IMRT treatment plans of left breast cancer: Comparison with 3DCRT

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Abstract

Introduction: IMRT becomes more suitable for treating complex target volumes as it is able to generate more complicated dose distributions and dose gradients with narrower margins than those allowed using traditional methods. As a consequence, IMRT can provide a clinical benefit in terms of increased tumor control through escalated dose and reduced normal tissue complications through OARs sparing.

Aim: To compare target conformity and sparing of lung, heart and contralateral breast for IMRT and 3DCRT plans for left breast cancer female patients underwent breast conservative surgery

Methods: CT studies of 20 patients with early stage left breast cancer who underwent breast conservative surgery were planned using 3DCRT and IMRT plans. PTV, lungs, heart and contralateral breast (CB) were outlined. 50 Gy was prescribed to the isocenter. Dose volume histogram parameters (DVPs) for both plans were compared and analyzed statistically using Wilcoxon Signed-Ranks test of SPSS (version 18).

Results: Both 3DCRT and IMRT achieved adequate and comparable target coverage. On the other hand, tangential IMRT showed insignificant higher PTV maximum dose with significant less dose homogeneity compared to 3DCRT. This is with greater sparing of the lungs, heart and contralateral breast in IMRT plans.

Conclusion: In the current study, our data shows that tangential beam IMRT for left breast cancer patients offers the potential to significantly reduce dose-volume parameters of the ipsilateral lung, heart and contralateral breast compared to tangential beam 3-DCRT with comparable target dose coverage. However 3DCRT technique is superior in term of dose homogeneity within the target.

I declare that there is no conflict of interest with any financial organization regarding the material in this manuscript.

Introduction

Breast cancer is the most common female cancer in the US and the second most common cause of cancer death in women. Approximately 232,620 new cases of invasive breast cancer are expected to be diagnosed in the United States in 2011, and 39,970 will die from the disease.[1] Management of invasive breast cancer should be based on the clinical extent and pathologic characteristics of the tumor, in addition to the age of the patient, menopausal status, some biologic prognostic factors, and the preference and psychological profile of the individual patient.[2]

Breast conserving therapy (BCT) which entails lumpectomy, axillary dissection and adjuvant radiotherapy is now clearly established as the standard of care for women with early stage invasive breast cancer. [3,4]

The value of radiation therapy as a breast conservation component has been further validated by studies comparing lumpectomy alone to lumpectomy and radiation therapy. According to results of these studies a three fold reduction in recurrence with the use of radiation therapy following breast conserving surgery especially in node positive and young women was demonstrated.[5]

Although the beneficial effect of postoperative radiotherapy for breast cancer is well documented, this treatment may be related to a number of complications. Acute effects to the skin, poor cosmetic results and increased risks of arm dysfunction and lymphedema in conjunction with extensive axillary lymph node dissection. Long term toxic effects may include carcinogenesis and cardiac or lung damage. [6,7]

The occurrence of previously mentioned complications is primarily related to the amount of the dose deposited in specific organs[8]. So the most efficient way to prevent these sequels is choosing a radiation technique that minimizes the exposure of internal organs. Radiation therapy for breast cancer has changed significantly in the last decades. For adjuvant breast radiotherapy, several new techniques have been introduced including IMRT.[9,10]

IMRT becomes more suitable for treating complex target volumes as IMRT enable variations of the radiation intensity within each beam so it is able to generate more complicated dose distributions and dose gradients with narrower margins than those allowed using traditional methods. As a consequence, IMRT can provide a clinical benefit in terms of increased tumor control through escalated dose and reduced normal tissue complications through OARs sparing[11-13]

Aim

The aim of this work was to compare target conformity and sparing of lung, heart and contralateral breast for IMRT and 3DCRT plans for left breast cancer female patients underwent breast conservative surgery

Methods

CT studies of 20 patients (age range 33-64 years, mean 51years) with early stage left breast cancer who underwent breast conservative surgery and referred to Alexandria Clinical Oncology Department (ACOD), Alexandria faculty of Medicine from May 2011 to October 2012 were planned and calculated with 6 MV photon beam on Precise treatment planning system. All patients scanned supine on breast board with ipsilateral arm above the head and patient head tilted to other side. CT slices at 5 mm thickness were taken from above the shoulder to include the neck superiorly and all of the ipsilateral lung and 5 cm below breast tissue inferiorly. The target volumes including clinical target volume (CTV) and planning target volume (PTV) were outlined according to RTOG breast cancer atlas for radiation therapy planning[14]. Organs at risk (OARs) including lungs, heart and CB were also outlined. Lung volume was automatically generated using the auto-contouring tool of the treatment planning system. CB tissue was defined as all glandular breast tissue (ranges from 817 cm^3 to 2817 cm^3, mean 1505 cm^3). Heart volume was defined as all visible myocardium, including the pericardium, from apex of heart to the right auricle, atrium, and infundibulum of the ventricle. 3DCRT was carried out using two tangential opposed wedged fields. Beam eye view (BEV) and MLCs used to shape target volume and shield OARs as possible in all cases. (Figure 1). Beam angles and wedge angles were chosen to optimize coverage of the PTV while minimizing exposure to ipsilateral lung, heart and CB. Gantry angles ranged from 286° to 314° for the medial fields and 122° to 143° for the lateral fields. Collimator rotation was used in 17 out of 20 cases and it ranged from 4° to 14° for the medial field and from 4° to 14° for the lateral field. Wedges were used in all cases (10°, 15°, 20° or 25°). 1-1.5 cm bolus was used in all cases to improve dose in build up region.

Inverse planned IMRT was carried out using step and shoot technique. The same beam orientations of the 3DCRT tangential beam plan were used. Five segments were generated for each field, segment 1 covering PTV, segment 2 including PTV & excluding heart, segment 3 including PTV & excluding lung, segment 4 including PTV & excluding both heart and lung and segment 5 including PTV & excluding build up region. (Figure 2). After defining planning parameters many trials were carried out to choose the best dose volume constrains (DVC).

Table 1: Optimization setup table

Structure	Type	Priority	Mean dose	Underdose (cGy)	Underdose Volume (%)	Overdose (cGy)	Overdose Volume (%)
PTV	target	100	-	5000	95%	5500	5
Left lung	OAR	30	1000	-	-	4000	-
Heart	OAR	10	-	-	-	4000	5

A total dose of 50Gy was prescribed and normalized to the isocentre of PTV according to the (ICRU) reports 50, 62 recommendations [15,16]. The ipsilateral lung tolerance dose was taken to be mean lung dose less than 30% of prescribed dose (15Gy), volume of lung receiving 20 Gy (V_{20Gy}) less than 15% and volume receiving 30 Gy (V_{30Gy}) less than 10%. The tolerance dose to the heart was taken to be V_{5Gy}, V_{20Gy} less than 5%, V_{30Gy} and V_{40Gy} less than 10%. As regard CB the aim was to keep mean dose to this volume as low as possible. [17]

3DCRT and IMRT plans for the twenty patients were compared using dose distribution, DVHs and DVPs for PTV, lung, heart, CB and the maximum body dose. PTV dose coverage, was assessed using dose to 95% of the volume ($D_{95\%}$) and the maximum point dose of the PTV ($D_{max\%}$). Dose homogeneity was assessed using homogeneity index HI (calculated as max dose /min dose). To evaluate the differences in the sparing of the lung, heart and CB between the two techniques, the selected dose volume parameters (DVPs) for each organ to keep their dose within tolerance were compared. Body maximum dose was also compared. This study had approval of Institutional Review Board as a retrospective one in which confidentially of records was considered

Statistical analysis

DVPs of PTV & OARs for 3DCRT & IMRT plans for the twenty patients were listed, compared and statistically analyzed using Wilcoxon Signed-Ranks test of SPSS (version 18). A P value of less than 0.05 was taken as statistically significant.

Results

3DCRT and inverse planned IMRT plans produced for 50Gy were compared for 20 patients with left sided breast cancer who underwent breast conservative surgery.

Dose distribution within target volume and organs at risk

Table 2 gives the statistical analysis for **PTV DVPs** comparing 3DCRT and IMRT plans. It shows that PTV $D_{95\%}$ ranged from 47Gy to 51Gy (mean 48.5Gy) for 3DCRT plans compared to 45Gy to 51.5Gy (mean 48Gy) for IMRT plans. The maximum dose ranged from 51.5Gy to 59.5Gy (mean 56.5Gy) for 3DCRT plans compared to 55Gy to 60Gy (mean 57.5Gy) for IMRT plans. The differences in PTV $D_{95\%}$ & maximum dose between both plans were not statistically significant (p=0.187 & 0.15 respectively). So PTV coverage was adequate and comparable in both plans. (Figure 3A). On the other hand, dose homogeneity index ranged from 1.07 to 1.2 (mean 1) for 3DCRT plans compared to 1.11 to 1.45 (mean 1.2) for IMRT plans. So the dose homogeneity within PTV was significantly better with 3DCRT than with IMRT plans (p=0.003).

Table 2: Relevant dose volume parameters of PTV comparing 3DCRT & IMRT plans.

PTV DVPs	Min	Max	Mean	±SD	P value
PTV Max dose (CR)	51.5	59.5	56.5	2.04	0.150
PTV Max dose (IM)	55	60	57.5	1.34	
PTV $D_{95\%}$(CR)	47	51	48.5	0.98	0.187
PTV$D_{95\%}$(IM)	45	51.5	48	1.81	
HI (CR)	1.07	1.2	1	0.03	0.003
HI (IM)	1.11	1.45	1.2	0.07	

CR, three-dimensional conformal radiotherapy; IM, intensity-modulated radiotherapy SD, standard deviation. The dose is in Gy.

Table 3 gives the statistical analysis for **lung DVPs**, **heart DVPs**, **CB mean dose and body maximum dose** comparing 3DCRT and IMRT plans. It shows that; **left lung mean dose** ranged from 9Gy to 21Gy (mean 13.5Gy) for 3DCRT plans compared to 5.5Gy to 19.5Gy (mean 11Gy) for IMRT plans. IMRT plans showed a significant reduction of 19.7% compared to 3DCRT plans (p= <0.001) , **left lung V_{20Gy}** ranged from 16% to 41% (mean 23%) for 3DCRT plans compared to 11% to 43% (mean 19%) for IMRT plans. IMRT plans showed a significant reduction of 15.8% compared to 3DCRT plans (p= 0.002) and **left lung V_{30Gy}** ranged from 15% to 39% (mean 23%) for 3DCRT plans compared to 8% to 38% (mean 19%) for IMRT plans. IMRT plans showed a significant reduction of 18%

compared to 3DCRT plans (p= 0.001). So IMRT plans achieved significant lung sparing compared to 3DCRT plans. (Figure 3B).

Table 3 also shows that; **heart V_{5Gy}** ranged from 3% to 62% (mean 32%) for 3DCRT plans compared to 7% to 58% (mean 28%) for IMRT plans. IMRT plans showed a significant reduction of 14% compared to 3DCRT plans (p= 0.001), **heart $V_{20\ Gy}$** ranged from 2% to 51% (mean 24%) for 3DCRT plans compared to 4% to 46% (mean 20%) for IMRT plans. IMRT plans showed a significant reduction of 16% compared to 3DCRT plans (p= 0.001), **heart V_{30Gy}** ranged from 2% to 47% (mean 21%) for 3DCRT plans compared to 2% to 42% (mean 17) for IMRT plans. IMRT plans showed a significant reduction of 22% compared to 3DCRT plans (p= <0.001) & **heart $V_{40\ Gy}$** ranged from 1% to 44% (mean 17%) for 3DCRT plans compared to 0% to 30% (mean 8%) for IMRT plans. IMRT plans showed a significant reduction of 51% compared to 3DCRT plans (p= <0.001). So IMRT plans achieved significant heart sparing compared to 3DCRT plans. (Figure 3C).

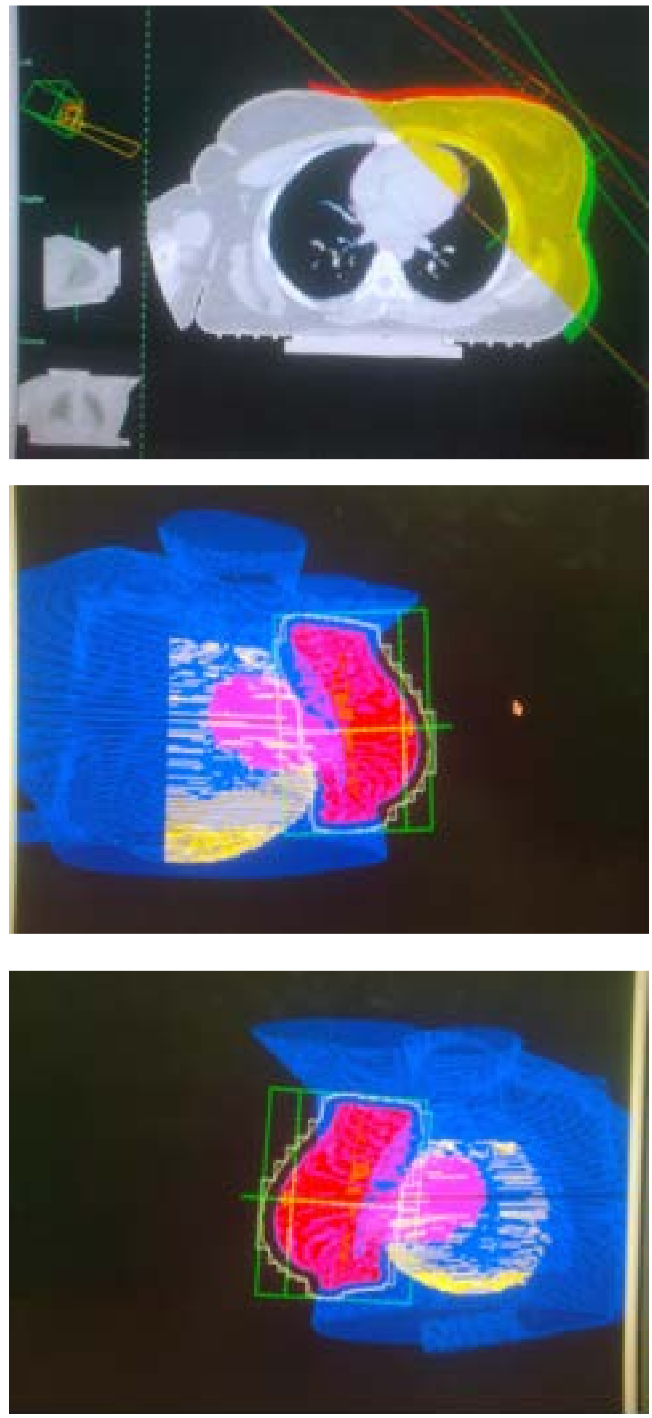
Regarding CB mean dose; it ranged from 0.5Gy to 12Gy (mean 5Gy) for 3DCRT plans compared to 0.5Gy to 8.5Gy (mean 3.5Gy) for IMRT plans. IMRT plans showed a significant reduction of 27% compared to 3DCRT plans (p= <0.001). (Figure 3D). **Table 3** shows that; body maximum dose ranged from 55Gy to 62.5Gy (mean 57.5Gy) for 3DCRT plans compared to 54Gy to 61Gy (mean 57Gy) for IMRT plans. The differences between plans were not statistically significant (p= <0.255).

Table 3: Relevant dose volume parameters of OARs comparing 3DCRT & IMRT plans.

DVPs	Min	Max	Mean	±SD	P value	Reduction % ±SD
Left lung						
Mean dose (CR)	9	21	13.5	2.66	<0.001	19.71 8.61
Mean dose (IM)	5.5	19.5	11	2.97		
V_{20Gy}(CR)	16	41	23	6.29	0.002	15.80 8.62
V_{20Gy} (IM)	11	43	19	7.55		
V_{30Gy} (CR)	15	39	23	6.08	0.001	18.18 11.46
V_{30Gy} (IM)	8	38	19	7.01		
Heart						
V_{5Gy} (CR)	3	62	32	14.80	0.001	14.07 9.75
V_{5Gy} (IM)	7	58	28	13.78		
$V_{20\ Gy}$ (CR)	2	51	24	13.14	0.001	16.23 11.17
V_{20Gy} (IM)	4	46	20	11.39		
V_{30Gy} (CR)	2	47	21	12.06	<0.001	22.02 14.41
V_{30Gy} (IM)	2	42	17	10.23		
V_{40Gy} (CR)	1	44	17	11.14	<0.001	50.94 28.26
V_{40Gy} (IM)	0	30	8	7.11		
Contralateral breast (CB)						
Mean dose (CR)	0.5	12	5	2.89	<0.001	26.88 13.56
Mean dose (IM)	0.5	8.5	3.5	2.01		
Body						
Max. dose (CR)	55	62.5	57.5	1.52	0.255	0.62 4.5
Max. dose (IM)	54	61	57	2.25		

The dose is in Gy & the volume receiving certain dose is in percent.

Reduction % is calculated as value of 3DCRT parameter - value of IMRT parameter / value of 3DCRT parameter x100 for each patient, and then the mean for 20 patients is calculated.



A

B

C

Figure 1: CT axial slices (A) and REV (B & C) show medial and lateral tangential fields of 3DCRT.

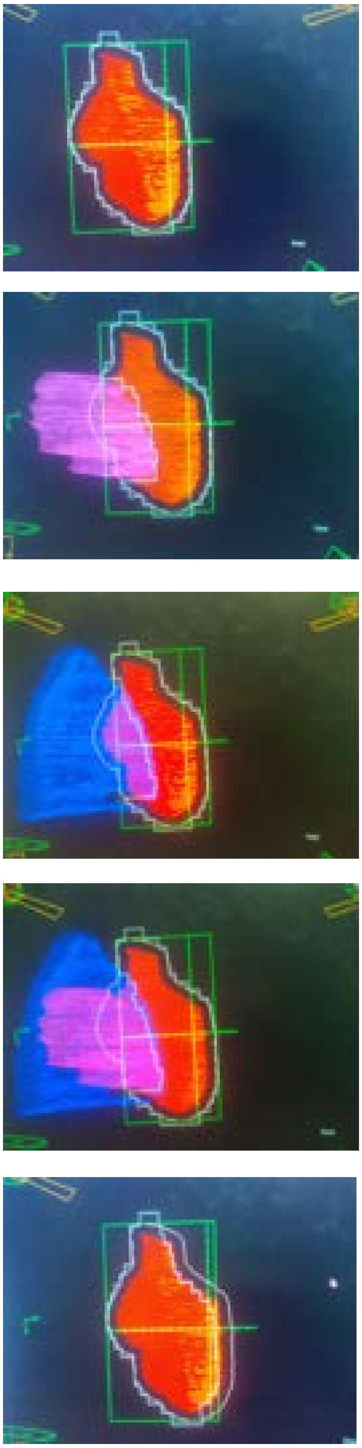


Figure 2: BEV of IMRT medial tangential beam show segments; segment 1 covering PTV, segment 2 including PTV & excluding heart, segment 3 including PTV & excluding lung, segment 4 including PTV & excluding both heart and lung and segment 5 including PTV & excluding build up region

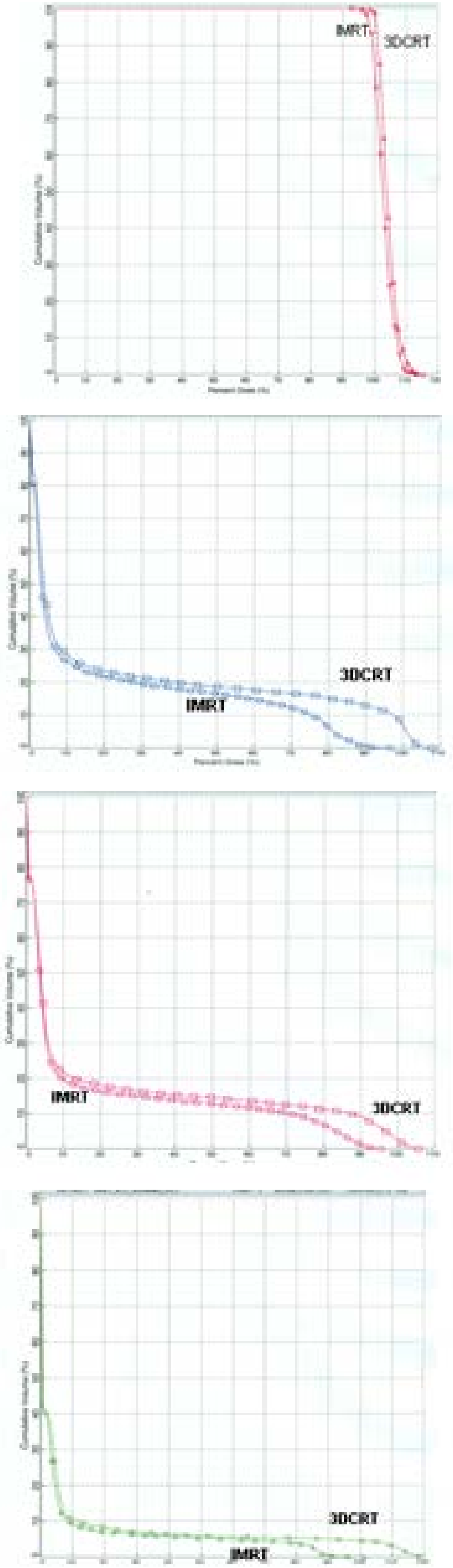


Figure 3: DVH in percentage for PTV (A), left lung (B), heart (C) & CB (D) comparing 3DCRT and IMRT plans

Discussion

Whole breast radiotherapy reduces risk of local recurrence and improves overall survival, but the main problems are the serious side effects on the heart, lung and contralateral breast. In this regard current study was carried out to evaluate the difference in dose distribution of tangential beam IMRT compared to tangential beam 3DCRT of whole breast in early breast cancer patients underwent breast conservative surgery.

As regard target coverage; both 3DCRT and IMRT in the current study achieved adequate and comparable target coverage. On the other hand, tangential IMRT showed insignificant higher PTV maximum dose with significant less dose homogeneity compared to 3DCRT. Target coverage is in accordance with that of Fong et al 2009[18]; who compared different IMRT techniques and standard wedge technique (SWT) for whole breast radiotherapy. But in contrast to current study dose homogeneity was not significantly different between tangential IMRT and SWT, and maximum dose was significantly reduced with tangential IMRT compared to SWT.

In Fong et al 2009[18] study, higher PTV maximum dose with SWT could be explained by using half beam block to shape the field and to prevent beam divergence within the lung without using MLCs. On the other hand, in the current study lower PTV maximum dose with 3DCRT is due to using well optimized technique by MLCs, different beam weighting and motorized variable wedges. Added to this, IMRT was limited by being two tangential fields with few segments.

The findings of the current study were supported by Mayo and colleagues [19] findings. They reported that the tangent inverse planning IMRT resulted in the worst dose homogeneity inside the breast and the worst maximum dose outside the target compared to 3DCRT and forward planning IMRT plans.

Regarding to lung sparing; in the current study IMRT resulted in better lung sparing compared with 3DCRT. This is in accordance with the results of Fong et al 2009 [18]; the mean lung dose was significantly reduced with tangential IMRT compared to SWT. The results of the current study were supported by R. Jagsi et al, 2010 [20] who compared many IMRT techniques including inverse tangential IMRT and forward planning segmental technique. They found that the left lung mean dose and V_{30Gy} with the inverse tangential IMRT technique were lower than forward planning segmental technique and also lower than that of the current study (7Gy and 20% compared to 11Gy and 19% in current study).

Regarding to heart sparing; current study showed that IMRT resulted in better heart sparing; V_{5Gy}, V_{20Gy}, V_{30Gy} and V_{40Gy} were significantly lower with IMRT than with 3DCRT. This is in accordance with the results of Fong et al 2009 [18]; they found that the volume of heart receiving large doses ($V_{47.5}$) was significantly decreased with the tangential IMRT (0.56% vs. SWT 1.7%, P = 0.011) whereas the volume receiving moderate doses (V_{30}) was not significantly differ with tangential IMRT compared with SWT. The results of the current study were also supported by Remouchamps et al, 2003 [21] who showed that heart V_{30Gy} was lower with IMRT than with wide tangent wedge technique (6.8% and 19.1% respectively). The introduction of deep inspiration breath hold technique to tangential IMRT reduced heart V_{30Gy} by 81%. Although current results were higher than results of tangential IMRT without deep inspiration breath hold technique (heart $V_{30\ Gy}$ was 17% for IMRT plans compared to 21% in 3DCRT plans) but reduction is still significant and results were within tolerance dose of the heart.

As regard to CB dose; current study revealed significant reduction of CB mean dose with IMRT compared with 3DCRT. This is in accordance with Fong, et al 2009 [18] study; the mean dose to the CB was significantly reduced with the tangential IMRT plans (1.8 Gy compared to 2.3 Gy with SWT).

Conclusion

In the current study, our data shows that tangential beam IMRT for left breast cancer patients offers the potential to significantly reduce dose-volume parameters of the ipsilateral lung, heart and contralateral breast compared to tangential beam 3-DCRT with comparable target dose coverage. However 3DCRT technique is superior in term of dose homogeneity within the target

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