

Determination and comparison of dosimetric parameters of three-dimensional conformal radiotherapy, field in field, and intensity-modulated radiotherapy techniques in radiotherapy of breast conserving patients

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ABSTRACT

Purpose: Three radiation therapy techniques for breast are common, namely three-dimensional conformal radiotherapy (3D-CRT), Field-in-Field (FIF), and Intensity-Modulated Radiotherapy (IMRT). The purpose of this study was to determine and compare dosimetric parameters of three different treatment planning types; 3D-CRT, FIF, and IMRT in target and normal tissues after breast-conserving surgery.

Methods: One hundred patients with left or right breast cancer cooperated in this study. They were divided into three categories (small, medium, and large size) based on breast volume. Three treatment planning techniques were carried out by planner for each patient in Prowess® 5.2 Treatment Planning System. The dosimetric parameters were obtained from dose-volume histograms using the CERR software (MATLAB Company, Washington, USA), which runs as an add-on in MATLAB software.

Results: 3D-CRT technique with the highest value of D_{max} creates more hot spots than the other techniques in the tumor region ($P = 0.013$). IMRT and FIF showed the best uniformity compared to 3D-CRT in all groups with respect to the values of the parameters D_{98} and D_2 . IMRT provided the best coverage in the tumor compared to other methods ($P < 0.001$). 3D-CRT technique yielded a high volume receiving $\geq 107\%$ of the prescription dose ($P < 0.001$). Among the three methods, the FIF method results in a lower dose to the lung for treatment based on the V_5 and V_{20} parameters ($P < 0.001$). Homogeneity index for IMRT was better than FIF, as well as, conformity index (CI) for IMRT and FIF was better than 3D-CRT.

Conclusion: IMRT and FIF plans offered excellent target coverage and uniformity, whereas FIF had better protection of healthy tissues. Thus FIF method is an efficient method to improve the quality of treatment for breast cancer patients.

KEY WORDS: Breast neoplasms, field-in-field, intensity-modulated radiotherapy, three-dimensional conformal radiotherapy

INTRODUCTION

Breast cancer is the most common cancer in women.^[1] It can be treated by using a multimodality approach of surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapy. Adjuvant radiotherapy following surgery is usually recommended for the treatment of breast cancer in patients.^[1] Radiotherapy has an important role in the prevention of local and regional recurrences after breast-conserving surgery. In radiotherapy, the goal is to deliver the dose to the tumoral tissue as well as sparing normal tissues.^[2]

To achieve the goal, various radiotherapy techniques developed dose distributions in the target and decreasing doses in healthy tissues.

Some studies^[3-6] aimed at finding the best therapeutic method to assess dosimetric parameters

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among current methods, including three-dimensional conformal radiotherapy (3D-CRT), Field-in-Field (FIF), and Intensity-Modulated Radiotherapy (IMRT).

3D-CRT technique was used as the standard care of irradiation of breast until 2000. It was frequently performed using two opposing tangential fields which allow acceptable coverage of the breast tissue while minimizing the dose to the adjacent critical structures (i.e., ipsilateral lung, contralateral lung, contralateral breast, and heart). FIF technique is designed by creating sub fields in the tangential fields using multileaf collimator (MLCs), while not using the physical wedge. In this method, hot spots and cold spots are reduced.^[7] In FIF technique, segment is designed and the dose distribution is obtained, but in IMRT technique, dose is presented and segment is obtained. IMRT uses special beam modifiers to vary or modulate the intensity of the radiation over the field of delivery.

Literature show much controversy on the use of these techniques;^[8,9] each technique has its own advantages and disadvantages. In 3D-CRT method, the main advantage is simplicity of planning and treatment process and the main disadvantage is nonuniform dose distribution.^[9] For FIF, uniform dose distribution and spare of normal tissues are important advantages, while requiring high skill and long time in planning are disadvantages.^[10] In IMRT method, the advantages include high coverage in breast and improvement conformity index (CI), and the disadvantages include the need for quality control and long time for planning and treatment.^[11]

There are several studies^[8,12] which have shown the superiority of IMRT method compared to the other two methods. On the other hand, there are several investigations^[13,14] reported that FIF is as an effective method. In Iran, 3D-CRT technique is common for breast radiotherapy and FIF and IMRT have not been sufficiently developed. Therefore, due to the increasing rate of breast cancer patients, finding the effective radiotherapy technique is an important issue.

The aim of this study was to determine and compare the dosimetric parameters in 3D-CRT, FIF, and IMRT techniques in breast-conserving patients.

METHODS

Patients

This study was approved by the Institutional Review Board (98-6389). Computed tomography (CT, 2 slice, Siemens, Munich, Germany) scan images of 100 patients with breast cancer were used. The patients referred to the XXX, during 2015 to 2018. Furthermore, all patients in our center signed the consent form regarding the use of their CT data for research agenda. At the time of CT scan, the patients were placed in the supine position on the breast board, while the ipsilateral

arm was placed above their heads. To position the patient reproducibly, the angulation of the breast board and X and Y-coordinate was noted using breast board coordinate scale. It is notable that, the breast board and marker positioning in the chest wall along with the tattoo markers used for patient reproducibility at the time of simulation and treatment. The CT images were obtained with a slice thickness of 5 mm using Siemens 2 Slice CT Scanner. The CT data in Digital Imaging and Communication in Medicine format were transferred to the Treatment Planning System (TPS) for both contouring and planning.

Target volume and delineation of organs at risk

The target volumes and critical structures were delineated on the CT data by a radiation oncologist using Prowess® Panther Version 5.2 (Prowess® Inc, Prowess Panther, California, USA) TPS. TPS was commissioned using CIRS phantom and validated by Atomic Energy Organization of Iran which is the principal authority for any radiation-related affairs. The whole breast tissue was outlined as the planning target volume (PTV). The ipsilateral lung, heart, contralateral lung, and contralateral breast were also contoured as organs at risk (OARs).

Treatment planning

All patient treatment plans were designed to dose 50 Gy to the PTV in 25 fractions with a 6-MV photon beam from Siemens ONCOR® treatment machine. The PTV of each patient was planned by planner, the CTV to PTV margins in different directions, were 9, 11, and 8 mm in lateral, anterior-posterior, and superior-inferior directions, respectively. These margins were choose regarding the patients setup errors and patients intra-fraction motions obtained from the Van Herk *et al.* method.^[15] In 3D-CRT plans, two opposite tangential beams were constructed to conform to whole breast PTV. A margin of 2 cm between the (OPTIFOCUS) MLC and PTV was set in anterior (air side) direction and 5 mm margin in the lung side direction as well. Physical wedge filters were used, and the angles or degrees were chosen according to PTV coverage and breast size [Figure 1]. Fields were set up to minimize the dose to ipsilateral lung, heart, contralateral breast, and contralateral lung and maximize the target coverage, using Beam Eye View (BEV). Critical organs were shielded using MLC without compromising with the PTV coverage. Beam weights were adjusted until the optimum coverage and acceptable hot spots were achieved. In addition PTV was set to receive 95% of the prescribed dose. In the FIF technique [Figure 2], each two tangential beams were divided into two different segments. One segment was designed to whole breast regions without filters (with 6 MV photons). A second segment (usually with photons of 18 MV energy to increase the dose to the deepest part of the breast while sparing the most superficial part) for the deepest area of under dosage to compensate tissue deficiency in thick breast. The MLCs were manipulated to shield the areas of the breast receiving any dose on the BEV (mainly at 105%–107% of the prescription dose). By the MLCs movement, hot and cold points were reduced in the subfields. For IMRT

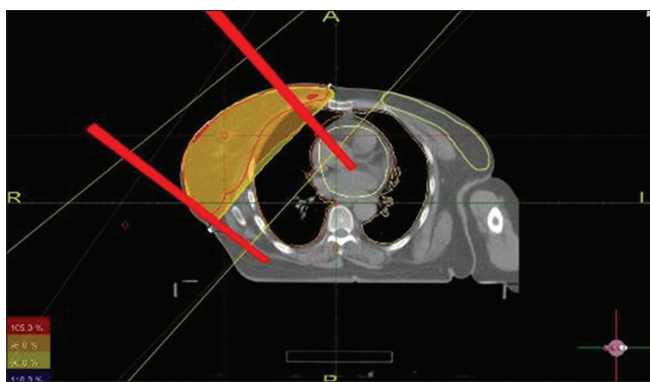


Figure 1: An example of three dimensional conformal radiotherapy fields (medial and lateral) used in current study. The planning target volume in red, the heart in yellow, the contralateral breast in green and the lungs in orange

technique [Figure 3], both tangential fields were copied in the new plan and nine segments per field were considered. Dose was prescribed to the PTV, and dose constraints were set to the TPS. Normal tissues constraints include: For ipsilateral lung, no more than 40% of the volume can receive the 30.0% of the prescribed dose ($V_{30\%} < 40\%$), and 20.0% of the volume can receive the maximum dose of 40.0% of prescribed dose ($V_{40\%} < 20\%$). For heart, no more than 30% of the volume can receive the 40.0% of the prescribed dose ($V_{40\%} < 30\%$), and the mean dose must be lower than 20 Gy (or 50% of the prescribed dose). For contralateral lung, no more than 20% of the volume can receive the 10.0% of the prescribed dose ($V_{10\%} < 20\%$).^[16]

The dose calculation was done by using Collapsed Cone Convolution Superposition (CCCS) algorithm.

Dosimetric comparisons

DVHs were drawn up for each technique and dosimetric parameters (D_x and V_x) were evaluated, using the CERR software, which runs as an add-on in MATLAB®:2016b software. D_x (cGy) is the minimum dose that delivered to the x% of the organ/structure volume and V_x (%) is the percentage volume of the organ/structure which received at least x% of the prescribed dose. We compared D_{98} (cGy), D_2 (cGy), D_{50} (cGy), V_{95} (%), and V_{107} (%) parameters for comparing PTV dose distribution among different radiotherapy techniques. Further parameters including V_5 (%) (for ipsilateral lung, contralateral lung, and contralateral breast), V_{10} (%) (for contralateral breast), V_{20} (%) (for ipsilateral lung, contralateral lung, and heart), V_{25} (%) (for heart), and V_{30} (%) (for heart) were used for comparing the doses received by OARs.

D_{max} (cGy) and D_{min} (cGy) as the maximum and minimum point doses received by the PTV were used for comparing the PTV dose; furthermore, homogeneity index (HI) and CI as explained by the (international commission of radiation units and measurements) report,^[17] were obtained and used for comparing the homogeneity and conformity of the dose distributions among different radiotherapy techniques.

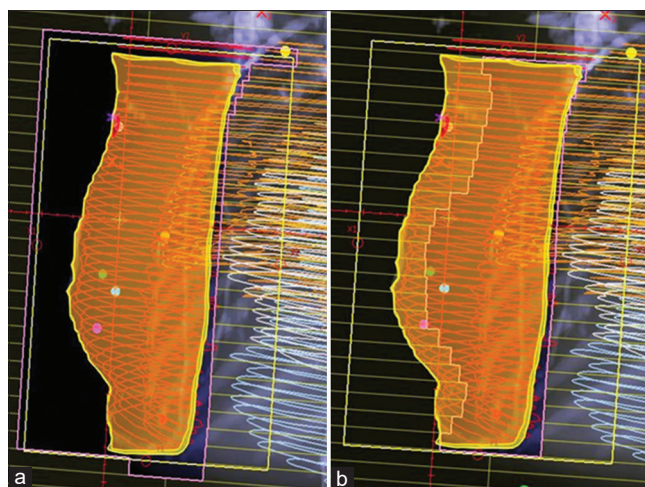


Figure 2: (a) An example of the main field without multileaf collimator blocking and (b) sub-field in the Field-in-Field technique

Statistical analysis

In this study, 100 female patients with a mean age of 43.2 ± 12.1 years were included. The patients were categorized into three groups according to the volume of the breast tissue: (a) 25 patients in the small breast volume group (< 1170 cc), (b) 50 patients in the medium breast volume group ($1170 \text{cc} \leq$ and ≥ 1721 cc), and (c) 25 others in the large breast volume group (> 1721 cc). Mean and standard deviation for each parameter were reported, and the comparisons were performed using the one-way analysis of variance (ANOVA) for all patients with and without considering breast volume in the three methods. In addition, intergroup comparisons of extracted parameters with and without breast volume were performed using *post hoc* test. The Statistical Package for the Social Sciences (SPSS) software version 22.0 (IBM Company, New YORK, USA) was used for the statistical analyses. For statistical analysis, P value less than 0.05 was considered to be statistically significant.

RESULTS

D_{max} , D_{min} , D_{98} , D_2 , V_{95} , and V_{107} along with the HI and CI values for PTV are presented for comparison of three techniques in Table 1. In *post hoc* test, significant differences for D_{max} were found ($P = 0.013$); further One-Way ANOVA indicated that there were no significant differences between IMRT and FIF ($P = 0.373$), and FIF and 3D-CRT ($P = 0.299$), while a significant difference was observed between IMRT and 3D-CRT ($P = 0.013$) [Table 2]. For D_{min} , the differences among the 3 techniques were statistically significant ($P = 0.011$) [Table 1], as well as, one-way ANOVA showed that there were significant differences between IMRT and FIF ($P = 0.032$), and IMRT and 3D-CRT ($P = 0.033$) [Table 2]. For D_{98} , the difference among the 3 techniques was statistically significant ($P < 0.001$), and in one-way ANOVA between two techniques (IMRT and FIF) this amount is a similar [Table 2]. Statistically significant differences for parameters including V_{95} , and V_{107} ($P < 0.001$) were recorded [Table 1], then one-way ANOVA showed

Table 1: Results of comparison of dosimetric parameters for target tissue and organ at risk among three dimensional conformal radiotherapy, field-in-field and intensity modulated radiotherapy regardless of breast size (post hoc)

| Structures | Parameters | 3D-CRT | FIF | IMRT | P |
|----------------------|------------------------|--------------------|--------------|----------------|----------|
| PTV | D _{max} (cGy) | 5462.6±525.5 | 5377.1±118.9 | 5300.0±406.4** | 0.013* |
| | D _{min} (cGy) | 0.5±0.0 | 0.4±0.0 | 97.1±427.0 | 0.011* |
| | D ₉₈ (cGy) | 1770.2±1053.8 | 3097.7±630.3 | 3813.1±412.4 | <0.001* |
| | D ₂ (cGy) | 5140.8±286.3 | 5145.5±88.9 | 5165.5±78.4 | 0.369 |
| | D ₅₀ (cGy) | 4115.4±518.1 | 4524.1±483.2 | 4822.6±377.5 | 0.402 |
| | V ₉₅ (%) | 88.1±12.4 | 93.9±10.3 | 99.0±9.1 | 0.028* |
| | V ₁₀₇ (%) | 2.0±5.2 | 0.0±0.2 | 0.0±0.2 | <0.001* |
| | HI | 0.82±0.16 | 0.46±0.08 | 0.28±0.04 | <0.001* |
| | CI | 0.46±0.05 | 0.59±0.06 | 0.72±0.06 | 0.044* |
| | Ipsilateral lung | V ₅ (%) | 41.7±9.6 | 31.8±8.2 | 45.3±7.7 |
| V ₂₀ (%) | | 25.4±8.3 | 20.0±6.4 | 28.2±6.5 | <0.001* |
| Contralateral lung | V ₅ (%) | 4.9±12.6 | 2.0±4.1 | 2.2±4.6 | 0.022* |
| | V ₂₀ (%) | 3.3±10.6 | 1.3±2.9 | 1.9±4.0 | 0.112 |
| Heart | V ₂₅ (%) | 7.0±8.6 | 6.7±9.8 | 7.9±9.6 | 0.652 |
| | V ₃₀ (%) | 6.3±8.1 | 6.3±9.4 | 6.6±8.5 | 0.973 |
| | V ₅ (%) | 1.1±2.4 | 0.9±2.6 | 1.1±1.9 | 0.717 |
| Contralateral breast | V ₂ (%) | 0.3±1.2 | 0.3±1.6 | 0.5±0.9 | 0.634 |
| | V ₅ (%) | 0.1±0.5 | 0.1±1.2 | 0.3±0.6 | 0.248 |
| | V ₁₀ (%) | | | | |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, FIF=Field-in-field, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

Table 2: Results of bivariate of dosimetric parameters for target tissue and organ at risk among three dimensional conformal radiotherapy, field-in-field and intensity modulated radiotherapy regardless of breast size (one-way ANOVA)

| Structures | Parameters | 3D-CRT | FIF | IMRT | P | | |
|----------------------|------------------------|--------------------|--------------|----------------|-------------------|--------------------|-----------------|
| | | | | | 3D-CRT versus FIF | 3D-CRT versus IMRT | FIF versus IMRT |
| PTV | D _{max} (cGy) | 5462.6±525.5 | 5377.1±118.9 | 5300.0±406.4** | 0.299 | 0.013* | 0.373 |
| | D _{min} (cGy) | 0.5±0.0 | 0.4±0.0 | 97.1±427.0 | 1.000 | 0.033* | 0.032* |
| | D ₉₈ (cGy) | 1770.2±1053.8 | 3097.7±630.3 | 3813.1±412.4 | <0.001* | <0.001* | <0.001* |
| | D ₂ (cGy) | 5140.8±286.3 | 5145.5±88.9 | 5165.5±78.4 | 1.000 | 0.473 | 0.473 |
| | D ₅₀ (cGy) | 4115.4±518.1 | 4524.1±483.2 | 4822.6±377.5 | 0.324 | 0.084 | 0.447 |
| | V ₉₅ (%) | 88.1±12.4 | 93.9±10.3 | 99.0±9.1 | <0.001* | <0.001* | 0.044* |
| | V ₁₀₇ (%) | 2.0±5.2 | 0.0±0.2 | 0.0±0.2 | <0.001* | <0.001* | 1.000 |
| | HI | 0.82±0.16 | 0.46±0.08 | 0.28±0.04 | <0.001* | <0.001* | <0.001* |
| | CI | 0.46±0.05 | 0.59±0.06 | 0.72±0.06 | 0.038* | <0.011* | 0.067 |
| | Ipsilateral lung | V ₅ (%) | 41.7±9.6 | 31.8±8.2 | 45.3±7.7 | <0.001* | 0.011* |
| V ₂₀ (%) | | 25.4±8.3 | 20.0±6.4 | 28.2±6.5 | <0.001* | 0.026* | <0.001* |
| Contralateral lung | V ₅ (%) | 4.9±12.6 | 2.0±4.1 | 2.2±4.6 | 0.048* | 0.069 | 0.988 |
| | V ₂₀ (%) | 3.3±10.6 | 1.3±2.9 | 1.9±4.0 | 0.126 | 0.351 | 0.839 |
| Heart | V ₂₅ (%) | 7.0±8.6 | 6.7±9.8 | 7.9±9.6 | 0.968 | 0.813 | 0.668 |
| | V ₃₀ (%) | 6.3±8.1 | 6.3±9.4 | 6.6±8.5 | 0.999 | 0.977 | 0.984 |
| | V ₅ (%) | 1.1±2.4 | 0.9±2.6 | 1.1±1.9 | 0.830 | 0.987 | 0.741 |
| Contralateral breast | V ₂ (%) | 0.3±1.2 | 0.3±1.6 | 0.5±0.9 | 1.000 | 0.705 | 0.715 |
| | V ₅ (%) | 0.1±0.5 | 0.1±1.2 | 0.3±0.6 | 0.792 | 0.252 | 0.619 |
| | V ₁₀ (%) | | | | | | |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, FIF=Field-in-field, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

that there was a similar significant difference between all techniques for V₉₅ (P < 0.044) [Table 2]. For V₁₀₇, there were no differences between IMRT and FIF, however, 3D-CRT technique had significantly higher values compared to other techniques (P < 0.001). The HI values were significantly lower in IMRT technique (P < 0.001), and CI values were higher in IMRT technique without significant differences between IMRT and FIF technique (P = 0.067).

Also, the parameters of V₅ and V₂₀ of the lung (P < 0.001), and V₅ of contralateral lung (P = 0.022) in intergroup test showed significant differences [Table 1]. For ipsilateral V₅ and V₃₀, FIF spared more than other techniques [Table 2]. V₂₀

value in contralateral lung was lower in FIF plan compared to 3D-CRT method (P = 0.048). As shown in Table 3, a significant difference was noted for dosimetric parameters including HI, D_{max}, D₉₈, V₉₅ and V₁₀₇ in small-size group. In medium-size HI, D₉₈, V₉₅, and V₁₀₇ yielded significant differences and listed in Table 4. Furthermore, significant differences existed for HI, D_{max}, D₉₈, V₉₅, and V₁₀₇ in large-size group [Table 5]. In general, it can be considered two techniques IMRT and FIF showed better coverage and uniformity than 3D-CRT technique, while the comparison between IMRT and FIF showed a better improvement for IMRT in V₉₅ (P = 0.001) and D₉₈ (P = 0.011) [Tables 6-8]. V₅ of ipsilateral lung in any 3 groups (P < 0.001), V₂₀ of ipsilateral lung in small and

Table 3: Results of comparison of dosimetric parameters for target tissue and organ at risk among three dimensional conformal radiotherapy, field-in-field and intensity modulated radiotherapy according to small breast size (*post hoc*)

| Structures | Parameters | 3D-CRT | FIF | IMRT | P |
|----------------------|------------------------|--------------------|--------------|---------------|----------|
| PTV | D _{max} (cGy) | 5460.5±31.6 | 5374.8±24.5 | 5313.3±15.6** | <0.001* |
| | D _{min} (cGy) | 0.5±0.0 | 0.5±0.0 | 91.5±91.0 | 0.373 |
| | D ₉₈ (cGy) | 1543.3±207.9 | 2997.4±108.2 | 3736.7±82.4 | <0.001* |
| | D ₂ (cGy) | 5126.3±52.1 | 5151.1±18.8 | 5170.7±15.2 | 0.641 |
| | D ₅₀ (cGy) | 3932.3±485.7 | 4456.4±402.9 | 4771.3±375.0 | 0.106 |
| | V ₉₅ (%) | 89.2±9.7 | 95.2±10.8 | 99.6±10.8 | <0.001* |
| | V ₁₀₇ (%) | 1.2±0.4 | 0.0±0.0 | 0.1±0.0 | <0.001* |
| | HI | 0.91±0.11 | 0.48±0.06 | 0.30±0.03 | 0.011* |
| | CI | 0.47±0.05 | 0.61±0.05 | 0.73±0.06 | 0.029* |
| | Ipsilateral lung | V ₅ (%) | 45.6±1.4 | 31.8±1.3 | 44.8±1.2 |
| V ₂₀ (%) | | 28.1±1.1 | 18.6±1.1 | 29.3±1.0 | <0.001* |
| Contralateral lung | V ₅ (%) | 9.1±4.7 | 1.5±0.7 | 1.7±0.7 | 0.104 |
| | V ₂₀ (%) | 5.7±4.1 | 1.0±0.5 | 1.6±0.6 | 0.336 |
| Heart | V ₂₅ (%) | 6.8±1.7 | 6.1±1.7 | 7.8±1.9 | 0.809 |
| | V ₃₀ (%) | 5.8±1.6 | 5.9±1.6 | 6.4±1.6 | 0.960 |
| Contralateral breast | V ₂ (%) | 1.6±0.7 | 1.4±0.6 | 0.6±0.3 | 0.464 |
| | V ₅ (%) | 0.6±0.4 | 0.5±0.4 | 0.2±0.1 | 0.757 |
| | V ₁₀ (%) | 0.2±0.2 | 0.2±0.2 | 0.1±0.1 | 0.949 |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, FIF=Field-in-field, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

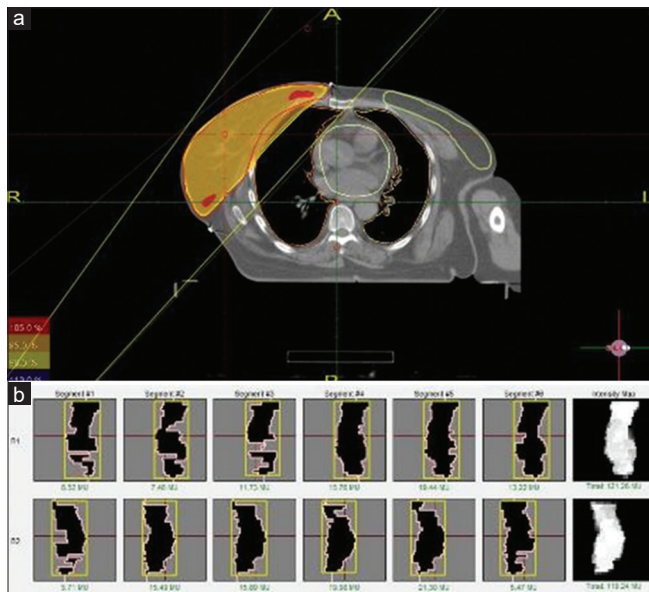


Figure 3: (a) An example of intensity modulated radiotherapy fields in current study and (b) An example of obtained intensity modulated radiotherapy fluence map

medium-size group ($P < 0.001$) and V_5 and V_{10} of contralateral breast in medium-size group ($P < 0.001$) all yielded significant differences in *post hoc* test [Tables 3-5]. In one-way ANOVA and bivariate FIF improved sparing in ipsilateral lung in any group, while 3D-CRT compared to IMRT significantly reduced ipsilateral lung dose. For V_5 and V_{10} of contralateral breast significant differences were found between 3D-CRT and IMRT ($P < 0.005$), and FIF and IMRT ($P \leq 0.001$) in medium-size group, and IMRT showed higher dose in contralateral breast compared to the other techniques [Table 7]. In overall sample, no statistically significant difference in heart and contralateral lung sparing was recorded among the 3 techniques [Tables 3-5].

DISCUSSION

A dosimetric analysis including 100 patients was performed with the aim to find the most effective method to treat breast cancer in postoperative treatment of breast carcinoma. IMRT and FIF techniques can improve the quality of treatment by providing a uniform dose distribution and better coverage of target tissue and protection of healthy organs.

The results of the comparison of dosimetric parameters of target tissues and OAR in two groups with and without breast tissue volume were evaluated. Regardless of breast size study, with the exception of D_2 and D_{50} parameters, the values of other parameters including HI, CI, D_{max} , D_{min} , D_{98} , V_{95} , and V_{107} in the target tissue varied statistically among the three methods. This means changing the treatment techniques, significantly changes the dose distribution in the target tissue. Tables 1 and 2 indicate the 3D-CRT method showed the greatest value of D_{max} among the three methods. Therefore, the 3D-CRT method leads to the creation of hot spots in the target tissue. Due to the larger values of D_{98} and lower values of HI in the IMRT and FIF methods and the position of these two points in the DVH diagram, it can be concluded that the tumor coverage in these two methods was improved compared to the 3D-CRT method.

In addition, the results showed better homogeneity (lower HI values) for IMRT and FIF methods, indicating better uniformity of these two methods compared to 3D-CRT method. However, the IMRT had statistically best homogeneity. On the other hand, conformity (CI values) were more similar in different techniques, however, the CI values were statistically better (having higher values) in FIF and IMRT methods compared to 3D-CRT method for patients having small and medium breasts. The comparison of V_x values in the target tissue, regardless of breast size, it was suggested that the

Table 4: Results of comparison of dosimetric parameters for target tissue and organ at risk among three dimensional conformal radiotherapy, field-in-field and Intensity modulated radiotherapy according to medium breast size (post hoc)

| Structures | Parameters | 3D-CRT | FIF | IMRT | P |
|----------------------|------------------------|--------------------|--------------|---------------|----------|
| PTV | D _{max} (cGy) | 5415.2±92.9 | 5385.2±16.4 | 5275.9±72.5** | 0.323 |
| | D _{min} (cGy) | 0.5±0.0 | 0.5±0.0 | 71.4±50.0 | 0.139 |
| | D ₉₈ (cGy) | 1892.1±145.5 | 3140.3±84.5 | 3829.2±53.1 | <0.001* |
| | D ₂ (cGy) | 5141.3±39.4 | 5142.0±11.8 | 5170.7±10.2 | 0.627 |
| | D ₅₀ (cGy) | 4224.3±417.7 | 4564.5±456.3 | 4855.7±377.8 | 0.128 |
| | V ₉₅ (%) | 88.3±9.9 | 93.5±8.7 | 99.1±8.1 | <0.001* |
| | V ₁₀₇ (%) | 1.4±0.3 | 0.0±0.0 | 0.0±0.0 | <0.001* |
| | HI | 0.77±0.08 | 0.44±0.05 | 0.28±0.03 | 0.010 |
| | CI | 0.45±0.05 | 0.60±0.05 | 0.71±0.05 | 0.071 |
| | Ipsilateral lung | V ₅ (%) | 40.4±1.3 | 32.1±1.0 | 45.8±1.2 |
| V ₂₀ (%) | | 24.3±1.0 | 20.6±0.8 | 28.6±0.9 | <0.001* |
| Contralateral lung | V ₅ (%) | 3.8±0.8 | 2.3±0.6 | 2.5±0.6 | 0.300 |
| | V ₂₀ (%) | 2.5±0.5 | 1.6±0.4 | 2.1±0.5 | 0.432 |
| Heart | V ₂₅ (%) | 6.2±1.0 | 5.7±1.1 | 7.9±1.3 | 0.392 |
| | V ₃₀ (%) | 5.7±0.9 | 5.4±1.0 | 6.7±1.2 | 0.674 |
| Contralateral breast | V ₂ (%) | 0.8±0.2 | 0.4±0.1 | 1.2±0.2 | 0.680 |
| | V ₅ (%) | 0.1±0.0 | 0.0±0.0 | 0.5±0.1 | <0.001* |
| | V ₁₀ (%) | 0.0±0.2 | 0.0±0.0 | 0.3±0.0 | <0.001* |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, FIF=Field-in-field, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

Table 5: Results of comparison of dosimetric parameters for target tissue and organ at risk among three dimensional conformal radiotherapy, field-in-field and intensity modulated radiotherapy according to large breast size (post hoc)

| Structures | Parameters | 3D-CRT | FIF | IMRT | P |
|----------------------|------------------------|--------------------|--------------|---------------|----------|
| PTV | D _{max} (cGy) | 5589.0±40.5 | 5359.5±24.3 | 5347.8±16.3** | <0.001* |
| | D _{min} (cGy) | 20.8±20.3 | 18.6±18.1 | 170.7±117.8 | 0.219 |
| | D ₉₈ (cGy) | 1710.3±224.8 | 3100.6±163.9 | 3858.2±103.6 | <0.001* |
| | D ₂ (cGy) | 5156.2±68.6 | 5148.0±19.9 | 5146.0±19.4 | 0.374 |
| | D ₅₀ (cGy) | 4147.4±413.1 | 4622.5±387.7 | 4887.1±377.6 | 0.255 |
| | V ₉₅ (%) | 87.1±8.6 | 94.6±9.0 | 98.6±8.2 | <0.001* |
| | V ₁₀₇ (%) | 4.2±2.2 | 0.0±0.0 | 0.0±0.0 | 0.041* |
| | HI | 0.84±0.07 | 0.44±0.05 | 0.26±0.04 | 0.007 |
| | CI | 0.47±0.06 | 0.58±0.08 | 0.74±0.06 | 0.208 |
| | Ipsilateral lung | V ₅ (%) | 40.4±1.3 | 32.1±1.0 | 45.8±1.2 |
| V ₂₀ (%) | | 24.3±1.0 | 20.6±0.8 | 28.6±0.9 | 0.680 |
| Contralateral lung | V ₅ (%) | 3.8±0.8 | 2.3±0.6 | 2.5±0.6 | 0.690 |
| | V ₂₀ (%) | 2.5±0.5 | 1.6±0.4 | 2.1±0.5 | 0.549 |
| Heart | V ₂₅ (%) | 6.2±1.0 | 5.7±1.1 | 7.9±1.3 | 0.843 |
| | V ₃₀ (%) | 5.7±0.9 | 5.4±1.0 | 6.7±1.2 | 0.661 |
| Contralateral breast | V ₂ (%) | 0.8±0.2 | 0.4±0.1 | 1.2±0.2 | 0.882 |
| | V ₅ (%) | 0.1±0.0 | 0.0±0.0 | 0.5±0.1 | 0.800 |
| | V ₁₀ (%) | 0.0±0.2 | 0.0±0.0 | 0.3±0.0 | 0.597 |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, FIF=Field-in-field, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

IMRT method leads to better tumor coverage and the FIF method leads to less hot spots. Therefore, it is not possible to recommend FIF or IMRT in terms of tumor coverage. Dean *et al.*^[18] reported that the coverage was better in IMRT plans than FIF plans for breast radiation therapy. In Kim and Choi^[19] study, it was shown that FIF had better uniformity and coverage in PTV compared to 3D-CRT. The above-mentioned studies agree with the present study. Table 1 showed that only in OAR located inside the beam trajectory (for example ipsilateral lung), the dosimetric parameters have a significant difference regardless of breast volume. It should be noted that V₅ of contralateral lung also has a significant difference among the three methods, which is only comparable between the 3D-CRT and FIF methods. However, V₅ and V₂₀ of ipsilateral lung in all three methods were statistically significant in bivariate.

Among three methods, the FIF method results in a lower dose to the lung for treatment based on the V₅ and V₂₀ parameters, which can be suggested for patients with pulmonary problems.

Regarding the heart dose parameters, we did not find any statistically significant differences between the evaluated radiotherapy techniques and for patients with different breast sizes. However, previous studies showed that IMRT and techniques with higher number of radiation fields (like FIF) resulted to better heart sparing.^[20-22] In our study, all the treatment plans were reviewed and corrected by an experienced medical physicist in a way that all the OARs will have as low as possible doses, and it can be the reason for the lack of differences of heart doses between different radiotherapy techniques.

Table 6: Results of bivariate of dosimetric parameters for target tissue and organ at risk between Three dimensional conformal radiotherapy and field-in-field according to breast size (one-way ANOVA)

| Structures | Parameters | Small | | | Medium | | | Large | | |
|----------------------|------------------------|--------------------|---------------|----------|--------------|--------------|----------|--------------|--------------|----------|
| | | 3D-CRT | FIF | P | 3D-CRT | FIF | P | 3D-CRT | FIF | P |
| PTV | D _{max} (cGy) | 5460.5±31.6 | 5374.8±24.5** | 0.055 | 5415.2±92.9 | 5385.2±16.4 | 0.953 | 5589.0±40.5 | 5359.5±24.3 | <0.001* |
| | D _{min} (cGy) | 0.5±0.0 | 0.5±0.0 | 1.000 | 0.5±0.0 | 0.5±0.0 | 1.000 | 20.8±20.3 | 18.6±18.1 | 1.000 |
| | D ₉₅ (cGy) | 1543.3±207.9 | 2997.4±108.2 | <0.001* | 1892.1±145.5 | 3140.3±84.5 | <0.001* | 1710.3±224.8 | 3100.6±163.9 | <0.001* |
| | D ₂ (cGy) | 5126.3±52.1 | 5151.1±18.8 | 0.870 | 5141.3±39.4 | 5142.0±11.8 | 1.000 | 5156.2±68.6 | 5148.0±19.9 | 1.000 |
| | D ₅₀ (cGy) | 3932.3±485.7 | 4456.4±402.9 | 0.203 | 4224.3±417.7 | 4564.5±456.3 | 0.255 | 4147.4±413.1 | 4622.5±387.7 | 0.355 |
| | V ₉₅ (%) | 89.2±9.7 | 95.2±10.8 | <0.001* | 88.3±9.9 | 93.5±8.7 | <0.001* | 87.1±8.6 | 94.6±9.0 | 0.001* |
| | V ₁₀₇ (%) | 1.2±0.4 | 0.0±0.0 | 0.013* | 1.4±0.3 | 0.0±0.0 | <0.001* | 4.2±2.2 | 0.0±0.0 | 0.090 |
| | HI | 0.91±0.11 | 0.48±0.06 | 0.009* | 0.77±0.08 | 0.44±0.05 | 0.006* | 0.84±0.07 | 0.44±0.05 | 0.015* |
| | CI | 0.47±0.05 | 0.61±0.05 | 0.018* | 0.45±0.05 | 0.60±0.05 | 0.047* | 0.47±0.06 | 0.58±0.08 | 0.226 |
| | Ipsilateral lung | V ₅ (%) | 45.6±1.4 | 31.8±1.3 | <0.001* | 40.4±1.3 | 32.1±1.0 | <0.001* | 40.4±2.1 | 31.2±2.3 |
| V ₂₀ (%) | | 28.1±1.1 | 18.6±1.1 | <0.001* | 24.3±1.0 | 20.6±0.8 | 0.025* | 25.2±2.5 | 20.0±1.5 | 0.149 |
| Contralateral lung | V ₅ (%) | 9.1±4.7 | 1.5±0.7 | 0.171 | 3.8±0.8 | 2.3±0.6 | 0.353 | 3.0±1.1 | 1.9±0.8 | 0.762 |
| | V ₂₀ (%) | 5.7±4.1 | 1.0±0.5 | 0.397 | 2.5±0.5 | 1.6±0.4 | 0.434 | 2.5±1.0 | 1.1±0.5 | 0.551 |
| Heart | V ₂₅ (%) | 6.8±1.7 | 6.1±1.7 | 0.962 | 6.2±1.0 | 5.7±1.1 | 0.956 | 9.2±2.2 | 9.8±3.0 | 0.990 |
| | V ₃₀ (%) | 5.8±1.6 | 5.9±1.6 | 1.000 | 5.7±0.9 | 5.4±1.0 | 0.986 | 8.5±2.1 | 9.3±2.9 | 0.972 |
| | V ₂ (%) | 1.6±0.7 | 1.4±0.6 | 0.964 | 0.8±0.2 | 0.4±0.1 | 0.505 | 1.1±0.4 | 1.4±0.8 | 0.959 |
| Contralateral breast | V ₅ (%) | 0.6±0.4 | 0.5±0.4 | 0.968 | 0.1±0.0 | 0.0±0.0 | 0.821 | 0.5±0.2 | 0.9±0.6 | 0.824 |
| | V ₁₀ (%) | 0.2±0.2 | 0.2±0.2 | 0.997 | 0.0±0.2 | 0.0±0.0 | 0.988 | 0.1±0.0 | 0.5±0.5 | 0.598 |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, FIF=Field-in-field, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

Table 7: Results of bivariate of dosimetric parameters for target tissue and organ at risk between three dimensional conformal radiotherapy and intensity modulated radiotherapy according to breast size (one-way ANOVA)

| Structures | Parameters | Small | | | Medium | | | Large | | |
|----------------------|------------------------|--------------------|---------------|----------|--------------|--------------|----------|--------------|--------------|----------|
| | | 3D-CRT | IMRT | P | 3D-CRT | IMRT | P | 3D-CRT | IMRT | P |
| PTV | D _{max} (cGy) | 5460.5±31.6 | 5313.3±15.6** | <0.001* | 5415.2±92.9 | 5275.9±72.5 | 0.360 | 5589.0±40.5 | 5347.8±16.3 | <0.001* |
| | D _{min} (cGy) | 0.5±0.0 | 91.5±91.0 | 0.476 | 0.5±0.0 | 71.4±50.0 | 0.227 | 20.8±20.3 | 170.7±117.8 | 0.323 |
| | D ₉₅ (cGy) | 1543.3±207.9 | 3736.7±82.4 | <0.001* | 1892.1±145.5 | 3829.2±53.1 | <0.001* | 1710.3±224.8 | 3858.2±103.6 | <0.001* |
| | D ₂ (cGy) | 5126.3±52.1 | 5170.7±15.2 | 0.642 | 5141.3±39.4 | 5170.7±10.2 | 0.698 | 5156.2±68.6 | 5146.0±19.4 | 0.477 |
| | D ₅₀ (cGy) | 3932.3±485.7 | 4771.3±375.0 | 0.106 | 4224.3±417.7 | 4855.7±377.8 | 0.161 | 4147.4±413.1 | 4887.1±377.6 | 0.005 |
| | V ₉₅ (%) | 89.2±9.7 | 99.6±10.8 | <0.001* | 88.3±9.9 | 99.1±8.1 | <0.001* | 87.1±8.6 | 98.6±8.2 | <0.001* |
| | V ₁₀₇ (%) | 1.2±0.4 | 0.1±0.0 | 0.017* | 1.4±0.3 | 0.0±0.0 | <0.001* | 4.2±2.2 | 0.0±0.0 | 0.087 |
| | HI | 0.91±0.11 | 0.30±0.03 | 0.012* | 0.77±0.08 | 0.28±0.03 | 0.041* | 0.84±0.07 | 0.26±0.04 | 0.011* |
| | CI | 0.47±0.05 | 0.73±0.06 | 0.031* | 0.45±0.05 | 0.71±0.05 | 0.058 | 0.47±0.06 | 0.74±0.06 | 0.123 |
| | Ipsilateral lung | V ₅ (%) | 45.6±1.4 | 44.8±1.2 | 0.914 | 40.4±1.3 | 45.8±1.2 | 0.008* | 40.4±2.1 | 44.7±1.3 |
| V ₂₀ (%) | | 28.1±1.1 | 29.3±1.0 | 0.738 | 24.3±1.0 | 28.6±0.9 | 0.007* | 25.2±2.5 | 25.6±1.3 | 0.991 |
| Contralateral lung | V ₅ (%) | 9.1±4.7 | 1.7±0.7 | 0.190 | 3.8±0.8 | 2.5±0.6 | 0.477 | 3.0±1.1 | 1.9±0.9 | 0.752 |
| | V ₂₀ (%) | 5.7±4.1 | 1.6±0.6 | 0.493 | 2.5±0.5 | 2.1±0.5 | 0.851 | 2.5±1.0 | 1.7±0.9 | 0.824 |
| Heart | V ₂₅ (%) | 6.8±1.7 | 7.8±1.9 | 0.933 | 6.2±1.0 | 7.9±1.3 | 0.601 | 9.2±2.2 | 7.8±2.0 | 0.917 |
| | V ₃₀ (%) | 5.8±1.6 | 6.4±1.6 | 0.967 | 5.7±0.9 | 6.7±1.2 | 0.797 | 8.5±2.1 | 6.4±1.8 | 0.814 |
| | V ₂ (%) | 1.6±0.7 | 0.6±0.3 | 0.497 | 0.8±0.2 | 1.2±0.2 | 0.507 | 1.1±0.4 | 1.6±0.5 | 0.883 |
| Contralateral breast | V ₅ (%) | 0.6±0.4 | 0.2±0.1 | 0.763 | 0.1±0.0 | 0.5±0.1 | 0.005* | 0.5±0.2 | 0.5±0.2 | 0.995 |
| | V ₁₀ (%) | 0.2±0.2 | 0.1±0.1 | 0.953 | 0.0±0.2 | 0.3±0.0 | 0.001* | 0.1±0.0 | 0.3±0.1 | 0.860 |

*P<0.05, statistically significant, **Mean±SD. 3D-CRT=Three dimensional conformal radiotherapy, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

Al-Rahbi et al.^[23] reported that the doses in the OAR significantly reduced in FIF technique compared to 3D-CRT. In another study by Aras et al.,^[24] they have reported that at low doses, IMRT delivered a higher dose to the ipsilateral lung but at higher doses, it protected the lung better compared to 3D-CRT, as well as, IMRT was also successful in sparing the heart. Compared to the present study, all patients in their study were left breast cancer and this can make a significant difference in heart sparing. Also, in their study, the Eclipse treatment planning software was used which in terms of dose and accuracy calculation algorithm is different from PROWESS® treatment planning software. It should be noted that comparing other tissues, CCCS algorithm has less accuracy

in lung.^[25] In the evaluation of dosimetric parameters with considering breast volume, in small breast size, a significant difference was observed for D_{max} parameter between 3D-CRT and IMRT methods.

In addition, the P value was borderline (0.055) in comparing FIF and 3D-CRT methods. This suggests that in terms of creating hot spots in small breasts, the IMRT method would result in a smaller volume hot spot. The evidence shows that in small, medium, and large breast groups, there are significant differences in D₉₅ and D_{max} values. More accurate evaluation shows that in IMRT, tumor coverage is better than the other two methods for all groups. The reason for this superiority can

Table 8: Results of bivariate of dosimetric parameters for target tissue and organ at risk between field-in-field and intensity modulated radiotherapy according to breast size (one-way ANOVA)

| Structures | Parameters | Small | | | Medium | | | Large | | |
|----------------------|------------------------|--------------------|---------------|----------|--------------|--------------|----------|--------------|--------------|----------|
| | | FIF | IMRT | P | FIF | IMRT | P | FIF | IMRT | P |
| PTV | D _{max} (cGy) | 5374.8±24.5 | 5313.3±15.6** | 0.231 | 5385.2±16.4 | 5275.9±72.5 | 0.532 | 5359.5±24.3 | 5347.8±16.3 | 0.960 |
| | D _{min} (cGy) | 0.5±0.0 | 91.5±91.0 | 0.476 | 0.5±0.0 | 71.4±50.0 | 0.227 | 18.6±18.1 | 170.7±117.8 | 0.313 |
| | D ₉₈ (cGy) | 2997.4±108.2 | 3736.7±82.4 | 0.002* | 3140.3±84.5 | 3829.2±53.1 | <0.001* | 3100.6±163.9 | 3858.2±103.6 | 0.011* |
| | D ₂ (cGy) | 5151.1±18.8 | 5170.7±15.2 | 0.917 | 5142.0±11.8 | 5170.7±10.2 | 0.711 | 5148.0±19.9 | 5146.0±19.4 | 0.477 |
| | D ₅₀ (cGy) | 4456.4±402.9 | 4771.3±375.0 | 0.255 | 4564.5±456.3 | 4855.7±377.8 | 0.273 | 4622.5±387.7 | 4887.1±377.6 | 0.306 |
| | V ₉₅ (%) | 95.2±10.8 | 99.6±10.8 | 0.023* | 93.5±8.7 | 99.1±8.1 | <0.001* | 94.6±9.0 | 98.6±8.2 | 0.001* |
| | V ₁₀₇ (%) | 0.0±0.0 | 0.1±0.0 | 0.996 | 0.0±0.0 | 0.0±0.0 | 1.000 | 0.0±0.0 | 0.0±0.0 | 1.000 |
| | HI | 0.48±0.06 | 0.30±0.03 | 0.022* | 0.44±0.05 | 0.28±0.03 | 0.031* | 0.44±0.05 | 0.26±0.04 | 0.015* |
| | CI | 0.61±0.05 | 0.73±0.06 | 0.106 | 0.60±0.05 | 0.71±0.05 | 0.085 | 0.58±0.08 | 0.74±0.06 | 0.216 |
| | Ipsilateral lung | V ₅ (%) | 31.8±1.3 | 44.8±1.2 | <0.001* | 32.1±1.0 | 45.8±1.2 | <0.001* | 31.2±2.3 | 44.7±1.3 |
| V ₂₀ (%) | | 18.6±1.1 | 29.3±1.0 | <0.001* | 20.6±0.8 | 28.6±0.9 | <0.001* | 20.0±1.5 | 25.6±1.3 | 0.114 |
| Contralateral lung | V ₅ (%) | 1.5±0.7 | 1.7±0.7 | 0.998 | 2.3±0.6 | 2.5±0.6 | 0.974 | 1.9±0.8 | 1.9±0.9 | 1.000 |
| | V ₂₀ (%) | 1.0±0.5 | 1.6±0.6 | 0.985 | 1.6±0.4 | 2.1±0.5 | 0.768 | 1.1±0.5 | 1.7±0.9 | 0.894 |
| Heart | V ₂₅ (%) | 6.1±1.7 | 7.8±1.9 | 0.810 | 5.7±1.1 | 7.9±1.3 | 0.426 | 9.8±3.0 | 7.8±2.0 | 0.854 |
| | V ₃₀ (%) | 5.9±1.6 | 6.4±1.6 | 0.974 | 5.4±1.0 | 6.7±1.2 | 0.704 | 9.3±2.9 | 6.4±1.8 | 0.679 |
| | V ₂ (%) | 1.4±0.6 | 0.6±0.3 | 0.657 | 0.4±0.1 | 1.2±0.2 | 0.068 | 1.4±0.8 | 1.6±0.5 | 0.978 |
| Contralateral breast | V ₅ (%) | 0.5±0.4 | 0.2±0.1 | 0.891 | 0.0±0.0 | 0.5±0.1 | 0.001* | 0.9±0.6 | 0.5±0.2 | 0.873 |
| | V ₁₀ (%) | 0.2±0.2 | 0.1±0.1 | 0.973 | 0.0±0.0 | 0.3±0.0 | 0.001* | 0.5±0.5 | 0.3±0.1 | 0.896 |

*P<0.05, statistically significant, **Mean±SD. FIF=Field-in-field, IMRT=Intensity modulated radiotherapy, PTV=Planning target volume, SD=Standard deviation, HI=Homogeneity index, CI=Conformity index

be the high number of beamlets (nine segments) per angle of the gantry. According to other studies, increasing dose delivery time in IMRT is one of the most controversial challenges,^[26] naturally increasing the number of beamlets will make the problem more serious. Statistically significant differences for V₉₅ and V₁₀₇ in all three groups were recorded.

Evidence showed that 3D-CRT causes hotter hot spots than the other two methods, while there is no significant difference between IMRT and FIF. The present study was performed on CT images of patients undergoing breast-conservation surgery and mastectomy patients were not included in this study.

Tables 3-5 indicated that for all three groups of patients with small, medium and large breast volume, in the OAR, only the ipsilateral lung made a significant difference. The V₂₀ ipsilateral lung, in the large breast group, is exception. Details show that the FIF method results in a lower V₂₀ value in ipsilateral lung. El-Sayed *et al.*^[27] Compared IMRT, FIF and 3D-CRT methods based on breast volume. In general, the obtained results showed that the FIF achieved the best of planning efficiency parameters for 3 groups of patients. The results of the present study show that in three treatment techniques, the values of the parameters outside the field are not different and this means that it is important to pay attention to the organs in BEV to choose the appropriate treatment technique.

CONCLUSION

It can be considered that from the perspective of covering the PTV and creating more uniformity with the ideal dosage distribution, in both studies with and without considering the volume of breast tissue, IMRT and FIF showed better results than the conventional 3D-CRT method. Sparing of healthy OAR

achieved by designing a FIF treatment plan. Referring to the fact that the use of IMRT technique requires more sophisticated equipment, facilities and time, FIF method is introduced as an efficient method to improve the quality of treatment for patients with breast cancer.

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Conflicts of interest

There are no conflicts of interest.

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