IMRT heart sparing in post-operative left breast cancer radiation therapy: A dosimetric study

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Abstract

Purpose: To compare and evaluate cardiac radiation doses in intensity modulated radiotherapy (IMRT) and 3D-conformal radiotherapy (3D-CRT).
Patients and methods: Sixty patients with left breast cancer were included in this study. IMRT and 3D-CRT plans were generated for each patient using XIO planning system and analyzed with respect to doses to heart. Parameters used were (V30Gy, V40Gy, Dmax, Dmean, NTCP).
Results: Heart radiation doses were significantly better in IMRT than in 3D-CRT particularly V30Gy (5.221±3.052% VS 13.184±5.868% with P-value=0.001), V40Gy (0.381±0.795% vs 8.791±4.546% with P-value=0.001), and NTCP (0.7563±0.287% vs 2.436±1.051% with P-value=0.001).
Conclusion: IMRT technique spared more heart volume from receiving excess radiation doses. NTCP values were significantly better in IMRT than in 3D-CRT technique.

Introduction

The rationale behind adjuvant post-operative radiotherapy following breast-conserving surgery (BCS) is the sterilization of the tumor bed of any residual subclinical disease that may be present after surgical excision. Adjuvant radiotherapy has been shown to be effective in reducing the risk of local recurrence in early stage disease and some studies also demonstrate improved survival in high-risk pre-menopausal women. The late widespread adoption of BCS and adjuvant post-operative radiotherapy, especially in good prognosis young women with early stage breast disease, increased the importance of late complications due to the long expected disease-free interval(1).

Concern exists regarding the inclusion of the IMNs in the target volume because of the potential for increased heart and lung radiation exposure. The concern is amplified because most patients referred for loco-regional radiotherapy are at increased risk of distant dissemination and will likely receive systemic agents with known cardiac and pulmonary toxicity. Therefore, the investigation of new techniques, such as IMRT, which have the potential to reduce heart and lung doses to levels lower than standard techniques, is of clinical importance(2).

Cozzi et al evaluated the effectiveness of IMRT in patients who might be considered at high risk of radiation- induced complications. These patients would have received a suboptimal treatment if irradiated with conventional or 3D- conformal techniques. With a relatively short mean follow- up of 10.4 months, no radiation pneumonitis and no heart complications were clinically observed after treatment. The authors concluded that IMRT proved to be technically feasible on a clinical basis for the treatment of the whole breast, including the IMC(3).

Hurkmans et al applied conformal tangential beam irradiation to the intact left breast with and without intensity modulation, instead of rectangular tangential treatment fields. The authors found that the use of conformal tangential fields decreases the NTCP for late cardiac toxicity on average by 30% compared to using rectangular tangential fields, while the tangential IMRT technique can further reduces this value by further 50% (4).

Patient and Methods

Sixty Stage I, II or III left-sided breast cancer patients who underwent breast conservative surgery (BCS) or modified radical mastectomy(MRM), Level I–II lymph node dissection, and loco-regional radiotherapy at Kasr El-Ainy cancer center (NEMROCK), chosen for this study. 3D-CRT and IMRT plans were generated for each patient.

Treatment Planning

Target delineation

A 3-D CT scan with 5-mm slice spacing was performed from mid-neck to upper abdomen. A radiation oncologist delineated the planning target volume (PTV). The PTV comprised the left breast and the chest wall in cases of breast conservative surgery (BCS), and the left chest wall in cases of modified radical mastectomy (MRM). .The IMC PTV was defined by an elliptical cylinder, with a major (lateral) and minor (anterior-posterior) axes of 30 and 20 mm, respectively, centered on the IMC vessels. This extended between the inferior aspect of the ipsilateral clavicular head and the fourth intercostals space to ensure only the first three intercostals spaces were included(5). The isocenter was positioned in the middle of the PTV.

Heart delineation

Heart was defined as all visible myocardium (excluding pericardium) from the apex to right auricle, atrium and infundibulum of the ventricle. The pulmonary trunk, root of ascending aorta & superior vena cava were excluded.

3D-conformal planning

In 3D-CRTplans, The PWTF plans were performed using standard forward planning methods, the gantry angle was optimized in the beam's eye view (BEV) for a minimum lung area and beam divergence toward the lung was compensated by adjusting the gantry angle of the beams. The ipsilateral lung was spared using a multileaf collimator (MLC). The shape of the MLC was defined in the BEV with a distance of 10 mm to the PTV to compensate the penumbra in craniocaudal direction and toward the lung, figures (1&2).

IMRT planning

In IMRT plans, seven co-planer equi-angular beams were used, figure *(3)*. The treatment planning system generated the beam intensity profiles with a bixel (or beam element) size of 5x5 mm², using step and shoot IMRT. Dose calculation was via pencil-beam method. Cost functions were selected and determined to satisfy the plan goals regarding the target coverage and risk organs protection. Optimization used superposition algorithm. All beam weights and intensity profiles were optimized using Helios inverse planning IMRT module. Optimization was performed by means of a steepest gradient search algorithm, then the segmentation process accomplished according to leaf motion calculator (LMC) algorithm. The maximum number of iterations was 100. Dose constrains to PTV & organs at risk were estimated numerically and also using constrains, and the optimization process was started and online modifications were attempted during optimization process to be able to get the best calculated fluence map and dose distribution. Then the segmentation process started to build the actual fluence for each beam according to leaf constrains of the treatment machine and the process accomplished via LMC algorithm. All plans were calculated at the XIO version 4.2 planning system. Photon energy of 6 MV at an Elekta accelerator was used.

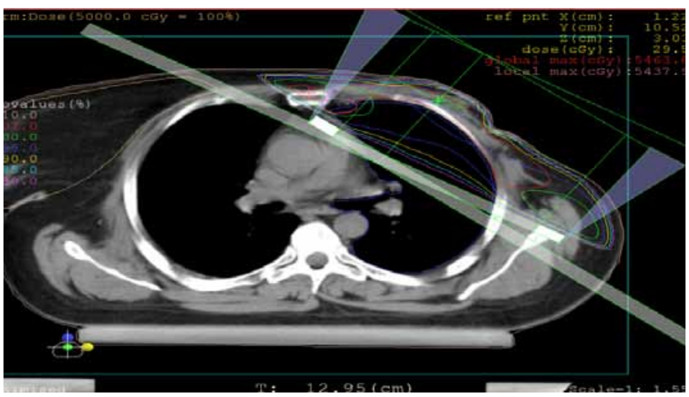

Fig 1: Shows the 3DCRT planning with the two PWTF.

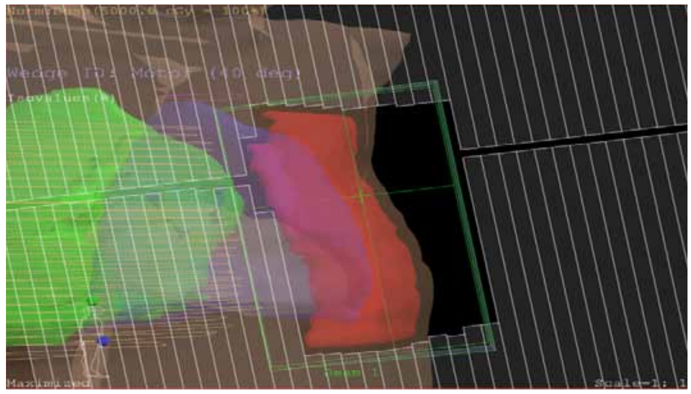

Fig 2: Shows the BEV for the 3d-CRT plan.

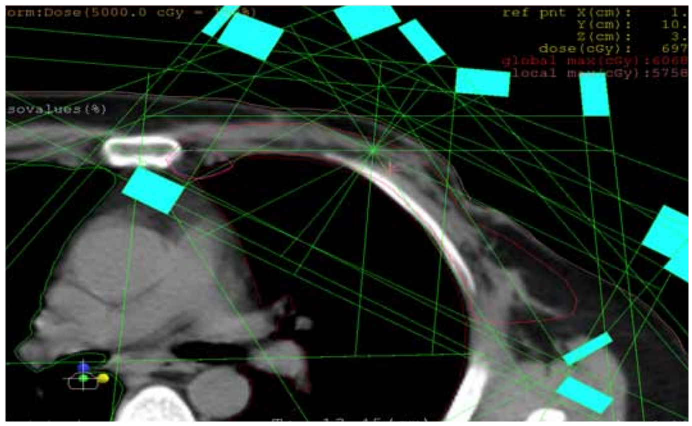

Fig 3: Shows the seven equi-distant co-planner beams in IMRT planning.

Dose–volume histograms (DVHs) were generated for all relevant structures for both techniques. Specific metrics were chosen for comparison of the IMRT and 3D-CRT plans figures (4&5). V30, V40, Dmax, Dmean, and NTCP (Normal Tissue Complication Probability) for late cardiac toxicity using model (incorporated in the planning computer system "XIO") with the parameters (n=0.35, m=0.10, and TD50= 48Gy) (6).

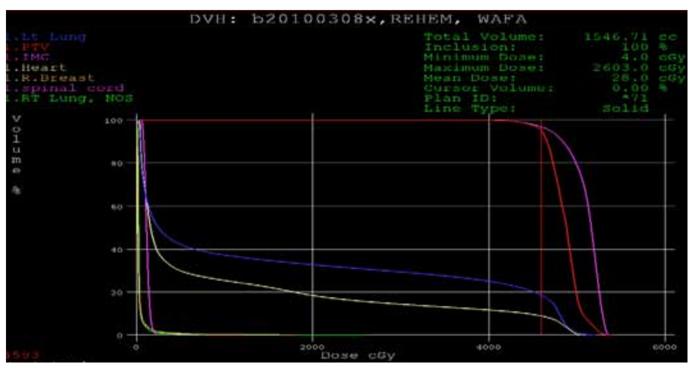

Fig 4: Shows the DVH for the 3D-CRT plan which display the doses to the targets and the organs at risk (heart in yellow color).

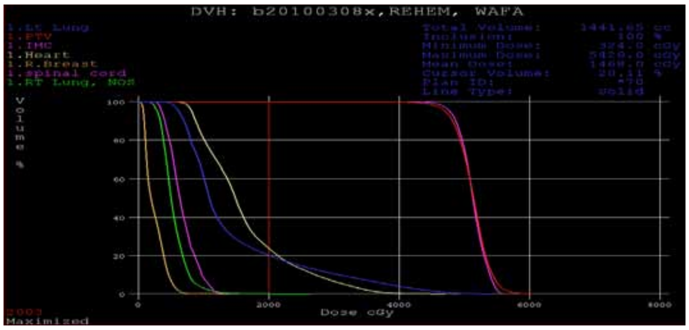

Fig 5: Shows the DVH for the IMRT plan which display the doses to the targets and the organs at risk (heart in yellow color).

Results

Five parameters were used to evaluate the radiation doses to the heart which were (V30Gy, V40Gy, Dmax, Dmean, and NTCP). These parameters were better in the IMRT than the 3D-conformal techniques which showed statistically significant differences (P-value <0.05) except in Dmean which was significantly less in 3D- conformal than in IMRT techniques, as shown in table (1).

Table 1: Evaluation of Heart Radiation Dose for all patients

Parameter	3D-CRT (60 plans) (mean ±Std)	IMRT (60 plans) (mean ±Std)	P-Value
V30 Gy	13.184±5.868%	5.221±3.052%	0.001
V40 Gy	8.791±4.546%	0.381±0.795%	0.001
Dmax	4737.48±402.271 cGy	3419.67±619.192 cGy	0.001
Dmean	837.25±265.945 cGy	1466.35±299.945 cGy	0.001
NTCP	2.436±1.051%	0.7563±0.287%	0.001

V30Gy = The percentage volume of the heart received at least 30Gy.
V40Gy = The percentage volume of the heart received at least 40Gy.
Dmax= Dose received by 2% of the heart.
Dmean= The mean dose received by the heart.
NTCP = Normal Tissue Complication Probability.

These significant differences in radiation doses to the heart were also maintained whether IMC was included or not in the planning, as shown in tables (2&3), and when the chest wall geometry was more curved (more than the normal ratio of AP/lat=5/7) table(4)

Table 2: Evaluation of Heart Radiation Doses with IMC

Parameter	3D-CRT (30 plans) (mean ±Std)	IMRT (30 plans) (mean ±Std)	P-Value
V30 Gy	15.240±4.968%	5.881±3.132%	0.001
V40 Gy	9.681±4.546%	0.862±0.341%	0.001
Dmax	4822.48±402.271 cGy	3454.59±709.192	0.001
Dmean	967.34±277.945 cGy	1483.35±302.945	0.001
NTCP	2.621±1.051%	0.846±0.279%	0.001

Table 3: Evaluation of Heart Radiation Doses without IMC

Parameter	3D-CRT (30 plans) (mean ±Std)	IMRT (30 plans) (mean ±Std)	P-Value
V30 Gy	10.364±6.11%	3.275±2.121%	0.001
V40 Gy	7.404±5.281%	0.381±0.795%	0.001
Dmax	4626.24±541.027 cGy	3037.45±609.443 cGy	0.001
Dmean	721.28±289.309	1336.90±224.951	0.001
NTCP	1.833±0.931%	0.573±0.218%	0.001

Table 4: Evaluation of Heart Toxic Dose with Chest Wall Ratio>0.71:

Parameter	3D-CRT (30 plans) (mean ±Std)	IMRT (30 plans) (mean ±Std)	P-Value
V30 Gy	13.827±6.158%	4.413±1.939%	0.001
V40 Gy	10.054±5.050%	0.0482±0.0108%	0.001
Dmax	4786.82288.763± cGy	3321.64316.691± cGy	0.001
Dmean	846.09271.658± cGy	1438.55173.408±	0.001
NTCP	2.501±1.491%	0.731±0.215%	0.002

Discussion

The parameters used to evaluate the radiation doses to the heart were significantly better in the IMRT than the 3D-conformal technique except Dmean was significantly better in 3D- conformal than in IMRT techniques. The benefit of IMRT technique has been kept valid whether IMC irradiation was given or not. ***Remouchamps, et al, 2003*** (7) showed that the mean volume of heart receiving > 30 Gy (heart V30) was lower with the IMRT technique than with the deep tangent wedged technique (6.8% and 19.1%, respectively; $p < .004$). The introduction of moderate deep inspiration breath-holds to the deep tangent IMRT technique reduced the heartV30 by 81% to a mean of 3.1% ($p < .0004$). Our results showed that heart volume which received more than 30 Gy; V40Gy was better than those results (<1.0% with IMC, and <0.5% without IMC).
Cho et al., 2002 (4) showed that the average NTCP for excess late cardiac mortality were 2.1 and 0.6% for the, wide split tangent and IMRT techniques, respectively, which was significant (P = 0:03). The individual NTCP values for the heart decreased by approximately 70% when going from the wide split to the IMRT plans. ***Krueger et al., 2003*** (2) in their study showed that IMRT matched the < 1% heart NTCP achieved using PWTFs (3D-conformal) technique. Our results agreed with the previous results in which the NTCP for late cardiac toxicity was kept below 1% (<0.75% with IMC, and <0.57% without IMC irradiation). Patients with increased chest antero-posterior/transverse ratio clearly had decreased lung and heart radiation doses with IMRT compared with 3D-conformal technique. ***Ung et al, 2000*** (8) showed that wide tangents were an appropriate treatment option for most patients. However, in some cases, excess heart or lung will be irradiated. This typically occurs for patients with anterior hearts, or barrel shaped chests. ***Cho et al, 2004*** (1) showed that concave targets are better covered with intensity modulated beams since they were able to conform more tightly around breast and spare the heart.

Conclusion

The IMRT technique was shown to reduce significantly heart radiation doses and the NTCP for late cardiac toxicity. This advantage of IMRT was valid whether IMC was included or not, and in geometrically more curved chest wall. Additional study of this technique, however, should be performed to analyze the unknown clinical implications of some of the dosimetric differences that result from the new plans and also to address the unsolved issues of treatment delivery associated with setup uncertainty, motion due to respiration, and the potentially increased sensitivity of the IMRT plans to those issues.

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