ORIGINAL RESEARCH ARTICLE

# Comparison of Doses received by Contralateral Breast during 3DCRT and IMRT Techniques used in Treatment of Breast Cancer

**Nirmal Kumar Mittal[1], Renu Goindani[2], Jagdish Kumar Gupta[3], Aparna Gupta[4]**

[1]Assistant Professor, [2]Associte Professor, [3]Department of Radio-Diagnosis, [4]Department of Radio-Diagnosis, Department of Radio-Diagnosis, Amaltas Institute of Medical Sciences, Dewas

**Corresponding author:** Dr. Renu Goindani, Associte Professor, Department of Radio-Diagnosis, Amaltas Institute of Medical Sciences, Dewas

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**A B S T R A C T**

**Introduction:** IMRT is considered as a feasible technique for delivering a homogenous dose to the whole breast and reducing the scattered dose to the contralateral breast. We conducted a prospective observational study comprising of 60 patients comparing the dose received by contralateral breast and other OAR's in both IMRT and 3DCRT technique and also the possible clinical toxicities seen in breast cancer patients during and after the chestwall irradiation.

**Material and Methods:** The present observational study entitled "Dose Received by Contralateral Breast During Radiotheraphy Techniques in the Treatment of Carcinoma Breast" was conducted on 30 patients attending the OPD of the Department of Radiation-Diagnosis, Amaltas Institute of Medical Sciences, Dewas (M.P.) during the period of Jan 2016 to June 2018. Radiotherapy was started 3 weeks after chemotherapy or surgery in selected group of patients. Patients who received radiotherapy by IMRT or 3DCRT technique were selected for the study purpose and were followed up on a regular basis upto a period of one year after completion of treatment.

**Result:** Distribution of age and their respective side of tumor among studied patients of breast cancer. Age of patients was found with little variation between the two groups. 18 (60.0%) patients had tumour in left breast while of 12 (40.0%) patients had right sided breast tumour, and the distribution of patients for side was noted equal in each of the two groups. The mean differences was highly significant at the 0.001 level of significance. The mean difference was not significant (insignificant) at the 0.05 level of significance. The degrees of freedom was 58.

**Conclusion:** So as to conclude, in our study it has been observed that acceptable target coverage as per the guidelines were achieved by both IMRT and 3DCRT techniques.

**Key words:** Contralateral Breast, 3DCRT and IMRT, Breast Cancer and OAR.

## INTRODUCTION

Breast Cancer is the most common cancer in women worldwide, with nearly 1.7 million new cases diagnosed in 2012, representing about 12% of all new cancer cases and 25% of all cancers in women. It is the fifth most common cause of death from cancer in women worldwide.[1] In India, for the year 2012, 144,937 women were newly detected with breast cancer and 70,2018 women died of it and has overtaken cervical cancer[2] and for the year 2015, there will be an estimated 1,55,000 new cases of breast cancer and about 76000 women in India are expected to die of the disease. It is now the most common cancer in most cities in India, and 2nd most common in the rural areas. In India, we are now witnessing more and more numbers of patients being diagnosed with breast cancer to be in the younger age groups (in their thirties and forties).

**New Advancements:** The journey of external beam radiation started in the last century with superficial X-rays and gradually moved on to high energy X-rays and photons including radionuclides like 60-Co (radioactive Cobalt) and 37-Cs (Cesium). Changes were notably apparent in technical aspects of radiation, starting from manual surface marking based planning to adoption of computer and software. The actual treatment planning advances from conventional fluoroscopic based methods to CT based simulation. These planning advances includes Accelerated Partial Breast Irradiation (APBI), Three Dimensional Conformal Radiotherapy (3DCRT), Intensity Modulated Radiotherapy (IMRT) and Image Guided Radiotherapy (IGRT). Techniques such as IMRT and IGRT need to be judiciously used. If IMRT is used, it should be forward planning IMRT with a predominantly tangential field arrangement.

However, a potential risk of primary breast irradiation is the development of asecondary malignancy in the contralateral breast. Boice et al.[3] have reported that incidence of radiation

induced breast cancer is a linear function of dose received by the contralateral breast and the latent period is over 10 years.

## MATERIAL AND METHODS

The present observational study entitled "Dose Received by Contralateral Breast During Radiotheraphy Techniques in the Treatment of Carcinoma Breast" was conducted on 30 patients attending the OPD of the Department of Radiation-Diagnosis, Amaltas Institute of Medical Sciences, Dewas (M.P.) during the period of Jan 2016 to June 2018. Radiotherapy was started 3 weeks after chemotherapy or surgery in selected group of patients.

**Inclusion criteria**

- All patients of breast cancer histologically proven.
- Patient of female sex and preferably of age <75years.
- Patient with performance status or KPS score >70.
- Patient with histologically proven invasive ductal carcinoma and AJCC stage 2 and 3.
- Patient having no distant metastasis.

**Exclusion Criteria**

- Patient with performance status or KPS score less than 70.
- Patient having distant metastasis.
- Patient having cancer in both breasts.
- Patient of age >75 years or with co-morbidities

**Preparation and organization of data**

The patient who had carcinoma breast and further met the inclusion criteria were selected as subjects during specified schedule.

Patients who had carcinoma breast and within age of less than 75 years and had performance status or KPS score >70 that further met all the inclusion criteria selected as subjects during specified schedule. Overall, a maximum of 60 patients were deemed fit into inclusion-exclusion criteria. Out of total 60 patients, 30 patients were allocated to one group planned to receive Intensity modulated radiotherapy technique (IMRT). The rest 30 patients were allocated to the second group planned to receive radiotherapy treatment by using Three dimensional conformal radiotherapy techniques (3DCRT). Both, the groups were study group. The patients were explained about the complete treatment procedure in his/her own language and his/her willingness to undergo the treatment had recorded in a consent form dually signed by them.

A proper detailed history was taken from all the selected patients. Patients then underwent proper physical examination, routine blood investigations, chest X-Ray and USG whole abdomen to rule out any distant metastasis. Staging of patient was done according to American joint society of cancer (AJCC) 2010.

Finally, comparison in dosimetric analysis of doses between the two radiotherapy treatments was carried out.

**Methods**

**Immobilization**

Prior to treatment a thermoplastic mould was made in the mould room to immobilise the chest region which was fixed on the breast board. This immobilisation was important to ensure accurate position of patient during the treatment. In immobilisation of breast cancer patients on breast board, both the hands were kept upwards and neck was rotated towards the opposite side from the treatment area. This was done so as to completely expose the axilla and supraclavicular region of the side which has to be treated.

**Planning Details**

**IMRT plan**

All the IMRT plans were done by 6 mega voltage (MV) energy with five to seven coplanar (CP) fields with couch angle 0 and no parallel opposed fields were chosen. The isocentre was placed at the geometrical centre of the PTV. The range of gantry angles chosen were 80° – 196° (counter clockwise) for right chestwall cases and 280° – 165° (clockwise) for left chestwall cases. No any field was placed at gantry angles 90 and 270 in any plan. Dose constraints as per the RTOG chest wall guidelines and adequate weights were given for OARs and target volumes. Varian leaf motion calculator version 8.9.08 was used to calculate the leaf motion for dynamic dose delivery. Dose volume optimizer (DVO) was used for plan optimization. AAA was used to calculate doses with grid size of 0.25 cc.

**3DCRT plans**

3DCRT plans were done by using 6 MV, 15 MV or combination of both photon energies. Two to five CP fields with couch angle 0° were used and two kinds of plans were prepared as per requirement of individual case as follows;

**(1) Only chest wall irradiation:** In the cases where only chest wall had to be treated were planned with only two tangential fields (couch 0°, gantry angles 310/50–325/35 and 130°/230°–145°/215°). In some of the cases one or two FIFs were also used to cover the cold spot. The isocentre was placed longitudinally at the geometrical centre of PTV. Lateral and vertical coordinates for isocentre were decided in such a way that it should live at equal depth from entry points of both the fields, and after fitting the MLCs to PTV, both the major fields should look like half beams which is important for low dose to lung (figure-1).

## STATISTICAL ANALYSIS

The responses of frequencies were calculated and analyzed by using the raw data of 60 subjects. The raw data were entered into the computer database. Statistical software, SPSS version 17.0 trial was used for analysis. Prevalence of an outcome variable along with 95% confidence limits was calculated. Both, descriptive and inferential statistics were used to study carcinoma breast in order to analyzed received doses between Intensity modulated radiotherapy technique and three dimensional conformal radiotherapy techniques.

Independent sample t-test is also used to know the significance of mean difference in age of patients of carcinoma breast between two radiotherapy techniques (3DCRT and IMRT) in order to confirm the non-biasedness with respect to age of patients of carcinoma breast in the present study.

The probability value, $p>0.05$ was considered as statistically not significant (insignificant) but the probability value from $p<0.06$ to $p<0.08$ was considered as suggestively or poorly significant. The probability value from $p<0.05$ to $p<0.02$ was considered as statistically significant while from $p<0.01$ to


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p<0.001, and above probability values were considered as statistically highly/strongly significant.

## RESULTS

### Patient characteristics

A total of 60 patients of breast cancer (post-operated) were included and distributed randomly in two groups with equal number of patients in each group. The scatter for age (Mean ± SD) of all subjects (N=60) was found to be 50.03±9.15 years and ranged from 35 to 70 years.

The scatter for age of patients who had carcinoma breast who received doses by using IMRT was found to be 49.50±8.10 years in carcinoma breast of left side (n=18) as compared to 50.42±8.45 years in carcinoma breast of right side (n=12). It was slightly lower for patients of carcinoma breast of left side. The scatter for age of patients who had carcinoma left breast (n=18) was found to be 50.17±9.70 years who received

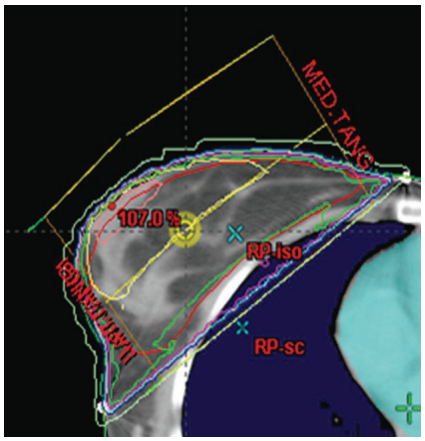
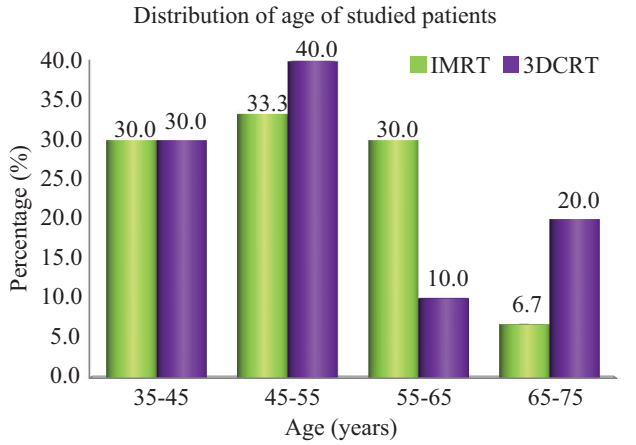


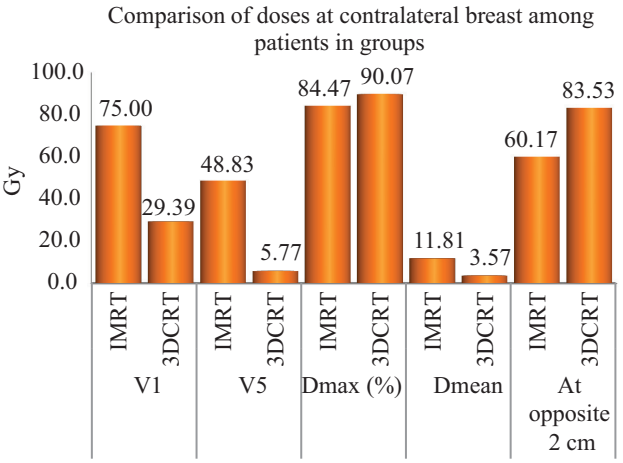

**Figure-1:** 3DCRTBEAMARRANGEMENT

| Variable | | IMRT | | 3DCRT | |
|---|---|---|---|---|---|
| | | $n_1$=30 | % | $n_2$=30 | % |
| Age (year) | 35-45 | 9 | 30.0 | 9 | 30.0 |
| | 45-55 | 10 | 33.3 | 12 | 40.0 |
| | 55-65 | 9 | 30.0 | 3 | 10.0 |
| | 65-75 | 2 | 6.7 | 6 | 20.0 |
| Side of tumor | Left sided | 18 | 60.0 | 18 | 60.0 |
| | Right sided | 12 | 40.0 | 12 | 40.0 |

**Table-1:** Age and side of tumor distribution of patients in groups




**Graph-1:** Bar diagram depicting the distribution of the age of breast carcinoma patients who belonged to IMRT group and 3DCRT group




**Graph-2:** Bar diagram showing the comparison of doses received by contralateral breast in breast carcinoma patients planned with IMRT and 3DCRT.

| Dosimetric parameter | Technique | Scatter Mean ± SD | Mean Diff | t-value | p-value (LOS) |
|---|---|---|---|---|---|
| Dose at Contralateral Breast | | | | | |
| $V_1$ (Gy) | IMRT | 75.00±28.04 | 45.61 Gy | 8.63 | p<0.001# |
| | 3DCRT | 29.39±7.18 | | | |
| $V_5$ (Gy) | IMRT | 48.83±20.93 | 43.06 Gy | 11.04 | p<0.001# |
| | 3DCRT | 5.77±4.27 | | | |
| $D_{max}$ (%) | IMRT | 84.47±10.34 | 5.60% | 1.22 | p>0.05⊗ |
| | 3DCRT | 90.07±22.99 | | | |
| $D_{mean}$ (Gy) | IMRT | 11.81±8.43 | 8.24 Gy | 5.11 | p<0.001# |
| | 3DCRT | 3.57±2.62 | | | |
| At opposite 2 cm (Gy) | IMRT | 60.17±8.15 | 23.36 Gy | 9.67 | p<0.001# |
| | 3DCRT | 83.53±10.43 | | | |

#The mean differences was highly significant at the 0.001 level of significance. ⊗The mean differences was not significant (insignificant) at the 0.05 level of significance. The degrees of freedom was 58. [Dmax (%) = Maximum dose in percentage of planned dose; $D_{mean}$ (Gy) = Mean dose (in Gy) to planned target volume; Mean Diff-Mean Difference; LOS-Level of Significance]

**Table-2:** Comparison of doses received by contralateral breast between IMRT and 3DCRTirrespective of cancerous breast side

doses by using 3DCRT which was a little lower as compared to patients (50.25±11.43 years) who had carcinoma right breast (n=12).

Table 1 reveals the distribution of age and their respective side of tumor among studied patients of breast cancer. Age of patients was found with little variation between the two groups. 18 (60.0%) patients had tumour in left breast while of 12 (40.0%) patients had right sided breast tumour, and the distribution of patients for side was noted equal in each of the two groups.

**Assessment and comparison of doses received by contralateral breast during 3DCRT and IMRT techniques**

Dosimetric comparisons were carried out for both the treatment plans (IMRT and 3DCRT) and dose received by contralateral breast was compared between the two techniques.

Average low dose volumes, $V_1$ and $V_5$ to the contralateral breast during IMRT showed larger values (75.00±28.04 Gy and 48.83±20.93 Gy) as compared to 3DCRT (29.39±7.18 Gy and 5.77±4.27 Gy) among all patients irrespective of cancerous breast side either left or right and thus the mean dose differences between the two techniques found to be statistically highly significant ($p<0.001$). But, there was not any statistically significant difference ($p>0.05$) noted between the average maximum dose ($D_{max}$) in the plans of both the techniques.

Volume of contralateral breast receiving $D_{mean}$ were significantly higher (11.81±8.43 Gy) for IMRT technique but doseat opposite two centimetre to breast were significantly lower (60.17±8.15 Gy) as compared to 3 DCRT (3.57±2.62 Gy and 83.53±10.43 Gy) amongall studied patients irrespective of cancerous breast side either left or right. Thus, the mean dose differences receiving $D_{mean}$ ($p<0.001$) and doseat opposite two centimetre to breast ($p<0.001$) between two techniques was found to be statistically highly significant.

## DISCUSSION

The use of radiation therapy in breast cancer patients have reduced risk of local recurrence and improved the overall survival, but the main problem with this modality of treatment is the dose received by contralateral breast, both lungs and heart and associated acute and late toxicities seen in the patients receiving the treatment. The breast tissue is highly sensitive and therefore the contralateral breast must be regarded as an organ at risk (sensitive organ) while planning for radiotherapy. With this context, the present work is aimed to compare the planning and dose delivery efficiency among two techniques of the radiotherapy namely 3-dimensional Conformal Radiotherapy (3DCRT) and Intensity Modulated Radiotherapy (IMRT) in breast cancer patients who underwent surgery and the acute and late clinical toxicities seen in the patients receiving the radiation therapy for the cancer.

A study by Ranete Muller et al.[4] stated that the skin dose measured at 5cm away from the medial border of the treatment field will be equal to the overall scattered dose received by the contralateral breast. In another study by Bhatnagar et al.[5] a total of 83 patients with breast carcinoma were treated(65 with tangential IMRT technique and 18 with 3-dimensional technique using tangential fields with wedges). Paired thermoluminescent dosimeters (TLDs) were placed on each patient's contralateral breast, 4 and 8 cm from the center of the medial border of the tangential field. The study represented a 36% and 57% reduction at the 4 and 8-cm contralateral positions, respectively, in the mean dose to the contralateral breast using IMRT compared to 3-DCRT technique.[6,7]

Few studies have concluded that the contribution of medial tangential field is almost twice of lateral tangential field in the dose received by contralateral breast. The reason could be that medial tangential field is close to the contralateral breast and hence the contribution by scatter photons and the collimator is more. Thus, dose to contralateral breast can be reduced by using IMRT or avoiding the medial tangential wedge in conventional tangential planning.

The use of IMRT has been proved to improve both dose homogeneity and target coverage as well as to spare normal tissue better than conventional tangential technique. In our study, we evaluated the target volume coverage, conformity index, homogeneity index and OAR dose in plans for both IMRT and 3DCRT using dose volume histogram (DVH) analysis. Both the plans achieved acceptable dose coverage to the planned target volume coverage i.e. 90% of PTV was covered with ≥ 90% of PD with acceptable hotspot, irrespective of malignant breast side.Although when dosimetric parameters were analyzed dose coverage to the planned target volume coverage with 90% volume planned with IMRT was found to be differed when compared to 3DRCT. Also, the conformity and homogeneity indices were found to be better in IMRT plans. Similar study by Smith et al.[8,9] compared three tangential beam IMRT plans with conventionaltangential beam 2D plans for the adjuvant radiotherapy of the whole breast in 20 patients with early breast cancer and showed a significant improvement of the PTV homogeneity index of 15% in IMRT technique compared to the conventional technique. Better target coverage and HI in the case of IMRT plans was mainly because of the multiple beam angles and adequate build up thickness before the PTV was present which made sufficient dose even at the edges of the PTV.[10]

Moving to the clinical benefits, Pignol et al.[9] reported first randomized trial ofbreast IMRT versus conventional RT in evaluation of acute radiation skin toxicity.The study demonstrated that 31.2% of breast cancer patients in the IMRT group experienced moist desquamation compared to 47.8% of patients that received standard treatment. Another retrospective analysis, by Harsolia et al.[10] reported thatgrade 2 acute breast dermatitis was significantly reduced with IMRT compared to conventional technique (41% vs 85%, respectively).

## CONCLUSION

So as to conclude, in our study it has been observed that acceptable target coverage as per the guidelines were achieved by both IMRT and 3DCRT techniques.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