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Dosimetric Comparison of 3DCRT Planning and Forward IMRT Field in Field Techniques in Early Stage Left Breast Cancer

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Abstract

Background: The objective of the study is to compare Forwarded IMRT FiF plan with Enhance Dynamic Wedge (EDW) tangential field radiotherapy in terms of dosimetric benefits for OARs early stage left side breast cancer radiotherapy.

Materials and Methods: Twenty patients of consecutive left side breast cancer who underwent breast conserving surgery were included and without surgery patients were also included in the study. Two different methods of treatment plans were created for the entire left side breast cancer patients. Forwarded IMRT Field in Field plans (FiF) plan and Enhance Dynamic Wedge (EDW) planning's are compared for doses in the planning target volume (PTV), the organs at risk (OARs) volume including ipsilateral lung, heart, left ascending coronary artery (LAD) and the contralateral breast, the dose homogeneity index (DHI), conformity index (CI) and the monitor units (MUs) counts required for the treatment.

Results: The homogeneity conformity of the dose to planning target volume (PTV) and the dose delivered to the heart, contralateral breast, and left ascending coronary artery (LAD) were compared with two techniques in all the 20 patients. Both the radiotherapy techniques achieved comparable radiation dose delivery to PTV-95% of the prescribed dose covering > 95% of the breast PTV as well as the mean doses of the heart, ipsilateral lung, contralateral lung, aorta, left atrium, right atrium, left ventricle, right ventricle, contralateral breast. Forwarded IMRT FiF technique achieving better uniform dose distribution and conformity with lower doses to OARs and less MUs.

Conclusion: The Forwarded IMRT FiF technique achieving better dose distribution in the PTV and spare the OARs. The lesser MUs required for treatment of the Forwarded IMRT FiF technique seems to be more advantageous compared to the Enhance Dynamic Wedge plan during whole left side breast irradiation.

Keywords: Breast cancer; Enhanced dynamic wedge; Dose volume histograms; Intensity modulated radiotherapy; Field in field technique; An organ at risk; Monitor units.

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Introduction

Breast cancer is one of the leading causes of cancer death in the less developed countries of the world. 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 loco-regional recurrence and distant metastases in patients with early-stage breast cancer.[1] Randomized clinical trials in early stage left breast cancer have shown that a whole breast radiotherapy plan after breast conserving surgery improves local control and disease free survival.[2] However, the treatment related toxicity, especially cardiotoxicity, increased the risk of death and also prevented observing the actual survival benefit.[3] "Treatment planning for medial tangential and lower tangential fields of breast irradiation revealed that the amount of organs at risk (OARs) including heart and lung can be spared by using computed tomography images (CT) based on conformal Enhanced Dynamic Wedge tangential radiotherapy when compared to standard tangential irradiation".[4] Physical wedge or enhanced dynamic wedges are added to the tangential beams to compensate the missing tissue or patients contour and improve the dose uniformity and tissue heterogeneity to the entire breast tissues.

Two Tangential fields of photon beam irradiation for the whole breast irradiation after breast conserving surgery are the standard techniques in early stage breast cancer.[5,6] With tangential field's photon beam irradiation, the exposure of the heart, lung, left ascending coronary artery (LAD) directly to the radiation beam prevents the left sided breast cancer patients. However, dose distribution obtained from the open field is difficult because of the different thickness volumes of the breast tissues. Therefore, the dose distribution can be improved by using a wedge filter.[7] "Physical wedge systems are commonly used to reduce dose inhomogeneity due to different thicknesses of breast surface irregularity and tissue heterogeneity, to improve dosimetric distribution benefits and spare OARs, several investigators have described the different techniques including intensity modulated radiotherapy (IMRT), three non-coplanar conformal fields, field-in-field (FIF) technique".[8] In addition, the use of 3D-CRT that covers all of the ipsilateral breast tissue results in dose to organs at risk (OARs): heart, lung, and contralateral breast.

Therefore the Forwarded IMRT plan to improve the dose distribution to decrease the higher dose (Hot spots) region and the dose to OARs would be desirable to try and reduce these side effects of whole breast radiotherapy.[9] Therefore, dose distribution can be improved by using Enhance Dynamic wedge filters. 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.[10] One study has shown increased cardiac morbidity in patients treated with radiotherapy for left sided breast cancer compared to right sided, due to the higher cardiac doses for patients with the left sided disease.[11] "Cardiac complications can be minimized by reducing the dose to the heart, which can be achieved by using intensity-modulated radiotherapy (IMRT).

Literature has shown that IMRT decreases the dose to the heart and ipsilateral lung more effectively than 3D-CRT for patients with left breast disease".[12,13] Multiple studies have shown that the volume of the breast is important for dose homogeneity. The inhomogeneity is worse in larger size breast radiotherapy plan side effects such as breast pain and the poor cosmetic outcome may be related to dose distribution.[14,15,16,17] Critical organs for left sided breast cancer include the heart, lung, and contralateral breast. After radiotherapy, there is a long-term risk in women younger than 40 for developing secondary primary breast cancer in the right breast.[18,19]

Even though the lungs are protected by developed treatment plans, radiation pneumonitis can occur in approximately 1-5% of patients after breast radiotherapy. In our study, whole breast radiation therapy after breast conserving surgery has been performed with conformal photon beam medial and lower tangential field irradiation using Enhanced Dynamic Wedge and Forwarded IMRT FiF technique. The Forwarded IMRT FiF technique helps us to increase dose distribution, homogeneity to the entered planning target volume (PTV) while decreasing the absorbed dose in irradiated tissues outside the PTV.

In this study, we have performed a dosimetric comparison of Forwarded IMRT FiF techniques and Enhanced Dynamic Wedge, which are regularly used in our clinic during whole breast irradiation.

Materials and Methods

Twenty consecutive left-side breast cancer patients ranging from 35-66 years of age (median 54 years) has taken in this treatment planning study. All the patients underwent breast conserving surgery and patients were scanned (Siemens SOMATON Definition AS computed tomography scanner) with a 3mm slice in the supine position with civco C-Qual breast Board inclined plane on a tabletop and each patient's left arm was raised above the head to exclude it from the treatment field. Civco breast and 2 clamp thermoplastic orfit were used for patients immobilization during treatment.

To maintain immobilization during treatment, a breast board was fixed to the CT and treatment couch with loc-bars. CT images data were taken with an adjacent axial slice thickness of 3 mm, covering the entire chest with free breathing. The data obtained from CT images were transferred to the treatment planning system (TPS) (Eclipse, version 13.7; Varian Medical Systems). Planning Target volumes, organs at risk, body, and both the lungs contours were created manually of TPS. The PTV, clinical target volume (CTV), heart, left anterior descending coronary artery (LAD) and contralateral breast were delineated by the same radiation oncologist.

The CTV of the whole breast including the all visible breast parenchyma was delineated in all slices. CTV was defined medially at the lateral edge of the sternum, inferiorly at the inframammary fold, superiorly at the caudal border of the clavicle head, and laterally to include all apparent breast tissue, excluding to latissimus dorsi muscle. PTV has obtained from CTV with 3 mm margin isotopically with the crop of the left lung. Anteriorly, the PTV was cropped outside the body with additionally 2 mm.

The cranial extent of the heart included the infundibulum of the right ventricle, the right atrium, and the right atrium auricle but excluded the pulmonary trunk, the ascending aorta, and the superior vena cava. The caudal border of the heart was the lowest border of the pericardium. The contralateral breast volume was defined as the breast tissue encompassed by the tangential line between the patient's midline and the contralateral posterior border was defined as being at the same level as the treated breast.

All the LAD volumes were delineated with the help of an experienced radiation oncologist. Details of the beam arrangements and objectives of plans are described below in Figure 1 and Figure 2. Planning Techniques: We used the ECLPSE TPS (Version 13.7, Varian Medical Systems) for treatment planning. In all the treatment plans the dose specification was 50Gy, prescribed at a reference point in all techniques, in 25 fractions of 2Gy per fraction with a 6-MV photon beam from a Varian DMX treatment machine. For all plans applied, 'Analytical Anisotropic Algorithm' (AAA) was used for dose calculation in a computerized radiation treatment planning system. All treatment plans were normalized to the isodose line to give a minimum of 95% of the PTV.

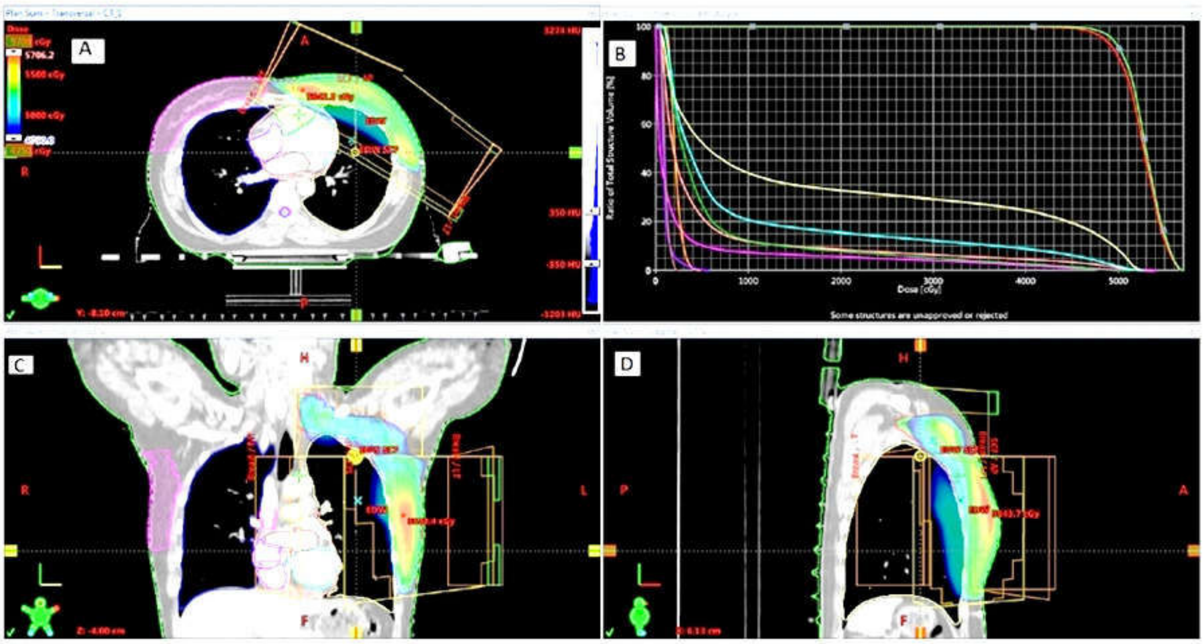


Fig. 1: Conformal radiotherapy with Enhanced dynamic wedges (DRT-EDW) technique. (A) Transverse slice of CRT-EDW. (B) Does volume histogram (DVH) red color: PTV, yellow color: ipsilateral lung, blue colour: contralateral lung, pink color: heart, cyan colour: left ventricle, dark green: right ventricle, orange colour: aorta, brown colour: left atrium, violet colour: right atrium and magenta color: contralateral breast. (C) Forntal slices of CRT-EDW. (D) Sagittal slice of CRT-EDW.

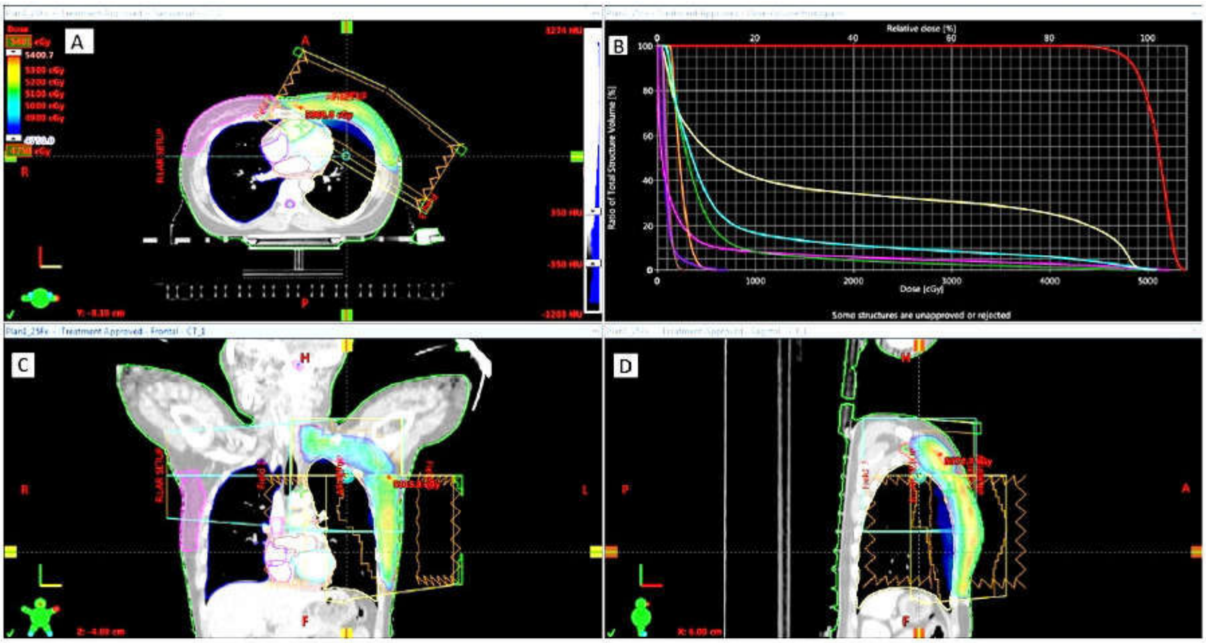


Fig. 2: Field-in-field (FIF) radiotherapy technique. (A) Transverse slice of FIF. (B) Dose volume histogram (DVH: red color: PTV, yellow color: insilateral lung, blue colour: contralateral lung, pink color: heart, cyan colour: left ventricle, dark green: right ventricle, orange colour: aorta, brown colour: left atrium, violet colour: right atrium and magenta color: contralateral breast. (C) Frontal slices of FIF. (D) Sagittal slice of FIF.

Conformal to the breast PTV, two opposing medial and lower tangential beams optimum gantry angle 45^0 to 60^0 used for PTV. We used the millennium 80 MLC to the PTV and beam's-eye-view projections used to get optimum gantry angle and also avoidance of heart, LAD, contralateral breast, and ipsilateral lung.

Enhance Dynamic wedges Technique

Enhance Dynamic wedges were used for both medial tangential and lateral tangential beams in order to achieve the dose uniformity to the PTV, and to compensate for the rapid dose changes in external contours, wedge angles were changed according to separation, thickness and curvature of the chest wall to achieve dose homogeneity, dose conformity and minimize volumes of heart, LAD and ipsilateral lung that unavoidably get included within the field borders and shielding was added the field in field adapted with the use of an 80-millennium multileaf collimator (MLC) which was 1 cm in thickness at isocentre. OAR blocked at near the PTV using MLC to reduce OAR dose.

Available Enhanced Dynamic Wedge 10^0, 15^0, 20^0, 25^0, 30^0, 45^0, 60^0 degree use on suitable Enhanced Dynamic Wedges both medial and lateral sides to reduce dose inhomogeneity in the target volume due to severe breast surface irregularity and tissue heterogeneity.

Forward IMRT Field-in-field Technique (FiF)

In the FIF technique, an open beam arrangement was first calculated and evaluated without any wedges then some subfields per gantry angle are used to produce an optimal breast plan. Generally, there are one lung MLC's block and three additional subfields per gantry angle. Lung block is formed by fitting the MLC's to the shape of the lung in lateral hot spots.

The initial calculation of the Forwarded IMRT FiF plan was performed with two equally weighted, open, tangential photon 6MV beams with the optimum gantry angle used for PTV. Hot spot blocked by using subfields which is help to achieve better dose homogeneity and also decreased the higher dose in to the PTV. After completion of plan, the main field and sub field merged as a single field.

Dosimetric evaluation: The DHI and CI were calculated for comparison of the two 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=(D5%/D95%) D5%/D95%; where D95% is the dose received by 95% of the target volume on the cDVH and is defined as the "minimum dose". D5% is the dose received by 5% of the target volume on the DVH and is defined as the "maximum dose" to the target volume. The ideal value of dose homogeneity is 1 and it increases as the plan becomes less homogeneity.

Dose volume histograms (cDVH) of PTV, contralateral breast, heart, ipsilateral lung, heart, and LAD were calculated for two different methods of the treatment plan in all patients. The dose changes in the PTV with Forwarded IMRT FiF and Enhanced Dynamic Wedge plans were compared using the dose homogeneity index (DHI) and conformity index (CI).

Conformity Index: Conformity index (CI) was used to evaluate the plan quality in terms of PTV conformity which is defined as:

CI = Reference Isodose Volume/Target Volume: Here, reference isodose volume was taken as 95% isodose volume of the PTV.

The target volume is the total volume of the PTV. CI was calculated for both sets of plans and compared.

Statistical analysis: Paired samples t-test was used for comparisons. A p-value of < 0.05 was considered to be significant.

Results

The mean volumes and standard deviations (SD) of the PTV and OAR are outlined in Table 1. The PTV volume range from 368.5cc to 932.4cc (mean and SD, 639.05±163.51). Forwarded IMRT FiF technique allowed us more homogeneity dose distribution when compared to the Enhanced Dynamic Wedge technique shown in Table 2.

Table 1: The volumes of the PTV and OAR (mean ± SD).

Parameter	Mean Volume ± SD (cc)	Maximum (cc)	Minimum (cc)
PTV	639.05±163.51	932.4	368.5
Ipsilateral Lung	1061.02±220.89	1384.3	720
Contralateral Lung	1187.13±249.78	1514.5	826.4
Heart	562.60±94.90	743.3	443.8
Breast Right	743.55±307.22	1419.4	395.9
Aorta	37.1±8.25	53.7	25.2
Left Ventricle	87.09±23.16	143.8	59.7
Right Ventricle	133.60±27.52	195.3	85.8
Left Atrium	52.72±14.67	84.6	28.5
Right Atrium	58.45±21.47	124.8	30.1

PTV: Planning target volume OAR: Organ at risk SD: Standard Deviation

Table 2: Dosimetric summary of the treatment volume and monitor units for the two planning techniques.

	FIF (mean & SD)	EDW (mean & SD)	P value (FiF vs. EDW)
PTV (V95%)	91.21±4.61	92.96±4.66	<0.001*
CI	1.75±0.21	1.97±0.31	<0.001*
DHI	0.84±0.04	0.83±0.03	0.007
MU	262.1±13.85	281.75±16.29	0.136

PTV: Planning target volume CI: Conformity index DHI: Dose homogeneity index
SD: Standard deviation FIF: Field in field MU: Monitor unit
EDW: Enhanced dynamic wed *:p<0.05, statistically significant

The average MU was 262±13.85 and 281±16.29 for Forwarded IMRT FiF and Enhanced Dynamic Wedge techniques respectively (p: 0.136). The HI values were 0.85±0.043 and 0.83±0.032 for Forwarded IMRT FiF and Enhanced Dynamic Wedge techniques respectively (p: 0.007). The CI values were 1.75±0.21 and 1.98 ±0.31 for Forwarded IMRT FiF and Enhanced Dynamic Wedge techniques respectively (p:< 0.001). The PTV V95% values were 91.21±4.61 and 92.96±4.66 for Forwarded IMRT FiF and Enhanced Dynamic Wedge techniques respectively (p :< 0.001).

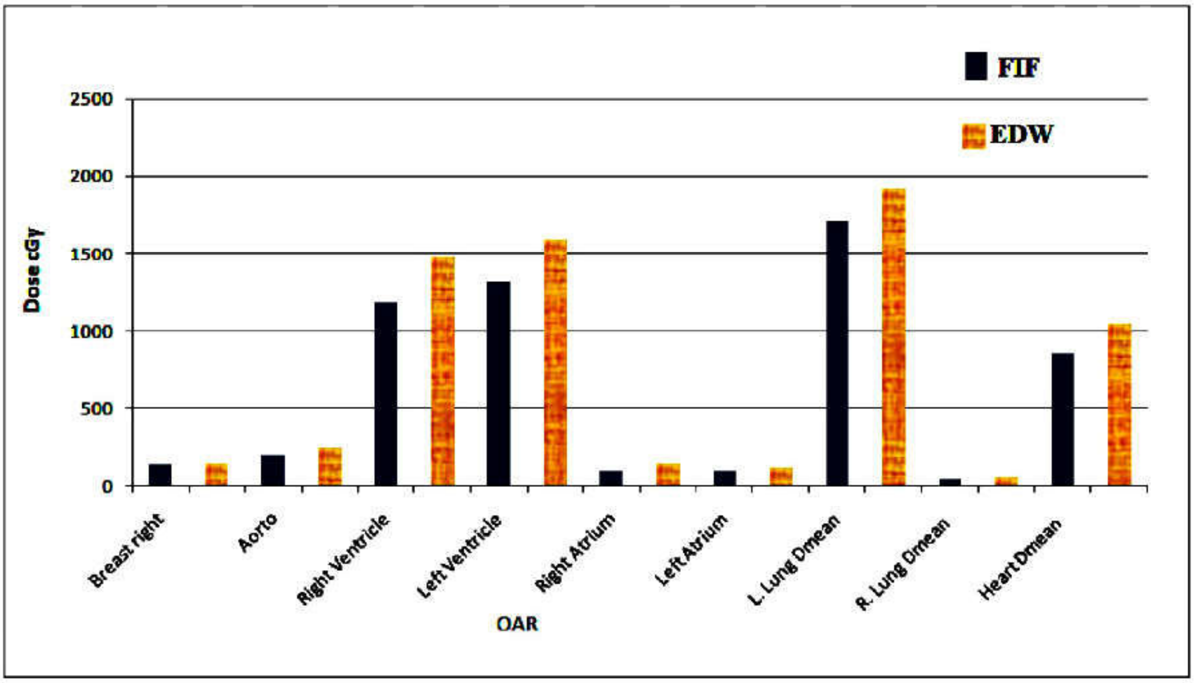
However, there wasn't any significant difference in terms of the PTV volumes that received 95% of the prescribed dose. The maximum dose of the PTV was significantly reduced with the Forwarded IMRT FiF technique (5599.6±129.72 for Enhanced

Dynamic Wedge and 5776.75±116.54for Forwarded IMRT FiF; p< 0.029). The mean dose of the PTV was significantly reduced with the Forwarded IMRT FiF technique (5083 ± 93.01for Enhanced Dynamic Wedge and 5165 ± 104.79 for Forwarded IMRT FiF (p: 0.181).

Table 3: The mean doses of the PTV and OAR

Parameter	FIF Mean ± SD (cGy)	EDW Mean ± SD (cGy)	P-value
PTV DMean	5083 ± 93.01	5165 ± 104.79	0.181
PTV DMax	5599.6±129.72	5776.75±116.54	0.029
Ipsilateral Lung	1709.6 ± 317.25	1922.7 ± 400.20	<0.001*
Contralateral Lung	48 ± 19.46	54.2 ± 15.69	<0.001*
Heart	856.1 ± 257.34	1048.6 ± 452.99	<0.001*
Breast Right	135.09 ± 94.22	150.54 ± 80.46	<0.001*
Aorta	203.98 ± 78.28	242.51 ± 122.40	<0.075
Right Ventricle	1183.7 ± 599.39	1471.42 ± 847.17	<0.001*
Left Ventricle	1314.35 ±426.7	1594.56 ± 612.83	<0.001*
Right Atrium	101.82 ± 41.98	142.83 ± 130.11	0.079
Left Atrium	102.06 ± 42.34	118.87 ± 47.38	<0.001*

PTV: Planning target volume OAR: Organ at risk SD: Standard deviation
FIF: Field in field EDW: Enhanced dynamic wedge cGy: centiGray
*:p<0.05, statistically significant



Graph 1: Graphical Representation of the mean dose of all OAR.

The mean doses of the OARs (ipsilateral lung, contralateral breast, Heart, right breast, aorta, right ventricle, left ventricle, right atrium, and left atrium) were significantly decreased with the Forwarded IMRT FiF technique (p values were <0.001 for each) Table 3 and Graph 1.

The Forwarded IMRT FiF only seems to reduce the mean dose of the ipsilateral lung when compared with Enhanced Dynamic Wedge (P=0.001). The heart mean dose values 856.1 ± 257.34 and 1048.6 ± 452.99 for Forwarded IMRT FiF and Enhanced Dynamic Wedge techniques respectively (p:< 0.001).

Discussion

This study was compared the dosimetric comparison of two treatment techniques in breast cancer patients FiF-IMRT vs. Enhanced Dynamic Wedge and to identify patient characteristics that can predict which patients would benefit the most from an intensive technique. It is difficult to directly compare the calculated mean values to the data from the literature because most studies do not include brief technical notes and there is great variability in the definitions of the planned targets. In addition, the volumetric parameters that were compared are very different, and different ways of calculating the DHI and CI were employed. Therefore, the results of this comparison were considered with other comparison studies in the literature.

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.[20] In this treatment planning study we compared two different techniques for left breast cancer patients and found that the Forwarded IMRT FiF technique was superior to the Enhanced Dynamic Wedge technique in terms of dose homogeneity and absorbed dose in irradiated tissues outside the PTV. Conservative surgery followed by postoperative radiotherapy is known as the gold standard treatment in early stage breast cancer.

Various three-dimensional CT-based breast radiotherapy techniques have been established to achieve uniform dose distribution in the PTV while sparing the OARs. The tangential field technique with Forwarded IMRT FiF, which is used to optimize the dose distribution, has been shown to provide excellent local control with rare long-term complications.[21,22] One of the main disadvantages of the wedge is that as the wedge angle increases, Mean dose of OAR and patients dose is increasing due to higher MU in Wedge field.[23,24]

On the other hand with treatment plans performed with tangential fields, as the Enhanced Dynamic Wedge wedge angle is used to decrease the extra dose at the top of the breast is increased dose in the medial and lateral beam entries are also increased as well as a degreased center of the PTV dose. It has been shown by many investigators that the use of the FiF technique improves dose distribution during whole breast irradiation.[25, 26,27]

In Enhanced Dynamic Wedge plans, the maximum dose was at the bottom of the wedge, so the contralateral breast dose was higher than that. The MLC is used instead of wedges for FiF technique.

The use of MLC allows decreasing scattered doses to the contralateral breast and other parts of the body when compared to Enhanced Dynamic Wedge tangential field technique with Enhanced Dynamic Wedge wedges.[28,29] Moreover some hotspots may persist even after the use of Enhanced Dynamic Wedge due to extreme tissue inhomogeneities and contour irregularities. This can be avoided by adopting the Forwarded IMRT FiF technique.[30] Radiotherapy may induce local tissue damage that in turn, depending on the severity and the volume affected, may lead to organ dysfunction. Organ dysfunction may be clinical (symptomatic) or subclinical (asymptomatic).

Within individual datasets, there are usually strong correlations between the different dosimetric parameters and thus this may partly obscure any "optimal" threshold. Furthermore, the correlations between dosimetric parameters are technique-dependent, and readers should carefully assess the similarity of their treatment technique to the historical reports before using any of these limits as clinical constraints. In the literature, in the current study, we used mean dose values to better define the dose constricts for each OAR. In our study, the Forwarded IMRT FiF tech significantly reduced the mean dose values of the contralateral breast.

Our analysis also indicate that with the Forwarded IMRT FiF technique heart mean dose receiving decreased significantly in FiF technique. Similarly, mean dose values for the ipsilateral lung were significantly reduced with the Forwarded IMRT FiF technique when compared to the conformal radiotherapy Enhanced Dynamic Wedge technique. Additionally, we evaluated the doses in the mean dose of LAD which is an important branch of the left main coronary artery supply the anterior and anterolateral walls of the left ventricle and the anterior two-thirds of the septum.

The LAD mean dose receiving reduced significantly with the FiF technique.[31] Our results showed that the CI is convenient in Forwarded IMRT FiF which means that healthy tissues were well protected. The DHI in Forwarded IMRT FiF plans was better, which means dose distribution in PTV volume is more homogeneous. The Forwarded IMRT FiF technique provided lower mean dose values for the entire OAR. The use of the Forwarded IMRT FiF effectively improved PTV conformity, while spare the OARs from tangential irradiation during whole breast irradiation treatment.

They also found that the Forwarded IMRT FiF technique required less MUs for delivering a plan as compared to Enhanced Dynamic Wedge based treatment planning which was at a statistically significant level. In our study, we have also demonstrated that the MUs required for the Forwarded IMRT FiF technique were lower when compared to the conformal radiotherapy Enhanced Dynamic Wedge technique. This is because in the Forwarded IMRT FiF technique, the MUs are adjusted among the sub-fields and even an increase in the number of sub-fields won't have much change in the MU. This is the biggest advantage of the Forwarded IMRT FiF technique in radiotherapy.

They also concluded that the Forwarded IMRT FiF technique provided an advantage in terms of quality assurance as it did not require quality control for pretreatment plan confirmation. The MUs required for the Forwarded IMRT FiF technique were also lower compared to the conformal radiotherapy technique in this study. The Forwarded IMRT FiF technique significantly improved homogeneity in the PTV and reduced Radiation Therapy Oncology Group (RTOG) grade II acute skin toxicity when compared to conventional tangential field RT with Enhanced Dynamic Wedges.

Our results were compatible with the results of these two studies. Additionally, we evaluated the LAD doses in the current study. Our results were in favor of the FIF technique in terms of the LAD doses. In our study, we did not consider the body mass index (BMI) and breast size of our patients. However, it has been known that there is a significant association between breast size and dose homogeneity.[32] Moreover, breast size is a risk factor for late adverse effects during whole breast irradiation. Our median PTV volume for 20 patients was 639.05 cc (range 932.4-368.5). We think that it is a limitation of our study.

Conclusions

The use of the postoperative forward IMRT planned field in field for whole breast radiation improved dosimetric parameters of homogeneity and conformity to the target, allowing a significant reduction in the doses received by OARs. The forwarded planning tangent FiF should be consider than Enhance Dynamic Wedge (EDW) whenever a homogenous dose distribution within the breast is desired reducing treatment time and scatter radiation to patients. Particularly in patients with large breast volumes and separation forward IMRT planning FiF also provides a slightly increased benefit in sparing the ipsilateral lung. The lower MU counts required for forward IMRT FiF techniques can be considered an advantage as it shortens the treatment time for most patients and more intensive techniques could be used for these patients.

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