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Significant reductions in heart and lung doses using IMRT for left sided breast cancer patients

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Abstract

Introduction
Various radiation techniques include Three Dimensional Conformal Radiotherapy (3DCRT), breath hold and Intensity Modulated Radiotherapy (IMRT) are used to irradiate the breast and to limit the dose to the heart and lungs. IMRT is used as a class solution for cardiac protection in left sided breast cancer patients.

Aim of the work
To evaluate heart and lung sparing effects of tangential beam IMRT whilst maintaining target coverage compared with tangential beam 3DCRT for left sided breast cancer patients

Methods
CT simulation was done for thirty left sided breast cancer patients who underwent conservative surgery. Planning target volume (PTV), heart and ipsilateral lung were contoured. 3DCRT and IMRT plans were generated for 50Gy using opposed tangential medial and lateral photon beams. Five segments were generated for each IMRT field. Heart V_{5Gy}, V_{20Gy}, V_{30Gy} and V_{40Gy} and ipsilateral lung V_{20Gy}, mean dose, PTV $D_{95\%}$, PTV D_{max} and dose homogeneity index were compared using Wilcoxon Signed-Ranks test.

Results
IMRT plans achieved significant reduction of 12%, 15%, 21% & 53% in heart V_{5Gy}, V_{20Gy}, V_{30Gy} and V_{40Gy} and of 18% & 11% in ipsilateral lung mean dose and V_{20Gy} compared with 3DCRT (p values <0.001). PTV coverage was adequate and comparable in both plans (P for PTV $D_{95\%}$ & $D_{max\%}$ =0.188 & 0.553). The dose homogeneity within PTV was significantly better with 3DCRT (P=0.004).

Conclusion
Tangential beam IMRT in left sided breast cancer leads to a significant dose reduction in heart and ipsilateral lung with comparable target coverage compared to tangential beam 3DCRT.

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 malignancy in women [1]. Early stage breast cancer is commonly treated using breast conserving surgery followed by adjuvant radiotherapy [2,3]. Although Three Dimensional Conformal radiotherapy (3DCRT) is widely used for treatment of breast carcinoma because it increases dose conformity to target volume and reduce heart and lungs doses but there is still a risk of fatal cardiovascular events [4].
Various radiation cardiac sparing techniques are recently used to irradiate the breast and to limit the dose to the heart and lungs [5]. These techniques include maneuvers that based on the increase in the distance between the heart and the chest wall such as breath hold, respiratory gating and prone patient positioning techniques[6].
Breath hold reduces the heart dose as the heart moves away from the chest wall so cardiac volumes exposed to radiation are reduced. Respiratory gating is anther technique for cardiac sparing as radiation is delivered during respiratory expansion of the thorax where the distance between the heart and the radiation fields is enlarged [7].
In prone positioning technique the breast falls away from the chest wall so the edge of the radiation beam is positioned away from the heart. This is useful for cardiac protection especially in patients with pendulous breasts [8].
Using advanced techniques as IMRT or proton beam radiotherapy is another way of cardiac sparing [9,10].

Computerized leaves and dose planning algorithms of IMRT allow for shaping of radiation field and help to escalate the dose to the target. This is with significant reductions in the cardiac dose [11]. IMRT is successfully used as a class solution for cardiac protection in left sided breast cases especially for patients with large breast [12,13,14]. Proton beam radiotherapy is based on rapid dose fall off beyond the Bragg peak. This allows the dose reduction to structures beyond the target volume as heart and so reduces cardiac toxicities [15].

As there is evidence that patients treated with these techniques have a lower risk of cardiac toxicity [16,17,18] so this study **aimed** to evaluate the heart and lung sparing effects of tangential beam IMRT whilst maintaining target coverage compared with tangential beam 3DCRT for left sided breast cancer patients.

Methods

CT simulation:

CT simulation was done for thirty left sided breast cancer patients who underwent breast conservative surgery and referred to Alexandria Clinical Oncology Department (ACOD), Alexandria faculty of Medicine from June 2014 to May 2015. CT Simulation was performed in the supine position on breast board with the ipsilateral arm positioned above the head and patient head tilted to other side.

Target and organs at risk delineation

The CT data were transferred to treatment planning system (Precise Elekta) where all required structures were contoured. The Planning target volume (PTV) was outlined according to RTOG breast cancer atlas for radiation therapy planning [19]. Organs at risk (OARs) including heart and ipsilateral lung were also contoured.

Treatment Planning

3DCRT Planning

3DCRT optimum plan was carried out using two opposed tangential medial and lateral 6MV photon beams. The gantry and wedge angles were chosen to optimize the coverage of the PTV and to protect the ipsilateral lung and heart which were also shielded using MLCs. To improve the target coverage in the buildup region one cm thickness of a tissue equivalent bolus was used.

IMRT Planning

Step and shoot IMRT optimized plans were generated using same beam orientations of the 3DCRT plan. Five segments were generated for each field; segment one covering PTV, segment two including PTV & excluding heart, segment three including PTV & excluding lung, segment four including PTV & excluding both heart and lung and segment five including PTV & excluding buildup region. The best dose volume constrains (DVCs) were selected after many trials (table 1).

Dose Prescription and dose limitation

The dose of 50Gy/25f was prescribed to the ICRU reference point which was located in the centre of the PTV volume. According to the International Commission on Radiation Units and Measurement (ICRU) Reports 50 [20] and 62 [21] recommendations the PTV dose coverage was assessed using dose to 95% of the volume ($D_{95\%}$) and the maximum dose point of the PTV (D_{max}). Dose homogeneity was assessed using homogeneity index HI (calculated as $D_{5\%}$ / $D_{95\%}$ where $D_{5\%}$ and $D_{95\%}$ are the minimum doses delivered to 5% and 95% of the PTV). For OARs; the volume of heart receiving 5Gy, 20Gy, 30Gy and 40Gy (V_{5Gy}, V_{20Gy}, V_{30Gy} and V_{40Gy}) were selected for the comparison of cardiac sparing between 3DCRT and IMRT plans. The ipsilateral lung mean dose and the volume of ipsilateral lung receiving 20Gy (V_{20Gy}) were also used for comparing lung protection.

This study had approval of Institutional Review Board as a retrospective one in which confidentially of records was considered

Statistical analysis

Dose volume histograms of the PTV, ipsilateral lung and heart of the 3DCRT and IMRT plans were generated for the thirty patients. Relevant dose volume histogram parameters of both plans were compared and tested for any statistically significant difference using Wilcoxon Signed-Ranks test of SPSS (version 16).

Results

Table 2 & Table 3 compares the relevant plan parameters of PTV, ipsilateral lung and heart of tangential beam IMRT and 3DCRT for the adjuvant radiotherapy of whole breast for thirty

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
ipsilateral lung	OAR	40	1200	-	-	4500	-
Heart	OAR	20	-	-	-	4500	5

left sided breast cancer patients. **Figure 1** demonstrates dose distributions of an IMRT and 3DCRT plan of the same patient.

Dose distribution within PTV

Table 2 & figure 2 (A) present the comparison and dosimetric analysis for the Planning Target volume (PTV) for

Table 2 Relevant plan parameters of PTV comparing tangential beam 3DCRT and tangential beam IMRT of the adjuvant radiotherapy of the whole breast in left sided breast cancer patients

PTV DVPs	Min	Max	Average	SD	P value
$D_{95\%}$ (3DCRT)	94	102	97.16	1.80	0.188
$D_{95\%}$ (IMRT)	90	103	96.40	3.15	
D_{max} (3DCRT)	103	119	114	4.06	0.553
D_{max} (IMRT)	110	120	114.9	2.74	
HI (3DCRT)	1.07	1.19	1.11	0.02	0.004
HI (IMRT)	1.10	1.21	1.14	0.03	

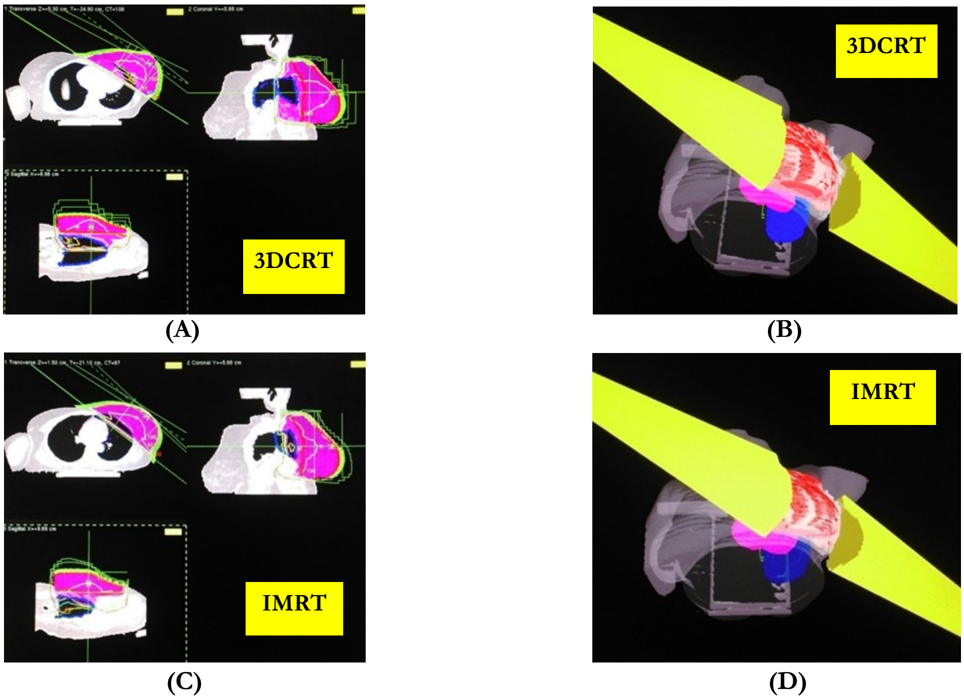


Figure 1. Dose distribution displayed in axial, coronal & sagittal views (A & C) for 3D-CRT & IMRT plans using opposed tangent fields for a left sided breast cancer patient and the room eye views of the same patient (B & D). Both show the colour wash of 95% of the dose (pink in A & C & white in B & D) match well the PTV shape.

tangential beam 3DCRT and IMRT plans. Regarding to target coverage; the average of PTV $D_{95\%}$ & $D_{max\%}$ 97.16% & 114% for 3DCRT plans compared to 96.40% & 114.9% for IMRT plans. So coverage is adequate in both plans but comparable as the differences in PTV $D_{95\%}$ & $D_{max\%}$ between the plans were not statistically significant (*P*=0.188 & 0.553). Regarding the dose homogeneity; 3DCRT plans shows significantly lower HI than IMRT plans (1.11 for 3DCRT plans Vs 1.14 for IMRT plans) so the dose homogeneity within PTV was significantly better with 3DCRT than with IMRT plans (P=0.004).

Dose distribution within organs at risk

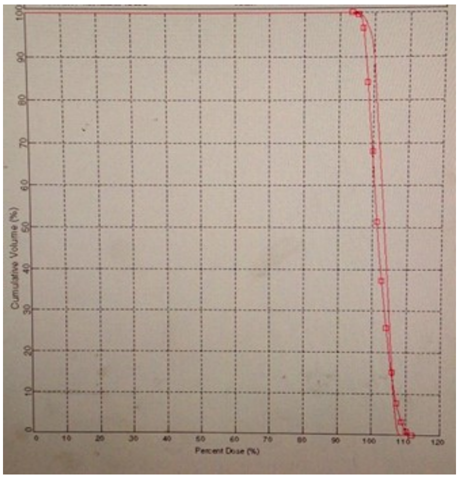
Regarding to ipsilateral lung; tangential beam IMRT statistically significantly reduced the ipsilateral lung mean dose by an average of 18% (average 10.80Gy versus 13.23Gy) & the ipsilateral lung V_{20Gy} by an average of 11% (average 21.10% versus 23.90%) for IMRT and 3DCRT respectively (P<0.001). So IMRT plans achieved a significant ipsilateral lung sparing compared to 3DCRT plans. **(Table 3 & figure 2 (B)**

Concerning the heart; tangential beam IMRT shows significant reduction of 12% (average 24.10% versus 28.53%), 15% (average 17.16% versus 21.10%), 21% (average 14.13% versus 18.36%) & 53% (average 6.80% versus 15.20%) in heart V_{5Gy}, V_{20Gy}, V_{30Gy} and V_{40Gy} for IMRT and 3DCRT respectively (P<0.001). So IMRT plans achieved significant heart sparing compared to 3DCRT plans. **(Table 3 & figure 2 (B)**

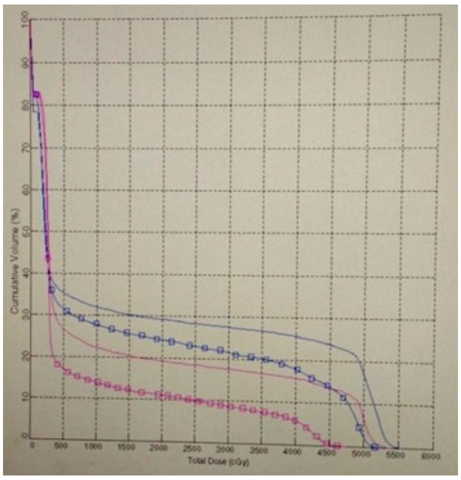
Discussion

In left sided breast cancer the target volume is located in close proximity to the heart, ipsilateral lung, and other critical organs. While conventional 3DCRT plans cannot adequately protect these organs, a number of studies reported the benefits of IMRT in protecting the heart and other critical organs compared to 3DCRT for the whole breast in early stage left sided breast cancer patients. So IMRT is successfully used as a class solution for cardiac protection [22, 23]. This study aimed to evaluate the heart and lung sparing effects of tangential beam IMRT whilst maintaining target coverage compared with tangential beam 3DCRT for thirty left sided breast cancer patients who underwent breast conservative surgery.

In the current study 3DCRT and IMRT plans showed adequate and comparable PTV dose coverage as the differences in PTV $D_{95\%}$ & $D_{max\%}$ between the plans were not statistically significant. On the other hand, tangential IMRT plans showed significant worst dose homogeneity compared to 3DCRT plans. The worst dose homogeneity inside the breast compared to 3DCRT plans was supported by Mayo CS et-al 2005[24] & Beckham WA et-al 2007[25]. On the other hand in contrast with the results of the current study, Rongsriyam K et-al 2008 [26] & Guang et-al study 2013[27] found that IMRT plans improved the target coverage, homogeneity and conformity compared with 3DCRT plans.



(A)



(B)

Figure 2. DVH for PTV (A), for Ipsilateral lung in blue and heart in pink (B) comparing 3DCRT (solid line) and IMRT plans for a left sided breast cancer patient

Regarding to heart sparing: current study showed that IMRT plans resulted in significant heart reductions in V_{5Gy}, V_{20Gy}, V_{30Gy} and V_{40Gy} compared to 3DCRT plans. The findings of the current study were supported by the results of Beckham WA et-al 2007[25] study; they found that heart V_{30Gy} was lower for IMRT plans (1.7% for IMRT Vs 12.5% for 3DCRT plans). Li J S et-al 2004 [28] showed also that heart V_{30Gy} was lower in IMRT plans compared with 3DCRT plans (0.5% in IMRT and 5% in 3DCRT plans); this is in accordance with the results of the current study. The results of the current study is also supported by Rongsriyam K et-al 2008[26] who found that heart V_{30Gy} was significantly lower for IMRT plans compared to 3DCRT plans (3.12% vs 5.84%). Moorthy S et-al 2013[29] also found that the average V_{40Gy} of heart was significantly lower for

Table 3. Relevant plan parameters of OARs comparing tangential beam 3DCRT and tangential beam IMRT of the adjuvant radiotherapy of the whole breast in left sided breast cancer patients

DVPs	Min	Max	Average	SD	P-value	Reduction%
Heart						
V_{5Gy} (3DCRT)	3	62	28.53	13.9	<0.001	12
V_{5Gy} (IMRT)	6	58	24.10	12.9		
V_{20Gy} (3DCRT)	2	51	21.10	12.1	<0.001	15
V_{20G} (IMRT)	3	46	17.16	10.56		
V_{30Gy} (3DCRT)	2	47	18.36	11.01	<0.001	21
V_{30Gy} (IMRT)	2	42	14.13	9.21		
V_{40Gy} (3DCRT)	1	44	15.20	10.12	<0.001	53
V_{40Gy} (IMRT)	0	30	6.80	6.17		
Ipsilateral lung						
Mean dose (3DCRT)	7	21	13.23	2.80	<0.001	18
Mean dose (IMRT)	5.5	19.5	10.80	2.69		
V_{20Gy}(3DCRT)	12	41	23.90	6.08	<0.001	11
V_{20Gy} (IMRT)	11	43	21.10	6.60		

IMRT compared with 3DCRT (7.5 % for 3DCRT and 2.13 % for IMRT).

Regarding to Ipsilateral lung sparing: In the current study IMRT resulted in significant lung sparing compared with 3DCRT plans. This is in accordance with Khullar P et-al 2014 [30]; they reported that IMRT achieved a significant reduction in V_{20Gy} of the ipsilateral lung with IMRT (49.2% versus 59.8% of the conventional technique). Moorthy S et-al 2013[29] also demonstrated that IMRT provided better dose distribution with significantly better mean dose and V_{20Gy} compared with 3DCRT (V_{20Gy} of ipsilateral lung was 37.9 % for 3DCRT and 22.4 % for IMRT). The results of the current study were also supported by Jagsi R et-al 2010[18]; they showed that the ipsilateral lung mean dose and V_{30Gy} with the inverse tangential IMRT technique were lower than with 3DCRT plans. The results of the current study is also supported by Rongsriyam K et-al 2008[26] who found that ipsilateral lung mean dose and V_{20Gy} were significantly lower for IMRT plans compared to 3DCRT plans (6.42Gy vs 8.82Gy & 0.88% vs 14.8%) respectively. Beckham WA et-al 2007[25] also found that ipsilateral lung V_{20Gy} was significantly lower for IMRT plans compared to 3DCRT plans (17.1% Vs 26.6%).

Conclusion

Tangential beam IMRT in left sided breast cancer leads to a significant dose reduction in heart and ipsilateral lung with comparable target coverage compared to tangential beam 3DCRT

References

1. Jemal A, Siegel R, Xu J, Ward E. cancer statistics, 2010. CA J Clin. 2010; 60:277-300.
2. Julien JP, Bijker N, Fentiman IS, et al. Radiotherapy in breast- conserving treatment for ductal carcinoma in situ: first results of the EORTC randomized phase III trial 10853. EORTC breast cancer cooperative Group and EORTC Radiotherapy Group. Lancet.2000; 355:528-533.
3. Fisher B, Anderson S, Bryant J, et al. Twenty- year follow-up of a randomized trial comparing total mastectomy, Lumpectomy, and Lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002; 347:1233-1241.
4. Smith W, Menon G, Wolfe N, Ploquin N, Trotter T,

Pudney D. IMRT for the breast: a comparison of tangential planning techniques. Phys Med Biol. 2010; 55:1231-1241.
5. Beck RE, Kim L, Yue NJ, Haffty BG, Khan AJ, Goyal S. Treatment Techniques to Reduce Cardiac Irradiation for Breast Cancer Patients Treated with Breast-Conserving Surgery and Radiation Therapy: A Review. Frontiers in Oncology. 2014; 4:327.
6. Chirag Shah, Shahed Badiyan, Sameer Berry, Atif J. Khan, Sharad Goyal, Kevin Schulte, Anish Nanavati, Melanie Lynch, Frank A. Vicini. Cardiac dose sparing and avoidance techniques in breast cancer radiotherapy. Radiotherapy and Oncology 2014; 112: 9–16
7. Remouchamps VM, Vicini FA, Sharpe MB, et al. Significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control and intensity-modulated radiation therapy for patients treated with locoregional breast irradiation. Int J Radiat Oncol Biol Phys 2003; 55:392–406.
8. Merchant TE, McCormick B. Prone position breast irradiation. Int J Radiat Oncol Biol Phys 1994; 30:197–203.
9. Fogliata A, Bolsi A, Cozzi L. Critical appraisal of treatment techniques based on conventional photon beams, intensity modulated photon beams and proton beams for therapy of intact breast. Radiother Oncol 2002; 62:137–45.
10. Fagundes M, Hug EB, Pankuch M, Fang C, McNeeley S, Mao L, Lavilla M, Schmidt SL, Ward C, Cahlon O, Hartsell WF. Proton Therapy for Local-regionally Advanced Breast Cancer Maximizes Cardiac Sparing. Int J Particle Ther.2015;1(4):827–844
11. Landau D, Adams EJ, Webb S, et al. Cardiac avoidance in breast radiotherapy: a comparison of simple shielding techniques with intensity-modulated radiotherapy. Radiother Oncol. 2001; 60:247–55.
12. Huang XB, Jiang GL, Chen JY, et al. Dosimetric evaluation of intensity modulated tangential beam versus conventional tangential irradiation for breast cancer. Ai Zheng. 2006:855–60.
13. Cozzi L, Fogliata A, Nicolini G, et al. Clinical experience in breast irradiation with intensity modulated photon beams. Acta Oncol 2005; 44:467–74.
14. Dogan N, Cuttino L, Lloyd R, et al. Optimized dose coverage of regional lymph nodes in breast cancer the role of intensity-modulated radiotherapy. Int J Radiat Oncol Biol Phys 2007; 68:1238–50.
15. Sarah C. Darby, Marianne Ewertz, Paul McGale, Anna M. Bennet, Ulla Blom-Goldman, Dorthe Brønnum, Candace Correa, David Cutter, Giovanna Gagliardi, Bruna Gigante, Maj-Britt Jensen, Andrew Nisbet, Richard Peto, Kazem Rahimi, Carolyn Taylor, and Per Hall. Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer. N Engl J Med 2013; 368:987-998
16. Fong A, Bromley R, Beat M, Vien D, Dineley J, Morgan G. Dosimetric comparison of intensity modulated radiotherapy techniques and standard wedged tangents for whole breast radiotherapy. J Med Imaging Radiat Oncol. 2009; 53:92-99.
17. Safae Mansouri, Asmaa Naim, Luis Glaria, Hugo Marsiglia: Dosimetric Evaluation of 3-D Conformal and Intensity-modulated Radiotherapy for Breast Cancer after Conservative Surgery. Asian Pacific Journal of Cancer Prevention.2014; 15 (11): 4727-4732.
18. Jagsi R, Moran J, Marsh R, et al. Evaluation of four techniques using intensity modulated radiation therapy for comprehensive locoregional irradiation of breast cancer. Int J Radiat Oncol Biol Phys 2010; 78:1594–603.
19. http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx
20. Prescribing, recording and reporting photon beam therapy. International commission on Radiological Units and Measurements (ICRU) Report # 50: ICRU 1993.
21. Prescribing, recording and reporting photon beam therapy. International commission on Radiological Units and Measurements (ICRU) Report # 62: ICRU 1997.
22. Vees H, Bigler R, Bieri S, et al. Assessment of cardiac exposure in left tangential breast irradiation. Cancer Radiother 2011; 15:670–4
23. Schubert LK, Gondi V, Sengbusch E, et al. Dosimetric comparison of left-sided whole breast irradiation with 3D-CRT, forward-planned IMRT, inverse planned IMRT, helical tomotherapy, and topotherapy. Radiother Oncol 2011; 100:241–6.
24. Mayo CS, Urie MM, Fitzgerald TJ. Hybrid IMRT plans –concurrently treating conventional and IMRT beams for improved breast irradiation and reduced planning time. Int J Radiat Oncol Biol Phys. 2005;61:922–932
25. Beckham WA, Popescu CC, Patenaude VV, et al. Is multibeam IMRT better than standard treatment for patients with left-sided breast cancer? Int J Radiat Oncol Biol Phys 2007; 69:918–24.
26. Rongsriyam K, Rojpornpradit P, Lertbutsayanukul C, et al. Dosimetric study of inverse-planned intensity modulated and conventional tangential techniques in breast conserving radiotherapy. J Med Assoc Thai 2008; 91:1571–82.
27. Guang-Hua Jin,Li-Xin Chen, Xiao-Wu Deng, Xiao-Wei Liu, Ying Huang, and Xiao-Bo Huang. A comparative dosimetric study for treating left-sided breast cancer for small breast size using five different radiotherapy techniques: conventional tangential field, field-in-field, Tangential-IMRT, Multi-beam IMRT and VMAT. Radiation Oncology 2013, 8:89
28. Li JS, Freedman GM, Price R, et al. Clinical implementation of intensity modulated tangential beam irradiation for breast cancer. Med Phys 2004; 31:1023–31.
29. Suresh Moorthy,, Hamdi Sakr, Shubber Hasan, Jacob

Samuel, Shaima Al-Janahi, Narayana Murthy. Dosimetric study of SIB-IMRT versus SIB-3DCRT for breast cancer with breath-hold gated technique. International journal of cancer therapy and oncology 2013; Vol 1 no 1. ISSN 2330-4049
30. Pooja Khullar, Niloy Ranjan Datta, G Venkadamanickam, Charu Garg and Sujeet Sinha. Comparative Dosimeteric Evaluation of Intensity Modulated Radiation Therapy versus Conventional Radiotherapy in Postoperative Radiotherapy of Breast. Cancer. J Nucl Med Radiat Ther 2014, 5:4