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Original Article

Dosimetric Comparison of Three-dimensional Conformal Radiotherapy versus Intensity Modulated Radiotherapy Following Breast Conservation Surgery in Early Stage Breast Cancer

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Abstract

Introduction: Breast cancer is the most frequent cancer among women. Radiotherapy is integral in the management of breast cancer. The purpose of this study was to compare two different types of treatment planning, standard wedged tangential-beam three-dimensional (3D) conformal radiotherapy (CRT), and dynamic intensity modulated radiotherapy (IMRT), in early breast cancer patients who have undergone breast conservation surgery. We aimed to improve dose distribution homogeneity in the breast and decrease the dose of organs at risk (OAR), that is, heart and ipsilateral lung.

Materials and Methods: This study is conducted using treatment plans done on the computed tomography (CT) simulation data sets of 20 patients. These patients were already treated with breast conservation surgery, consisting of removing the primary tumor with a margin followed by 3D CRT at the Department of Radiotherapy, Government Medical College, Kozhikode from 2015 to 2017. A CT scan was taken with the patient in treatment position from the level of the C6 vertebra to below the level of the diaphragm. The breast clinical target volume was contoured according to Radiation Therapy Oncology Group guidelines and reference radio-opaque wires placed. The same CT data set with target volumes and OAR volumes were used for the IMRT study. Plans were compared according to cumulative dose-volume histogram analysis in terms of planned treatment volume (PTV) and volume parameters of OARs.

Results: Our study 3D CRT gives a much better dosimetry coverage for breast PTV and reduces the dose to the OARs than IMRT. IMRT is more cardiac sparing at higher doses than 3D CRT, especially at v25 and the dose receiving 33% of heart is less on IMRT. Hence, IMRT may be beneficial in patients with a high risk of cardiac events. The ipsilateral lung dose parameters were observed to have higher values in the IMRT technique than the 3DCRT technique.

Conclusion: 3D CRT enables better dose distribution in the PTV and reduces OARs in breast cancer radiotherapy compared to IMRT.

Key words: Breast cancer, Dynamic intensity modulated radiotherapy, Organs at risk, Three-dimensional conformal radiotherapy, Whole breast irradiation

INTRODUCTION

Breast cancer is the most frequent cancer among women; most patients with breast cancer are diagnosed at an early stage (61.1%), largely because of widespread mammography screening programs. The standard of care for these patients is lumpectomy or mastectomy plus lymph node sampling followed by adjuvant radiotherapy (RT) to the tumor bed or the whole breast as indicated. RT is integral in the management of breast cancer. Long-term data establish the efficacy of RT in the adjuvant management of breast cancer the 25-year results of NSABP B04 published in 2002 indicate radiation leads to less extensive surgeries while maintaining relapse-free and overall survival.[2] Meta-analyses show that locoregional control as well as

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breast cancer mortality benefit from adjuvant radiation therapy following breast conservation surgery or following mastectomy with node-positive disease.[1,2]

The focus has now shifted from just treatment to high-quality, precise treatment delivery to reduce long-term treatment-related toxicity. Radiation to the breast, with or without additional fields for nodal coverage, has the potential to negatively impact long-term cosmetic outcome of the treated breast. It can also cause rare but severe complications due to incidental dosage to the heart, lungs, and contralateral breast. In fact, cardiac mortality is reported to be higher in left-sided breast cancer patients than in right-sided breast cancer patients because higher incidental cardiac radiation doses were delivered in patients with left-sided breast cancer.

Due to the proximity of the lung beneath the breast tissue, this organ receives the highest incidental dose in women receiving radiation for breast cancer. The mean total lung dose has been reported as 5.7 Gy using modern three-dimensional (3D) conformal techniques. The contralateral breast is also an important organ at risk (OAR) due to its exposure to scattered radiation. While we have established the indispensable role of RT in the management of breast cancer, it is also important to deliver this at the lowest possible, most effective dose to ensure patient safety. Furthermore, the best mode of delivery of RT must be established. It was either used as tangential preoperative treatment of the breast or as post-operative treatment of the chest wall during the initial years.

In the 1980s, breast-conserving surgery (BCS) started and post-operative treatment of the remaining breast tissue became standard. Prospective randomized trials have confirmed that long-term mortality from breast cancer and overall patient survival are comparable for BCS plus radiation treatment and for mastectomy[3] the past decade has seen considerable advances in the delivery of post-operative radiation that aim to optimize the treatment for each person's anatomy and reduce acute or long-term toxicity. 3D planning with a computed tomography (CT) simulator and either field-in-field three-D conformal radiation therapy (CRT) (forward planning) or intensity-modulated radiation therapy (IMRT) (inverse planning) has replaced the simple 2-D tangential treatment. By reducing dose non-homogeneity, these advances in techniques are associated with lower rates of complications, such as acute skin desquamation, edema, late fibrosis, or negative cosmetic effects on the breast.[6,7] In addition, techniques involving the prone position and deep-inspiration breath-holding are now used for left-side breast cancer or larger breast size to reduce toxicity, particularly cardiac dose sparing.[8,9]

This study aims to compare the dosimetry characteristics of IMRT and 3D RT techniques and evaluate each modality's characteristics when applied to whole breast radiation therapy in early-stage breast cancer.

MATERIALS AND METHODS

Patients with left-sided breast cancer who have already been undergone breast conservation surgery and post-operative RT from Government Medical College, Calicut, from 2015 to 2017 were included in the study after informed consent and ethical clearance obtained from the Institutional ethics committee, Medical College Kozhikode. At the time of recruitment, the following data were collected: Name, age, address, menopausal status, parity, presence of comorbid illness, stage at diagnosis, histopathological report, details of surgery performed, and chemotherapy are taken. RT was planned and administered after obtaining informed consent. Dose volume histogram (DVH) data were collected from the Treatment Plans of individual patients.

Simulation and Treatment Planning

External Beam Radiation using the 3D Conformal technique 3D CRT was used. The patient was placed in the supine position with both the arms flexed and abducted to more than 90°. Both hands were made to hold the handgrip placed on the board above the head. The arms were held in position by arm supports which were also attached to the board and the head was turned to the right. Headrest and hip rest were also used to aid in the patient's position reproducibility.

The field borders were determined clinically and marked by radio-opaque wires. The medial border was 1 cm from the mid-line, the superior border was at the caudal border of the clavicular head, the inferior border was 1 cm below the inframammary fold and the lateral border was at the mid-axillary line. A contrast-enhanced CT scan was taken with the patient in the treatment position from the level of the C6 vertebra to below the level of the diaphragm. The chest wall or breast clinical target volume, the regional lymphatics, and the supraclavicular field (when indicated) were contoured according to the Radiation Therapy Oncology Group guidelines.

CT data were exported to a computerized treatment planning system (Eclipse, Version13.6). Beam weights and wedges were optimized based on the dose distribution for the central axis plane. All patients were planned with 6MV photons. Field borders were not modified to reduce or avoid cardiac irradiation and cardiac shielding was not used. All patients were treated with a tumor dose of 50Gy to the isocenters in 25 fractions, 5 days/week.

The dose distribution was calculated with full 3D CT density information, including lung correction using the Anisotropic Analytical Algorithm algorithm. In the IMRT technique, the fluence-based sliding window IMRT optimized plans were generated to achieve the same objectives described for the 3D CRT plans, the number of beam segments was not restricted during optimization.

The planned treatment volume (PTV) for IMRT was the same as used for the 3D CRT plans. The ECLIPSE 15.1 treatment planning system was used to analyze the PTV's mean, maximum and minimum doses and for organs at risks (OARs) mean, maximum, minimum doses, percentage of volume receiving 3000 cGy (V30), percentage of volume receiving 2000 cGy (V20), percentage of volume receiving 1000 cGy (V10), and isodose volumes for 50%, 30% and 10%. The OAR that was assessed was the heart and lungs. The heart is contoured with the aid of a heart contouring atlas "Development and Validation of a Heart Atlas to study Cardiac exposure to Radiation following treatment for Breast Cancer".[10] For each treatment plan, DVHs for the heart and lungs, with a 1-cm radial margin, were generated. The superior limit of the heart included the right and left atria and excluded the pulmonary trunk, ascending aorta, and superior vena cava. The caudal border of the myocardium was taken as the inferior limit of the heart. For each OAR, the mean and maximum dose was assessed for each patient. For each of these quantities, the average value for all assessed patients (referred to as mean) was calculated with its standard deviation (SD).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using the SPSS version 23.0 software and analyzed with the help of descriptive statistics such as mean, SD, percentage, and statistical tests such as the Independent *t*-test.

RESULTS

Twenty patients with post BCS status who satisfied the inclusion criteria were selected and data were analyzed. The majority of the women enrolled in the study were in the age group 31–40 years, comprising 40% of the study population. The mean age of the population was 40.3 years. About 80% of the study population (16 patients) was postmenopausal and 10% (2 patients) were nulliparous. Most women (95%) enrolled into the study had no pre-existing cardiac disease. About 15% were hypertensive. About 50% were found to be Luminal subtype A and 25% constitute triple negative. Nine patients (45%) in our study presented with T1 stage while most of the patients (55%) had T2 disease. Ten patients (50%) received chemotherapy with AC, followed by Taxol.45% of patients received FAC schedule and 5% received FEC.

Comparison of PTV

This study shows that the mean of maximum dose and minimum dose received by PTV is high in IMRT planning than 3D CRT with a statistically significant *P* value. However, the mean dose received by PTV is less with IMRT planning.

Comparison of Heart Dose

The dosimetry comparison between 3D CRT and IMRT shows that the mean of the maximum dose and minimum dose received by heart was higher in IMRT planning than 3D CRT. The mean of v25 dose and dose received by 33% of heart is more on 3D CRT when compared to IMRT. Thus, IMRT is more cardiac sparing.

Comparison of Lung Dose

This data analysis shows that the mean of v10, v20, and v30 doses received by lung is less on 3D CRT when compared to IMRT [Table 1] and this is found to be statistically significant with a *P* value of 0.001 as per *t*-test. Similarly,

Table 1: Comparison of dose distribution of PTV and OAR in 3D CRT versus IMRT

Group		Mean	Std.Deviation	*P*-value
PTV				
Max dose	3D CRT	5553.095	49.04559	0.049
	IMRT	5584.255	48.05061	
Min dose	3D CRT	1422.68	59.1518	0.001
	IMRT	2631.327	239.91481	
Mean dose	3D CRT	5259.25	85.81385	0.001
	IMRT	4998.635	96.51326	
Heart				
Max	3D CRT	4521.25	85.72546	0.001
	IMRT	4666.9	72.5084	
Min	3D CRT	41	4.66792	0.001
	IMRT	347.45	19.67225	
Mean	3D CRT	1159.75	79.02956	0.001
	IMRT	1537.65	76.44212	
33% Vol	3D CRT	1480.3	54.65885	0.001
	IMRT	1077.8	60.60624	
V25	3D CRT	23.7	2.51522	0.001
	IMRT	15.914	1.16765	
V10	3D CRT	33.35	3.01357	0.001
	IMRT	48.321	5.3049	
Lungs				
V5	3D CRT	50.785	3.27242	0.001
	IMRT	59.85	5.66322	
V20	3D CRT	32.2	2.10488	0.001
	IMRT	37.25	1.05954	
V30	3D CRT	26.78	0.89006	0.001
	IMRT	28.39	1.44072	
V10	3D CRT	41.9	2.72261	0.001
	IMRT	55.07	5.08218	
Mean dose	3D CRT	1043.35	46.1511	0.001
	IMRT	1489.35	108.14185	

PTV: Planned treatment volume, OAR: Organ at risk, CRT: Conformal radiotherapy, IMRT: Intensity-modulated radiation therapy the mean dose is also less with 3D CRT (1043.35 cGy) than IMRT plans (1489.35 cGy). So from this study, we can see that more lung volume is irradiated with IMRT than 3D CRT planning.

DISCUSSION

BCS plus radiation treatment is associated with very high local control rates (90–95%). These rates are comparable to those obtained with mastectomy, with more women having a good or excellent cosmetic result.[4,5] In India, BCS is preferred mostly by young women, whereas most older women undergo mastectomy. Since our study included only women who received radiation after BCS, we have a study population with a majority of them in their forties.

This study aimed to quantify the radiation dose received by ipsilateral breast, heart, and ipsilateral lung. All the patients included in this study had left-sided disease and all of them had undergone BCS.

Out of the 20 patients studied, only two patients (10%) were nulliparous, while 18 patients (90%) were multiparous. In our study population, 15% had a history of hypertension which is also a risk factor for coronary artery disease. One patient (5%) already had a history of heart disease, increasing their chances of developing radiation-induced coronary artery disease. All of the patients had received anthracycline-based chemotherapy, which on its own is a known cardiotoxic drug. This increases cardiac morbidity and mortality in addition to radiation-induced cardiac disease.

Dosimetry analysis shows that in the 3D CRT plan, the maximum dose received by PTV is 5553.09 cGy (111%), whereas, in the IMRT plan, it is 5584.25cGy (111.68%). This proves that IMRT has a higher maximum dose exposure because IMRT is known to cause focused areas of hot spots, causing more radiation on the breast tissue.

In the 3D CRT plan mean minimum dose received by PTV is 1422.68cGy (28.4%), while in the IMRT plan mean minimum dose received by PTV is 2631.32cGy (52.62%). Hence, our study showed that the IMRT plan achieved high minimum doses. These minimum doses are only point doses in PTV explained by the fact that we can only achieve the prescribed dose delivery for more than 90% of the prescribed isodose to encompass greater than 95% of the PTV, so at some points in every plan, there will be doses lesser than mean doses. These results are comparable with the previous studies by Ashraf *et al*.[10]

The present study mean of maximum dose received by heart is 4521.25 cGy y with 3D CRT plan, while in IMRT plan; it is 4666.9 cGy, which means maximum dose received by heart much higher by IMRT plan. Similarly, the mean minimum dose received by the heart is 41 cGy with 3D CRT, whereas the heart in IMRT is 347.45 cGy. Hence, the mean minimum dose received by the heart is more on the IMRT plan.

This data analysis shows that the mean of v25 dose received by the heart is 23.7% and 15.91% for 3D CRT and IMRT plans. This is significant with a $P = 0.001$.

Hence, mean V25 dose received by the heart is lesser using IMRT planning. The mean dose received by 33% of the heart is also less with IMRT. From this data, we can infer that IMRT is more cardiac sparing at higher doses compared to 3D CRT.

Different studies show that the mean dose received by the heart ranges from 0.8 Gy to 13.3 Gy.[11-14] In our study, the mean cardiac dose received is 14.89 Gy which is higher with IMRT. Higher doses on the heart in IMRT may be because we were not using breath-holding/respiratory gating techniques in IMRT planning.

In the case of the lung, the mean dose is 1043.3 cGy in the 3D CRT plan in contrast to the IMRT plan, where the mean dose received by the lung is 1489.3 cGy. Hence, it can be concluded that the mean dose received by the lung is more on the IMRT plan. The v5, v10, v20, and v30 doses received by lung in 3D CRT is 50.7%, 41.9%, 32.2%, and 26.8%, respectively, whereas they are 50.85%, 55.07%, 37.25%, and 28.39%, respectively, in IMRT plan with a statistically significant $P = 0.001$. This shows that more lung is exposed in IMRT planning at low doses and higher doses. At low doses, it can increase the risk of radiation-induced second malignancies. The risk of radiation pneumonitis is related to the volume of lung irradiated at higher doses.

CONCLUSION

3D CRT gives a much better dosimetry coverage for breast PTV and reduces the dose to OARs than IMRT. At higher doses, IMRT is more cardiac sparing than 3D CRT, especially at V25 A dose receiving 33% of heart is less in IMRT. Hence, IMRT may be beneficial in patients with a high risk of cardiac events. The ipsilateral lung dose parameters were observed to have higher values in IMRT techniques than 3D CRT. The risk of Radiation-Induced Pneumonitis is related to the volume of ipsilateral lung irradiated.

However, the quality of the treatment plan depends on the patient geometry and technology available in a RT center, such as treatment planning system, beam energy, and TPS algorithm. The selection of treatment techniques for whole breast irradiation is an important factor in sparing the adjacent normal structure and determining the associated risk. The IMRT technique delivers a modestly higher dose to adjacent normal tissues. The main concern with this is the increased risk of late secondary malignancy.

Quantification of dose to OARs may be useful for clinicians as they counsel women with early-stage breast cancer about their treatment options. The IMRT plans contribute a modestly higher dose to adjacent normal tissues. The main concern with this is the increased risk of late secondary malignancy. 3D CRT technique is superior in better coverage of PTV volumes and delivering lower dose to adjacent normal tissue, and treatment time.

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REFERENCES

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, Cutter D, Duane F, *et al*. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: Meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet 2014;383:2127-35.
2. Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: An overview of the randomised trials. Lancet 2005;366:2087-106.
3. Jatoi I, Proschan MA. Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: A pooled analysis of updated results. Am J Clin Oncol 2005;28:289-94.
4. Anderson SJ, Wapnir I, Dignam JJ, Fisher B, Mamounas EP, Jeong JH, *et al*. Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in patients treated by breast-conserving therapy in five national surgical adjuvant breast and bowel project protocols of node-negative breast cancer. J Clin Oncol 2009;27:2466.
5. Haviland JS, A'Hern R, Bentzen SM, Whelan T, Bliss JM. Radiotherapy for breast cancer, the TARGIT-A trial. Lancet 2014;383:1716-7.
6. Freedman GM, Li T, Nicolaou N, Chen Y, Ma CC, Anderson PR. Breast intensity-modulated radiation therapy reduces time spent with acute dermatitis for women of all breast sizes during radiation. Int J Radiat Oncol Biol Phys 2009;74:689-94.
7. Keller LM, Sopka DM, Li T, Klayton T, Li J, Anderson PR, *et al*. Five-year results of whole breast intensity modulated radiation therapy for the treatment of early stage breast cancer: The fox chase cancer center experience. Int J Radiat Oncol Biol Phys 2012;84:881-7.
8. Formenti SC, DeWyngaert JK, Jozsef G, Goldberg JD. Prone vs supine positioning for breast cancer radiotherapy. JAMA 2012;308:861-3.
9. Eldredge-Hindy H, Lockamy V, Crawford A, Nettleton V, Werner-Wasik M, Siglin J, *et al*. Active breathing coordinator reduces radiation dose to the heart and preserves local control in patients with left breast cancer: Report of a prospective trial. Pract Radiat Oncol 2015;5:4-10.
10. Ashraf M, Janardhan N, Bhavani P, Shivakumar R, Ibrahim S, Reddy PY, *et al*. Dosimetric comparison of 3DCRT versus IMRT in whole breast irradiation of early stage breast cancer. Int J Cancer Ther Oncol 2014;2:020318.
11. Taylor CW, Povall JM, McGale P, Nisbet A, Dodwell D, Smith JT, *et al*. Cardiac dose from tangential breast cancer radiotherapy in the year 2006. Int J Radiat Oncol Biol Phys 2008;72:501-7.
12. Bartlett FR, Yarnold JR, Donovan EM, Evans PM, Locke I, Kirby AM. Multileaf collimation cardiac shielding in breast radiotherapy: Cardiac doses are reduced, but at what cost? Clin Oncol 2013;25:690-6.
13. Sato K, Mizuno Y, Fuchikami H, Kato M, Shimo T, Kubota J, *et al*. Comparison of radiation dose to the left anterior descending artery by whole and partial breast irradiation in breast cancer patients. J Contemp Brachyther 2015;7:23.
14. Karacetin D, Baycan D, Nazli MA, Trabulus DC, Gunes ME, Barut Y. Dosimetry comparison of dynamic IMRT, field-in-field IMRT and 3D-CRT in left-sided breast cancer after breast-conserving surgery. Acta Sci Cancer Biol 2018;2:6-10.

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