwide. Breast cancer can be treated by using a multimodality approach of surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapy.

The administration of adjuvant radiotherapy following breast conserving surgery (BCS) is effective in reducing the risk of locoregional recurrence and distant metastases in patients with early stage breast cancer [1,2].

The most adopted treatment methods for breast cancer patients are BCS or mastectomy followed by adjuvant radiotherapy. Adjuvant radiotherapy improves local control with minumum toxicity and improves overall survival [3].

The adjuvant radiotherapy of the chest wall or whole breast is commonly delivered by three-dimensional conformal radiotherapy (3D-CRT) or field-in-field intensity modulated radiotherapy (FiF-IMRT) techniques [4]. One study has shown increased cardiac morbidity and mortality in patients treated with radiotherapy for left-sided breast cancer compared to right-sided, due to the higher cardiac doses for patients with left-sided disease [5]. Cardiac complications can be minimized by reducing the dose to the heart, which can be achieved by using intensity modulated radiotherapy (IMRT) [6].

The high-dose region is located in the anterior heart, which includes the left anterior descending coronary artery (LAD), causing increased perfusion defects after radiotherapy. Radiotherapy can also increase the risk for ischemic heart disease [7].

Literature has shown that IMRT decreases the dose to heart and ipsilateral lung more effectively than 3D-CRT for patients with left breast disease [6,7].

Multiple studies have shown that volume of breast is important for dose homogeneity. The inhomogeneity is worse in larger breasts, and radiotherapy side effects such as breast pain and poor cosmetic outcome may be related to dose distribution [8-11].

Critical organs for left-sided breast cancer include the heart, lung, and contralateral breast. After radiotheraphy, there is a long-term risk in women younger than 40 for developing a second primary breast cancer in the right breast [12-13].

Even though the lungs are protected by developed treatment plans, radiation pneumonitis can occur in approximatelly 1 - 5% of patients after breast radiotherapy [14,15].

This study generated three different treatment plan types: 3D-CRT, FiF-IMRT, and dynamic IMRT (d-IMRT). We checked all treatment plan dose distributions, OAR doses, specifically doses to heart structure.

Materials and Methods

Patients

Eighteen female patients were chosen for this dosimetric study. All patients had left breast cancer and had undergone BCS. Their primary diagnosis was only left breast carcinoma (without supraclavicular or axillary lymph nodes). Patients were treated with 3D-CRT, FiF-IMRT, or d-IMRT, and the results were compared with each other.

Target Volume and Delineation of Organs at Risk

All patients were immobilized in the supine position and scanned with a helical scanner (Siemens SOMATOM® Spirit® computed tomography scanner) with 3 mm slices over the neck and at the end of the twelfth rib. Immobilization was achieved with a Civco fiber breastboard, and each patient's left arm was raised above the head to exclude it from the treatment field.

Target volumes and OAR were determined by the radiation oncologist in the presence of a radiologist at the treatment planning system (TPS) (Varian Eclipse™ V10). The following structure sets were delineated: planned treatment volume (PTV), ipsilateral lung, contralateral breast, cardiac volumes, and cardiac vessels such as left and right atria, left and right ventricles, pulmonary artery, aorta, superior and inferior vena cava, and left anterior descending artery. All organ and treatment volume delineations were based on report 83 of the International Commission on Radiation Units and Measurements (ICRU).

The left breast was identified as PTV, and the lumpectomy cavity was contoured on the computed tomograph (CT) images as the gross tumor volume (GTV), which included surgery clips and seromas. The boost planning target volume was defined by providing the GTV with a 1.5 cm margin, except when there was close proximity to skin and chest wall.

Planning Techniques

We used the Eclipse™ TPS (Version 10, Varian Medical Systems, Palo Alto, CA). All patient treatment plans were designed to dose 50 Gy to the PTV in 25 fractions with a 6-MV photon beam from a Varian UNIQUE™ treatment machine, as well as a PTVboost dose of 10 Gy in 5 fractions. The PTV of each patient was planned with a technique of 3D-CRT, FiF-IMRT or dIMRT. In 3D-CRT plans, wedge filters were used, and the angles or degrees were chosen according to PTV volumes. In FiF-IMRT plans, a Varian Millennium 120 leaf multi-leaf collimator (MLC) was used to block unwanted high doses in the PTV. Sliding window techniques were used in five fields for dIMRT plans. This technique supplied homogeneity and conformity with moving MLC leaves in the various treatment plans (Figures 1-4).

Figure 1: Beam Arrangements of treatment plans.

Figure 2: Medial portal of the main field with field-in-field intensity-modulated radiation treatment (FIF-IMRT) plans.

Figure 3: Medial portal of the main field with 3D conformal radiotherapy.

Figure 4: Medial portal of subfields (IMRT) of the left breast.

All treatment plans aimed to achieve a minimum dose greater than 95% and a maximum dose lower than 107% of the prescribed dose, so all treatment plans were normalized to the isodose line to give a minimum of 50 Gy to 95% of the PTV.

Dose constraints for OARs were V5, V10, V20 of the ipsilateral lung; V1, V2, V5 of the contralateral breast; V2, V5, V10, V20, V30 of the heart; V2, V5, V10, V20, V30 of the left and right ventricles and LAD artery; and V2 of the aorta, superior and inferior vena cava, pulmonary artery, and right and left atrium.

Plan Comparison

DHI and CI were calculated for comparison of the three types of treatment plans. To define both indices, a cumulative dose-volume histogram (cDVH) was used. The DHI provided information about PTV dose differences between treatment plans, and the CI provided information about OAR doses. DHI was defined as follows:

DHI = (D2-D98)/Dp x 100%

D98 is the dose received by 98% of the target volume on the cDVH and is defined as the "minimum dose". D2 is the dose received by 2% of the target volume on the cDVH and is defined as the "maximum dose". Dp is the prescribed dose to the target volume.

Statistical Analysis

Analysis was performed using one-way analysis of variance (ANOVA) and Tukey's range test.

Results

In this study, patients with cancer of the left breast who had 3D-CRT, FiF-IMRT and dIMRT plans, as well as OAR doses to the total heart, left lung, ipsilateral breast, and cardiac veins (right and left ventricles, right and left atria, LAD, aorta, and pulmonary arteries) were compared.

When the total heart dose was examined in the study, V5 doses in the d-IMRT plan were higher and statistically significant when compared with 3D-CRT and FiF-IMRT plans ($p < 0.01$). Total heart doses of V10 in d IMRT were higher but not statistically significant ($p > 0.05$). When high-dose areas of V20 and V30 were examined, the total heart doses in the three treatment plans were nearly equal and not statistically significant. ($p > 0.05$) (Table 1).

	Total Heart			
	FiF IMRT	**3D-CRT**	**DIMRT**	**p**
V1				
V2				
V2.5				
V5	10,88 ± 6,11*	14,58 ± 9,42*	29,5 ± 12,1	< 0,001
V10	6,88 ± 4,10	7,54 ± 5,61	10,8 ± 5,81	0,218
V20	5,24 ± 3,50	5,76 ± 4,83	4,56 ± 3,5	0,798
V30	4,25 ± 3,12	4,80 ± 4,40	2,3 ± 2,37	0,243

Table 1: Comparison of total heart doses with field-in-field intensity-modified radiotherapy (FIF IMRT), IMRT and 3D conformal radiotherapy (CRT) plans.

	Left Lung			
	FiF IMRT	**3D-CRT**	**DIMRT**	
V1				
V2				
V2.5				
V5	28,02 ± 9,76*	30,80 ± 13,53*	62,4 ± 13,8	< 0,001
V10	20,18 ± 8,69	20,39 ± 10,01	30,3 ± 9,58	0,037
V20	15,93 ± 7,71	15,67 ± 8,43	15,8 ± 6,1	0,997
V30				

Table 2: Comparison of left lung doses.

In assessments of the left lung, V5 doses in d-IMRT plans were higher and statistically significant when compared with 3D-CRT and FiF-IMRT plans ($p < 0.01$). V10 doses in d-IMRT plans were higher and statistically significant ($p < 0.03$), and V20 doses in the three treatment plans were nearly equal and not statistically significant (Table 2).

The V1 dose was higher and statistically significant for the ipsilateral breast in d-IMRT plans ($p < 0.01$). V2 and V5 doses among the three treatment plans were nearly equal and not statistically significant (Table 3).

The cardiac vessels were examined separately (Table 4). The right ventricleV2 and V5 doses in the d-IMRT plans were higher and statistically significant, compared to 3D-CRT and FiF-IMRT plans ($p < 0.01$). V10 value in the right ventricle was higher in the d-IMRT plan but not statistically significant ($p > 0.05$). V20 and V30 values were lower in the d-IMRT plan but not statistically significant ($p > 0.05$).

	Contralateral Breast			
	FiF IMRT	**3D-CRT**	**DIMRT**	**p**
V1	4,45 ± 5,15#	29,52 ± 15,2*$	11 ± 5,5#	< 0,001
V2				
V2.5	0,64 ± 1,12	2,66 ± 3,17	2,94 ± 2,04	0,064
V5				
V10				
V20				
V30				

Table 3: Comparision of the contralateral breast doses.

The left ventricle showed statistically significant higher values of V5 doses in the dIMRT plans ($p < 0.01$). With V10, V20, and V30 values, the left ventricle doses in the d-IMRT plans were lower but not statistically significant ($p > 0.05$).

The left and the right atria revealed V2 doses in d-IMRT plans to be higher and statistically significant ($p < 0.01$), when compared to the 3D-CRT and FiF-IMRT plans.

V5 doses for the LAD in d-IMRT plans were higher and statistically significant ($p < 0.021$), when compared to 3D-CRT and FiF-IMRT plans. V10 doses in the d-IMRT plans were again higher but not statistically significant ($p > 0.05$). V20 and V30 values were lower in d-IMRT plans.

V2 aorta doses in d-IMRT plans were higher and statistically significant ($p < 0.01$)

The pulmonary artery V2, V5, and V10 doses were higher and statistically significant in d IMRT plans, but V20 and V30 doses, although higher, were not statistically significant in FiF-IMRT plans.

The maximum PTV doses (105% and 110%) decreased with the d-IMRT plan, but not with the other plans.

The CI assessment found that d-IMRT treatment plans were much better and statistically significant ($p < 0.01$), followed by FiF-IMRT and 3D-CRT. The d-IMRT treatment plans were better and statistically significant ($p < 0.01$) by DHI assessment, followed by FiF-IMRT and then 3D-CRT plans (Table 4). The d-IMRT plans were also found to be much better in patients with breast volumes smaller than 500 cc than in patients with breast volume greater than 1000 cc.

Right Ventricle				Left Ventricle			
FiF IMRT	3D-CRT	DIMRT	p	FiF IMRT	3D-CRT	DIMRT	p
0 ± 0*	3,89 ± 12,30*	80,3 ± 14,5	<0,001				
9,39 ± 7,47*	14,24 ± 8,91*	36,2 ± 18,4	<0,001	17,51 ± 10,60*	23,18 ± 13,18*	40,6 ± 14,8	0,001
4,24 ± 4,26	5,42 ± 5,98	8,07 ± 6,3	0,307	10,90 ± 6,53	12,40 ± 8,69	17 ± 10,03	0,267
2,76 ± 3,37	3,65 ± 4,89	2,31 ± 3,8	0,757	8,28 ± 5,51	9,56 ± 7,74	7,31 ± 5,84	0,738
2,08 ± 2,71	2,82 ± 4,11	1,08 ± 2,39	0,476	6,56 ± 4,89	6,85 ± 7,54	3,18 ± 3,91	0,289

Right Atrium				Left Atrium			
FiF IMRT	3D-CRT	DIMRT		FiF IMRT	3D-CRT	DIMRT	
0,17 ± 0,54*	3,89 ± 6,23*	40,76 ± 29,98	<0,001	1,19 ± 2,55*	7,68 ± 8,58*	35,93 ± 27,33	<0,001

LAD				AORTA			
FiF IMRT	3D-CRT	DIMRT	p	FiF IMRT	3D-CRT	DIMRT	p
				0,46 ± 1,46*#	14,13 ± 13,94*$	79,16 ± 14,3#$	<0,001
49,83 ± 14,52*	59,14 ± 14,40	70,6 ± 17,6	0,021				
35,26 ± 19	37,5 ± 19,54	46,1 ± 16,1	0,388				
19,28 ± 19,50	30,74 ± 20,05	25,6 ± 17,6	0,416				
25,81 ± 19,65	26,41 ± 19,91	15,5 ± 16,3	0,355				

Table 4: Cardiac vessels doses with three techniques.

MU counts were four times higher in d-IMRT plans than other treatment plans because intensity is provided by MLC movements in dynamic plans.

Discussion

This study is a dosimetric comparison of three treatment techniques in breast cancer patients; d-IMRT, FiF-IMRT, and 3D-CRT. Results revealed doses to the OAR (lung, contralateral breast, total heart, and cardiac vessels), dose homogeneity, and how much healthy tissue is protected with each treatment plan used in this study [16,17].

Developing treatment techniques like d-IMRT and FiF-IMRT can affect cosmetic results and long-term treatment-related toxicities. Despite these benefits, long-term observation should be employed to monitor for cardiac toxicity and secondary cancer risk (lung and contralateral breast) in breast cancer patients treated with d-IMRT and FiF-IMRT.

Our study was performed to compare dose distribution of the d-IMRT, FiF-IMRT,and 3D-CRT plans in breast cancer patients following lumpectomy. When the targeted volumes receiving 105% and 110% of the prescribed dose in the PTV were compared, significant decreases were found with the d-IMRT technique. Maximum doses in the PTV were significantly decreased with d-IMRT plans (6%). In 3D-CRT plans, the maximum dose was at the bottom of the wedge, so the contralateral breast dose was higher than that.

During assessment of breast volume, we observed that homogeneity and conformity were worse for larger breasts (breast volume > 1,000 cc), especially with the 3D-CRT plan. Dose homogeneity was better in smaller breasts (breast volume < 500 cc) with the d-IMRT plans. In their trial, Herrick., *et al.* classified patients into three groups according to breast volumes: small (< 975 cc), medium (976 - 1,600 cc), and large (> 1,600 cc). They concluded that, with small and medium-sized breast volumes, targeted volumes receiving between 105% and 110% of the prescribed dose were more homogeneous with the d-IMRT plan [18].

Another study showed that an increased risk of secondary tumors has been observed in breast cancer patients treated with older radiation techniques, which combined higher radiation doses with larger tissue volumes [7,19,20].

Our results showed that the CI is convenient in d-IMRT, which means that healthy tissues were well protected. The DHI in d-IMRT plans were better, which means dose distribution in PTV volume is more homogeneous.

In this study, d-IMRT MU counts outnumber FiF-IMRT and 3D-CRT. This situation results in increase to the lower-dose area. D-IMRT plans have worse results in lower-dose areas because intensity is provided with MLC movement.

Rudat., *et al.* showed that intensity modulated radiotherapy (IMRT) decreases high doses to heart and ipsilateral lung for patients with left breast disease, compared with 3D-CRT [7].

Our study confirms these results in higher-dose areas.

In literature, modern radiotherapy techniques, such as d-IMRT, are likely to reduce secondary cancer risk by reducing the lung dose volume. The secondary cancer risk stems from lower-dose areas rather than the higher-dose areas. Therefore, it is thought that d-IMRT has more possibility to increase the secondary cancer risk [21].

Ercan., *et al.* showed that V10, V20, and V30 of the irradiated heart volumes were decreased with FiF-IMRT [20]. In this study, we defined atria, ventricles, and large vessels, as well as the total heart for evaluation by dose-volume histogram. V2 and V5 doses in the d-IMRT plan were higher and more meaningful than in 3D-CRT and FiF-IMRT plans but, in higher-dose areas, the d-IMRT plan produced lower OAR volumes.

Our data showed that FiF-IMRT of the breast significantly reduces contralateral breast dose volume compared with d-IMRT and 3D-CRT ($p = 0.001$). V1 of the contralateral breast was significantly lower with the FiF-IMRT technique. This can be demonstrated by MU counts and radiation scatter. The reason for this result is that the wedges increase the disseminated doses for 3D-CRT, and density is provided with MLC movement for dynamic IMRT.

Conclusion

Cardiac morbidity has long been considered a risk of adjuvant breast cancer radiotherapy, so measuring the cardiac dose exposure is important. DHI, CI, and PTV dose distribution in consideration of cardiac, vessel, and organ doses should be important elements of treatment plans.

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