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Dosimetric comparison of whole breast radiotherapy using field in field and conformal radiotherapy techniques in early stage breast cancer

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Background: We aimed to compare field-in-field technique (FIF) with conformal tangential field radiotherapy (CRT) in terms of dosimetric benefits for early stage breast cancer radiotherapy. ***Materials and Methods:*** Twenty consecutive left-side breast cancer patients who underwent breast-conserving surgery were included to the study. For each patient, two different treatment plans were created for the entire breast. FIF plans and CRT plans were compared for doses in the planning target volume (PTV), the organ at risk (OAR) volume including ipsilateral lung, heart, left ascending coronary artery (LAD) and the contralateral breast, the homogeneity index (HI), and the monitor unit (MU) counts required for the treatment. Paired samples *t*-test was used for statistical analysis. ***Results:*** The FIF technique significantly reduced the maximum dose of the PTV as well as the mean doses of the heart, LAD, ipsilateral lung and the contralateral breast (p values were <0.001 for each). When the OAR volumes irradiated with 2, 5, 10, 20, 30 and 40 Gy were compared, the results were in favor of the FIF technique. The volume receiving <20 Gy of the prescription dose for the ipsilateral lung was significantly decreased using FIF technique (p<0.001). FIF technique allowed us more homogenous dose distribution with lower MUs. ***Conclusion:*** The FIF technique provided better dose distribution in the PTV and significantly reduced the doses in the OAR. Considering the lower MUs required for treatment the FIF technique seems to be more advantageous than CRT during whole breast irradiation. **Iran. J. Radiat. Res., 2012; 10(3-4): 131-138**

Keywords: *Breast cancer, conformal radiotherapy, dose volume histograms, field-in-field technique.*

INTRODUCTION

Randomized clinical trials in early stage breast cancer have shown that whole breast radiotherapy (RT) after breast conserving surgery improves local control and disease free survival (1). However the treatment related toxicity, especially cardiotoxicity, increased the risk of death and also prevented to observe the actual survival benefit (2). In parallel to the developments in the field of radiation treatment deleterious side effects of whole breast RT have been decreased. Treatment planning for tangential breast irradiation revealed that the amount of organ at risk (OAR) including heart and lung can be spared by using computed tomography (CT) based conformal tangential radiotherapy (CRT) when compared to standard tangential irradiation (3).

Tangential photon beam irradiation to whole breast after breast conserving surgery is regarded as the standard approach in early stage breast cancer (4-6). With irradiation from tangential fields, exposure of heart directly to the radiation is prevented in patients with left-sided breast cancer. However, dose distribution obtained from open field beams is complicated because of the complex volume of the breast. Therefore, dose distribution can be improved by using wedge filters (7). Conventional hard wedge (HW) systems are commonly used to reduce dose inhomogeneity due to severe breast surface irregularity and tissue heterogeneity.

In order to improve dosimetric benefits and spare OAR, several investigators have

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described the different techniques including intensity modulated RT (IMRT), three non-coplanar conformal fields, field-in-field (FIF) technique (8). In our clinic, whole breast RT after breast conserving surgery has been performed with conformal tangential field irradiation using HW and/or FIF technique. The FIF technique helps us to increase dose homogeneity to the planning target volume (PTV) while decreasing the absorbed dose in irradiated tissues outside the PTV. In this study we performed a dosimetric comparison of FIF RT and CRT with HW, which are frequently used in our clinic during whole breast irradiation.

MATERIALS AND METHODS

Twenty consecutive left-side breast cancer patients ranging from 39-73 years of age (median 54 years) were examined in this treatment planning study. All the patients underwent breast-conserving surgery. Patients were scanned in the supine position with Civco C-Qual breast inclined plane on a table top. To maintain the treatment position, a breast board was fixed to the CT and treatment table with the help of the loc-bars. CT data were acquired with adjacent axial slice spacing 5 mm, covering the entire chest with normal free breathing. The data obtained from CT were transferred to the treatment planning system (TPS) (Eclipse, version 8.6; Varian Medical Systems).

Target volumes and organs at risk

Body and lung contours were created using an automatic contouring feature 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 all visible breast parenchyma was delineated on each slice. CTV was defined medially at the lateral edge of the sternum, inferiorly at the inframammarian fold, superiorly at the caudal border of the clavicle head and laterally to include all apparent breast tissue, excluding to latissimus dorsi muscle. A PTV was generated by expanding the CTV 5 mm isotopically. Anteriorly, the PTV was corrected for being 5 mm inside the skin surface.

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 by the help of an experienced radiologist.

Tangential field radiotherapy with conventional hard wedges

All the treatment planes were created by the same medical physicist. Conformal to the breast PTV, two opposing tangential beams were constructed. We used 1cm margin between the MLC and PTV. With the use of beam's-eye-view projections gantry angles were determined to achieve maximum avoidance of heart, LAD, contralateral breast and ipsilateral lung. Shielding was adapted with use of a multileaf collimator (MLC) which was 1 cm in thickness. We used MLC especially for the shielding of the entire OAR which located nearby the PTV. We used HW systems on both medial and lateral sides to reduce dose inhomogeneity in the target volume due to severe breast surface irregularity and tissue heterogeneity (figure 1).

Field-in-field radiotherapy

The initial calculation of FIF plan was performed with two equally weighted, open, tangential photon beams with the same gantry angle used for CRT with physical wedges (figure 2). Hot spot volumes blocking two or three subfields were determined to improve dose homogeneity while decrease to overdoses in the PTV. The main field and the subfields were merged into one portal.

Dosimetric evaluation

In this study, Varian millennium 80-leaf collimators (MLC) (Varian Medical Systems) were used. The treatment dose for each patient was 2 Gy/fraction with a total 25 fractions. The plan was normalized to the isodose line to give a minimum of 50 Gy to %95 of the PTV. Dose volume histograms (DVHs) of PTV, contralateral breast, heart, ipsilateral lung, heart and LAD were calculated for each treatment plan in all patients.

Dose changes in the PTV with CRT and FIF RT plans were compared using the dose homogeneity index (DHI). The homogeneity index was defined as follows (9):

$$DHI = \frac{D2 - D98}{D_{prescription}} \times 100$$

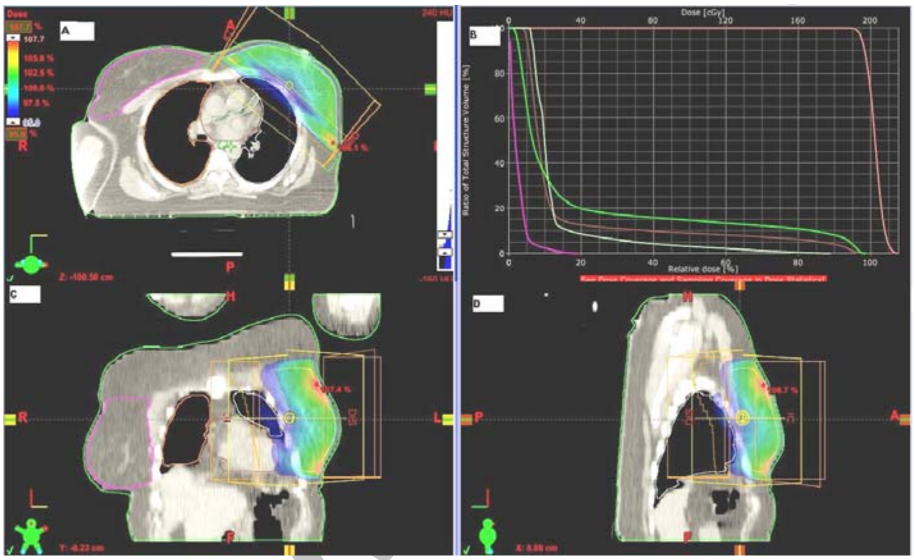

Figure 1. Conformal radiotherapy with hard wedges (CRT-HW) technique. a) Transverse slice of CRT-HW. b) Dose volume histogram (DVH): pink color: PTV, green color: ipsilateral lung, brown color: heart, light green color: LAD and magenta color: contralateral breast. c) Frontal slice of CRT-HW. d) Sagittal slice of CRT-HW.

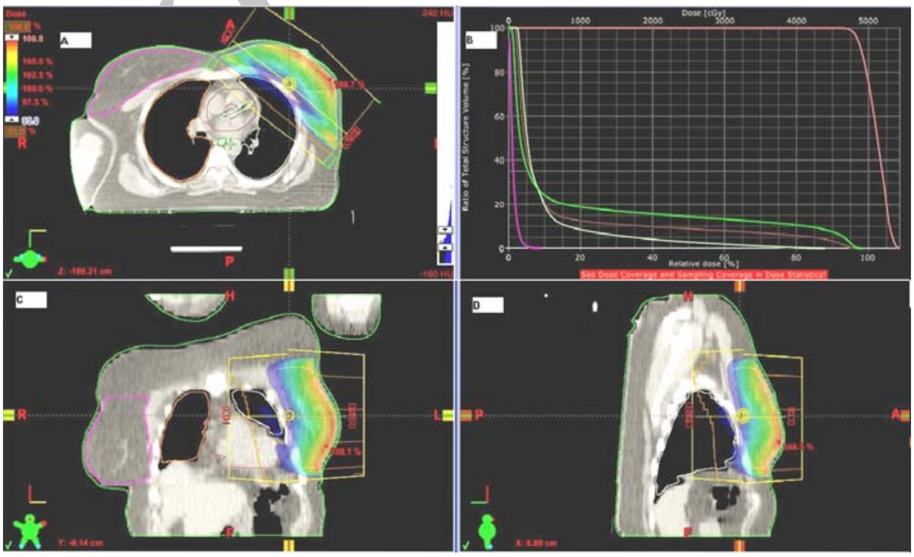

Figure 2. Field-in-field (FIF) radiotherapy technique. a) Transverse slice of FIF. b) Dose volume histogram (DVH): pink color: PTV, green color: ipsilateral lung, brown color: heart, light green color: LAD and magenta color: contralateral breast. c) Frontal slice of FIF. d) Sagittal slice of FIF.

In this formula, D98 represents the dose to the 98% of the volume as displayed on the cumulative DVH. It means that 98% of the target volume receives this dose or higher and considered to be the “minimum dose.” D2 is the dose to the 2% of the target volume, as displayed on the DVH, indicating that only 2% of the target volume receives this dose or higher. This is considered to be the “maximum dose.”

PTV doses were compared on the basis of the maximum, minimum and the mean doses as well as the percent volumes receiving at least 95 of the prescribed dose (V95). The maximum, minimum and the mean doses of contralateral breast, heart, ipsilateral lung, LAD and Monitor Unit (MU) settings required for each plan were also compared. Tissue volumes in the all critical organs receiving 2, 5, 10, 20, 30 and 40 Gy were evaluated.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 11.0 was used for statistical analysis (SPSS Inc. Chicago, II., USA). 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. FIF technique allowed us more homogenous dose distribution when compared to CRT technique. The DHI values were 1.14±0.30 and 1.16 ±0.04 for FIF and CRT techniques respectively (p: 0.02).

The maximum dose of the PTV was significantly reduced with the FIF technique (5444.8±162.1 for CRT and 5307.4±150.6 for FIF; p< 0.001). However there wasn’t any significant difference in terms of the PTV volumes that received % 95 of the prescribed dose (p: 0.067).

The mean doses of the OAR (heart, LAD, ipsilateral lung and the contralateral breast) were significantly decreased with FIF technique (p values were <0.001 for each) (table 2). When the OAR volumes irradiated with 2, 5, 10, 20, 30 and 40 Gy were evaluated, the results were in favor of the FIF technique (table 3). The ipsilateral lung volumes irradiated with 2, 10, 20, 30 and 40 Gy were significantly reduced with FIF technique (p values were: 0.001, 0.004 for V2 and V10 and <0.001 for V20, V30 and V40). The V2, V30 and V40 values for the heart were significantly lower with the FIF technique when compared to CRT technique (p values were 0.034, <0.001 and <0.001 respectively). When the LAD volumes irradiated with 20, 30 and 40 Gy were evaluated, the FIF technique allowed lower values when compared to CRT (p values were 0.007, <0.001 and <0.001 respectively). The V2, V5, V10, V20, V30 and V40 values for the contralateral breast were significantly lower with FIF technique (p values were 0.001 for V2 and V5 and <0.001 for others).

The average MU values used in the FIF technique were significantly lower than the CRT technique (p<0.001). The mean MU counts ± SD required for CRT and FIF techniques were 284.8±30.4 and 224.5±9 respectively.

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

Parameter	Mean Volume ± SD (cc)	Maximum (cc)	Minimum (cc)
PTV	595.6±301.3	1015	198.3
Ipsilateral Lung	1080.1±221.4	1433.7	716.4
Heart	543.7±133.1	884.1	395.5
LAD	5.6±1.5	7.6	3.3
Contralateral Breast	647.6±202.5	1078.1	452.5

PTV: Planning target volume
SD: Standard Deviation
OAR: Organ at risk
LAD: Left Ascending Coronary Artery

Table 2. The mean doses of the PTV and OAR.

Parameter	HW mean ± SD (cGy)	FIF mean ± SD (cGy)	P
PTV	5063.3±101.1	5057±89.5	0.632
Ipsilateral Lung	984.4±258.5	765.0±223.3	<0.001*
Heart	702.6±178.0	509.9±217.8	<0.001*
LAD	658.1±392.5	447.4±423.3	<0.001*
Contralateral Breast	129.5±64.1	57.0±33.8	<0.001*

PTV: Planning target volume
LAD: left anterior descending coronary artery
*: p< 0.05, statistically significant
OAR: Organ at risk
HW: Hard wedge
SD: Standard Deviation
Gy: Gray

Table 3. V2, V5, V10, V20, V30 and V40 values of OAR.

Parameter	HW mean ± SD (cGy)	FIF mean ± SD (cGy)	p
V2			
Ipsilateral Lung	4859.1±314.7	4679.0±364.9	0.001*
Heart	4238.2±816.0	3986.3±1105.7	0.034*
LAD	2086.9±1549.9	1866.1±1805.6	0.337
Contralateral Breast	387.9±261.9	211.2±187.7	0.001*
V5			
Ipsilateral Lung	4495.8±841.5	4344.6±836.6	0.093
Heart	3084.6±1262.1	2886.7±1521.9	0.203
LAD	1666.4±1379.6	1517.5±1677.4	0.468
Contralateral Breast	309.1±120.7	153.1±120.7	0.001*
V10			
Ipsilateral Lung	3677.2±1367.4	3347.1±1429.2	0.004*
Heart	1635.4±1309.7	1406.2±1252.4	0.106
LAD	1352.4±1038.2	1138.4±1072.7	0.242
Contralateral Breast	242.6±135.1	99.7±51.6	<0.001*
V20			
Ipsilateral Lung	921.9±433.8	661.7±446.9	<0.001*
Heart	853.9±969.8	603.6±1009.3	0.437
LAD	1056.2±1234.6	764.3±1232.6	0.007*
Contralateral Breast	178.4±75.4	73.5±38.6	<0.001*
V30			
Ipsilateral Lung	520.7±205.9	265.4±112.7	<0.001*
Heart	487.0±127.4	246.0±64.7	<0.001*
LAD	726.1±575.9	466.7±600.3	<0.001*
Contralateral Breast	138.2±63.7	57.3±29.7	<0.001*
V40			
Ipsilateral Lung	382.2±164.9	172.6±53.6	<0.001*
Heart	413.1±109.8	223.5±105.4	0.001*
LAD	502.4±194.6	265.2±120.9	<0.001*
Contralateral Breast	106.7±53.6	45.8±24.0	<0.001*

OAR: Organ at risk
HW: Hard wedge
SD: Standard Deviation
Gy: Gray
LAD: left anterior descending coronary artery
*: p< 0.05, statistically significant

DISCUSSION

In this treatment planning study we compared two different techniques for tangential breast irradiation in left-side breast cancer patients and found that FIF technique was superior to CRT technique in terms of dose homogeneity and absorbed dose in irradiated tissues outside the PTV.

Conservative surgery followed by postoperative RT is known as gold standard treatment in early stage breast cancer. Various three-dimensional CT-based breast RT techniques have been established to provide homogenous dose distribution in the target volume while sparing the nearby tissues. The tangential field technique with wedge filters, which is used for in optimize the dose distribution, have been shown to provide excellent local control with rare long-term complications (10, 11). One of the main disadvantages of wedge is that as the angle increases, the scatter component from the wedge also increases resulting in increased unwanted dose to the patients (12-14). On the other hand with treatment plans performed with tangential fields, as the wedge angle 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 (6).

In has been shown by many investigators that use of the FIF technique improve dose distribution during whole breast irradiation (6, 8, 15-18). 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 conventional tangential field technique with wedges (19-20). Moreover some hotspots may persist even after the use of wedge due to extreme tissue inhomogeneities and contour irregularities. This can be avoided by adopting the FIF technique (12).

RT 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) (21). Various Vx values (percentage organ volume receiving ≥ x Gy) are associated with radiation induced normal tissue damage risk. Within individual datasets there are usually strong correlations between the different dosimetric parameters (e.g., V5 and V20), 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 (22). Like the similar studies in the literature, in the current study we used V2, V5, V10, V20, V30 and V40 values in order to better define the dose constricts for each OAR.

In our study, in parallel to the literature data, the FIF technique significantly reduced the V2, V5, V10, V20, V30 and V40 values of the contralateral breast. Our results also showed that with the FIF technique heart volumes receiving 2, 30 and 40 Gy were decreased significantly. Similarly V2, V10, V20 and V30 and V40 values for the ipsilateral lung were significantly reduced with FIF technique when compared to CRT technique.

Additionally we evaluated the doses in LAD which is an important branch of the left main coronary artery supplying supply the anterior and anterolateral walls of the left ventricle and the anterior two-thirds of the septum. Although the DVHs of coronary vessels from irradiation of the intact left breast was reported by Storey and colleagues (23) to best of our knowledge there is no dosimetric study assessing the LAD during left-side breast irradiation using two different techniques in the literature. The LAD volumes receiving 20, 30 and 40 Gy were reduced significantly with FIF technique. The FIF technique provided lower V30 and V40 values for the entire OAR.

There are several studies in the literature comparing the dosimetry in the FIF and standard radiotherapy techniques for whole breast RT (6, 7, 12, 18, 24, 25). Prabhakar and colleagues showed that the use of FIF effectively improved PTV conformity, while saving the OARs from tangential irradiation during whole breast irradiation treatment (12). They also found that FIF technique required less MUs for delivering a plan as compared to a physical wedge based treatment planning which was at statistically significant level. In our study we have also demonstrated that the MUs required for the FIF technique was lower when compared to CRT technique. This is due to the fact that in 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 MUs. This is the biggest advantage of advocating FIF technique in radiotherapy (12).

Ercan and colleagues reported in their study that the FIF technique, compared to CRT, for whole breast RT enables significantly better dose distribution in the PTV while decreasing the doses received by heart, the ipsilateral lung and surrounding tissue (6). They also concluded that the 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 FIF technique was also lower compared to CRT technique in this study. Sasaoka and Futami also showed that 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 physical wedges (8). 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 (26). Moreover breast size is a risk factor for late adverse affects during whole breast irradiation. Our median PTV volume for 20 patients was 595.6 cc (range 1015-198.3). We think that it is a limitation of our study.

In conclusion FIF technique for breast irradiation after breast conserving surgery enables significant increase in dose homogeneity in the PTV while allowing significant reduction in the doses received by OAR. The lower MU counts required for FIF techniques can be considered an advantage as it shortens the treatment time for most patients and could result in increased patient throughput on a linac.

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