Influence of different treatment planning techniques on radiation doses to the heart, left anterior descending coronary artery and left lung in the radiotherapy of left-sided breast cancer patients

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▸ ***Original article***

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Revised: September 2017
Accepted: December 2017

Int. J. Radiat. Res., January 2019; 17(1): 119-125

DOI: 10.18869/acadpub.ijrr.17.1.119

ABSTRACT

Background*:** Breast-conserving surgery (BCS) followed by radiotherapy (RT) is the standard of care for women with breast cancer. Evidence shows that RT dose to the heart can result in ischemic heart disease. In this study we compared 3 different RT techniques were for heart, left anterior descending coronary artery (LAD) and lung doses in left breast cancer patients after breast-conserving surgery. ***Materials and Methods*:** Three different plans were designed for each patient using conventional tangential fields, 6+18 MV combination beams, and field-in-field (FIF) technique. These were compared in terms of doses to the planning target volume (PTV), ipsilateral lung, heart and LAD. ***Results: Forty left breast cancer patients were included in this study. Mean PTV V95% was 95.74% for conventional, 90.45% for FIF and 87.89% for 6+18 MV combination beams ($p<0.05$). Mean left lung dose was 11.22 Gy for FIF, 12.25 Gy for 6+18 MV and 12.95 Gy for conventional technique ($p<0.05$). Mean heart dose was 4.52 Gy for FIF, 4.85 Gy for 6+18 MV and 5.13 Gy for conventional technique ($p<0.05$), and mean D2% for LAD was 40.06, 43.43 and 45.25 Gy ($p<0.01$) in FIF, 6+18 MV and conventional techniques, respectively. ***Conclusion:*** These results indicated that FIF and 6+18 MV combination techniques significantly reduced the doses received by the heart, LAD and left lung compared to conventional tangential fields, while FIF was superior to 6+18 MV considering the above-mentioned variables. The lower doses to the organs at risk were achieved with a small but statistically significant loss in PTV coverage.

Keywords: *Left breast cancer, radiotherapy, heart dose, coronary artery dose, tangential fields, field-in-field technique.*

INTRODUCTION

Breast cancer is a major public health problem for women throughout the world. Worldwide, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females [1]. Breast-conserving surgery (BCS) followed by radiation therapy to the intact breast is now the standard of care for the majority of women with early-stage invasive breast cancer [2]. Nevertheless, effects on the heart are a potentially significant and serious clinical problem in radiation therapy treatment of early breast cancer [3]. In the history of breast cancer RT regimens, the range of dose to the heart has changed due to the development of new techniques, beam energy, target doses, and different volumes and contouring modalities [4]. Previous studies have shown that breast cancer radiotherapy can increase the risk of cardiovascular disease, including pericarditis, coronary artery disease (CAD), conduction abnormalities, congestive heart failure and valvular disease [5]. Patients with left-sided breast cancer who received RT, had a statistically significant increased rate of stenosis in the coronary artery branches on the left-anterior surface of the heart (the mid and distal branch of left anterior descending artery (LAD)) when compared with right-sided breast cancer [6]. The whole heart is often selected for the evaluation of cardiac dose but some of the newer studies demonstrated that the dose to the coronary arteries, irradiated left ventricular volume and highest dose to the small cardiac volume especially to the anterior portion of the heart might be more important. The appropriate site for evaluation of the dose relevant to radiation-induced coronary artery disease has not been fully determined, but arteries particularly LAD are sensitive to radiation [7].

Tangential photon beam irradiation to whole breast after BCS is the standard approach in early breast cancer. With irradiation through tangential fields, exposure of heart directly to the radiation is minimized in patients with left-sided breast cancer; however, achieving a good dose distribution from open fields is complicated because of the complex volume of the breast. In conventional technique, wedges are commonly used to reduce dose inhomogeneity [8]. In patients treated with 6 MV or lower energy photons with wide tangential fields, for whom separation is >22 cm, there may be significant dose inhomogeneity in the breast. This problem can be minimized by using higher-energy photons (10 to 18 MV) to deliver a portion of treatment [2]. In order to improve dosimetric benefits and spare organ at risk (OAR), several investigators have described different techniques such as intensity modulated radiation therapy (IMRT) or field-in-field (FIF) techniques [9]. The benefit of FIF technique is to increase the dose homogeneity to the targeted volume while decreasing the absorbed dose in irradiated tissues outside the targeted tissue [10]. FIF plan for whole-breast irradiation is based on a standard tangential beam arrangement, employing two directly opposed fields. Sub-fields are added using forward planning to even out volumes of high and low doses [11]. The development of advanced breast treatment techniques such as multi-segmented intensity-modulated field-in-field irradiation allows for the use of clinical applications that can minimize the risk of a secondary breast malignancy [12].

Breast radiotherapy also delivers some unwanted irradiation to the lungs. Side-effects to the lungs are in the form of acute pneumonitis and sub-acute/late lung fibrosis [13]. Radiation pneumonitis is a rare complication of breast RT affecting about 1% of patients [14]. The incidence of radiation pneumonitis is known to be correlated with the volume of the irradiated lung and the radiation dose [15]. Several studies have reported that FIF or forward-planned IMRT technique decrease the dose to lungs compared with conventional tangential techniques with wedges [16].

In our center, breast RT is performed with 3D -planned conventional tangential field irradiation using wedges with 6MV photon beam. Considering the potential cardiac (and pulmonary) side effects of radiotherapy as mentioned above, we performed a comparison of FIF and 6+18 MV combination beam techniques with tangential fields evaluating the doses to the PTV, lung, heart and LAD.

MATERIALS AND METHODS

Forty left-side breast cancer patients 35-67 years of age undergoing breast-conserving surgery were included in our study. The study was approved by the Ethical Committee of Tehran University of Medical Sciences. It is noteworthy that we performed our study on CT-simulation data of real patients. All the patients were scanned in the supine position. CT data were acquired with axial slice spacing 5 mm covering the entire chest.

Planning target volume (PTV) and OARs

(heart, ipsilateral lung, contralateral lung and LAD artery) contours were defined according to the Radiation Therapy Oncology Group (RTOG) Atlases. LAD contouring was performed with the help of a radiologist.

For each patient 3 different treatment plans were designed, as follows: Conventional 3D RT, FIF and 6+18 MV combination. In conventional 3D RT technique, two medial and lateral tangential fields with 6 MV photon beam and wedges were used. In 6+18 MV combination beams, first two 6 MV medial and lateral tangential fields and then two smaller lateral and medial 18 MV tangential fields with 15% of total monitor units (MU) were designed so that the existing hot points in 6 MV fields fall out of 18 MV fields. Figure 1 shows an example of the treatment plan for a patient using 6+18 MV combination beam technique.

In field-in-field (FIF) technique, first two 6 MV lateral and medial tangential fields were planned. Then heart and left lung were shielded by multi-leaf collimator (MLC) and a smaller field called segment 1 with the same energy but with 10% of total MU was designed. In the following stages segments 2 and 3 with 5% and 6% of total MU were designed to shield the hot points. Figure 2 demonstrates the treatment plan of a patient using FIF technique.

Statistical analysis

SPSS version 18 was used in this study for statistical analysis. Paired samples t-test was used for comparisons. A p value of < 0.05 was considered to be significant.

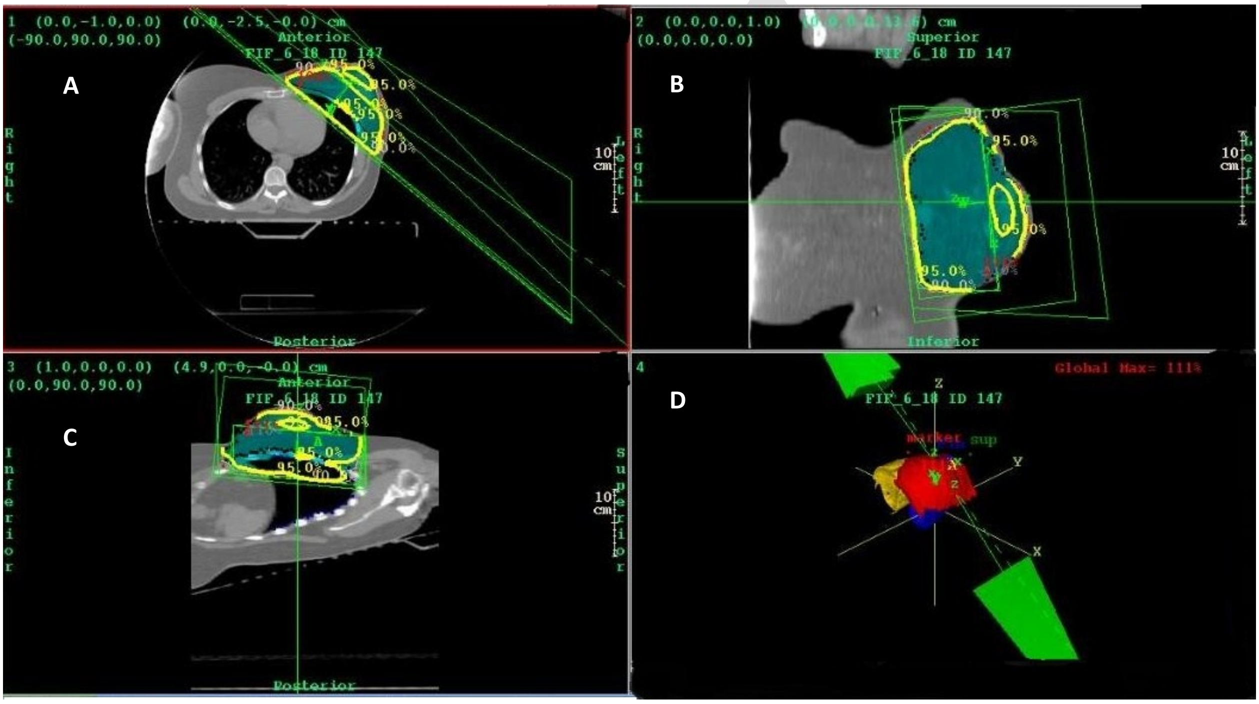

Figure 1. The treatment plan for a patient using 6+18 MV combination beams. **A** transverse view presenting two beams configuration. **B** control view. **C** sagittal view. **D** 3D view.

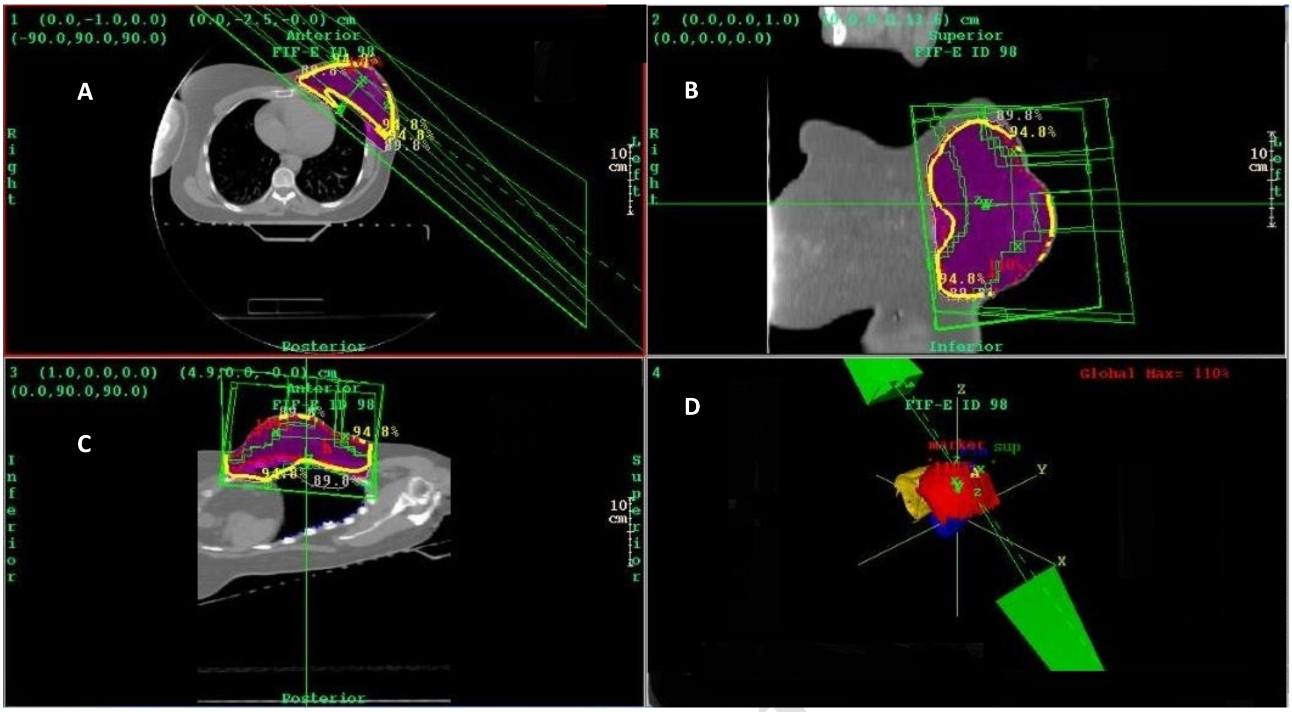

Figure 2. The treatment plan of a patient using FIF technique. **A** transverse view presenting two beams configuration. **B** control view. **C** sagittal view. **D** 3D view.

RESULTS

Main results of our study are shown in table 1. The mean doses of heart, LAD artery, left and right lungs were significantly decreased with FIF and 6+18 MV combination compared to conventional technique ($p<0.01$) while FIF was superior to 6+18 MV considering the above-mentioned variables ($p< 0.05$).

The V5 Gy and V25 Gy values for heart were significantly lower with FIF and 6+18 MV compared to conventional techniques ($p<0.05$), whereas FIF was superior to 6+18 MV in terms of V25 value of heart ($p<0.05$).

The D2% values for LAD coronary artery were significantly lower with FIF and 6+18 MV compared to conventional technique ($p<0.01$), while FIF was superior to 6+18 MV ($p<0.01$).

Left lung V20 Gy value was lower with FIF and 6+18 MV compared to conventional technique ($p<0.05$), but there were no significant difference between FIF and 6+18 MV in this regard.

The V95% of PTV was higher in conventional technique compared with FIF and 6+18 MV, while FIF was superior to 6+18 MV.

Figure 3 shows the dose-volume histogram (DVH) of a patient's different plans for the above -mentioned volumes. We didn't find any significant relationship between whole-breast field separation and the studied doses to the OARs.

Table 1. Dose parameters of heart, LAD artery, left lung and PTV in conventional, 6+18 MV and FIF techniques.

	Heart mean dose (cGy)	LAD mean dose (cGy)	Left lung mean dose (cGy)	Right lung mean dose (cGy)	Heart V25Gy	LAD D2% (cGy)	PTV V95%	PTV Dmax (per fraction) (cGy)
Conventional	513	2330	1295	65	%6.65	4525	95.74%	228
18+6	485	2149	1225	64	% 6.35	4343	87.89%	227
FIF	452	2005	1122	63	% 6.1	4006	90.45%	221

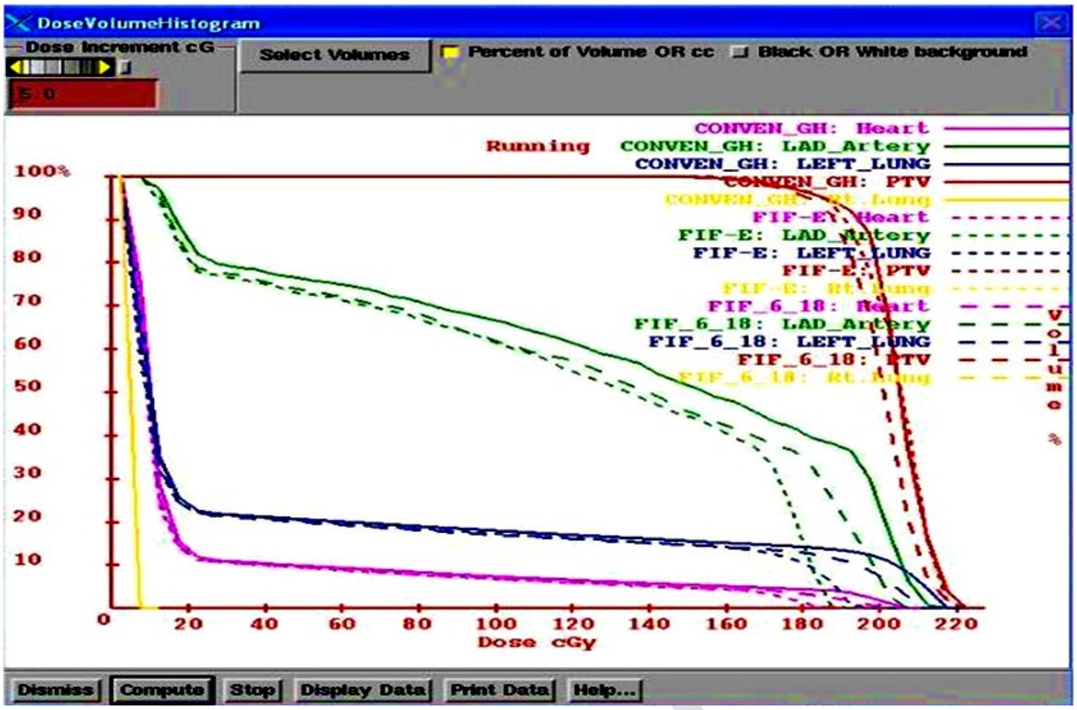

Figure 3. The dose-volume histogram (DVH) of a patient's different plans.

DISCUSSION

Breast-conserving surgery followed by radiation therapy is now established as the most acceptable standard of care for the majority of early-stage invasive breast cancer patients [(2)]. The number of breast cancer survivors is increasing and the long-term survivors may display adverse events related to cardiovascular and pulmonary disease [(7)].

The 'Early Breast Cancer Trialists Collaborative Group' reported excessive mortality from heart disease in patients receiving radiation therapy [(17)]. In fact, cardiac mortality is reported to be higher in left-sided breast cancer patients than in right-sided breast cancer patients because whole Breast Irradiation can deliver higher cardiac radiation doses in patients with left-sided breast cancer [(18-20)].

Thimoty *et al.* showed that among all of women who received RT, those with left-sided breast cancer had a statistically significant increase rate of stenosis in the coronary artery branches on the left anterior surface of the heart when compared with those with right-sided cancer [(6)].

Left Anterior Descending (LAD) artery is an important branch of the left main coronary artery supplying the anterior and anterolateral walls of the left ventricle and the anterior two-thirds of the septum [(8)].

Taylor *et al.* reported that the Irradiation of the breast or chest wall in the late 1980s and in the 1990s was usually delivered using 6 MV tangential beams, and some women irradiated in the 1990s received CT-planning [(4)]. The heart received mean radiation doses of 2.8 Gy (BED Gy2= 3.5) for left-sided irradiation from this technique.

The corresponding mean heart doses for patients irradiated in2008 for stage I and II left breast cancer are thus about 2.8 and 3.3 Gy, respectively (prescribed dose: 46 Gy, 2 Gy/ fraction). Of the cardiac structures considered, the LAD coronary artery received the highest radiation doses from most left-sided regimens due to its proximity to the left breast and IMC (12 Gy) [(4)].

According to our data the mean heart dose with conventional techniques was 512.75 cGy and LAD mean dose was 2330.42 cGy, but with using other different techniques for radiotherapy of left-sided breast cancer patients, found that FIF and 6+18 MV combination beam techniques were superior to conventional tangential fields in terms of dose to the heart (484.78 c Gy and 451.73cGy), LAD artery (2148.97 and 2004.62 cGy).

There are several studies in the literature comparing the dosimetry in the FIF

with standard radiotherapy techniques for whole breast RT.

Yavas *et al*. in their study showed that the FIF technique significantly reduced the V2, V5, V10, V20, V30 and V40 values of the contralateral breast [8].

Their results also showed that with the FIF technique heart volumes receiving 2, 30 and

40Gy were decreased significantly. Similarly V2, V10, V20 and V30 and V40 values for

ipsilateral lung were significantly reduced with FIF technique when compared to CRT technique. 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 [8].

Ercan *et al*. reported in their study The FiF technique, compared to CRT, for breast radiotherapy enables significantly better dose distribution in the PTV. Significant differences are also found for soft tissue volume, the ipsilateral lung dose, and the heart dose [10].

Prabhakar *et al.* showed that the use of FIF effectively improved PTV conformity, while saving the OARs from tangential irradiation during the whole breast irradiation [21].

In this study we compared three different techniques for radiotherapy of left-sided breast cancer patients and found that FIF and 6+18 MV combination beam techniques were superior to conventional tangential fields in terms of dose to the OARs (heart, LAD artery, and ipsilateral lung). We found that heart mean dose, LAD mean dose and LAD D2% were better in FIF and 6+18 MV compared to conventional tangential technique.

In our study in accordance with other studies, FIF and 6 18+MV combination beams techniques were superior to conventional technique in terms of; Heart mean dose, Heart V5, Heart V25, LAD artery D2%, LAD means dose, Left and Right Lung mean doses and Left Lung V20. We also found that FIF technique was superior in terms of mentioned variables except V20 value of left lung, compared to 6-18 combination beam technique.

The main limitations of our study were lack of access in our center to inverse-planned IMRT or other photon energies except 6 and 18 MV. Thus we could not compare our plans to an IMRT plan, or use medium energy photons. Another limitation that we came across in this study was that we could not take CT simulations from both breasts simultaneously so we did not able to calculate contralateral breast dosimetric parameters.

CONCLUSION

The present study showed that for left-sided whole breast RT, FIF and 6+18 MV combination beam techniques provided better sparing of organs at risk (heart, LAD artery, and left lung) compared to conventional tangential fields. Our study also demonstrated that FIF technique was superior to 6+18 MV in terms of heart and LAD doses. The lower doses to the organs at risk were achieved with a small but statistically significant loss in PTV coverage.

Conflicts of interest: *Declared none.*

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