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Study of Impacts on Lung Dose-Distribution as Increasing Number of Beams in Left-Sided Breast Irradiation

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Abstract: Objectives: The aim of this study was to analyze the impacts of increasing number of IMRT-beams on left lung dose-distribution in left-sided breast irradiation. **Methods:** We selected 105 patients retrospectively for this study diagnosed with left-sided breast cancer aged ranging from 33 to 74 years. There were 52 cases of chest wall (CW) irradiation including SCF, 20 cases of BCS and 33 cases were of CW including supra-clavicular fossa (SCF) and internal mammary lymph nodes (IMLN). **Result:** Our main objective was to analyze dose-distribution of left lung. Monitor Units (MUs) were also recorded and found almost same in these three modalities ranging from 1200 to 2000. The mean value of V_{20Gy} (cc) in 11-bIMRT technique was found less by 8-17cc as compared to 7-and 9-bIMRT technique. It was observed that 11-bIMRT technique yielded slightly better outcomes in terms of V_{20Gy} (cc). **Discussion:** For this purpose, patients diagnosed with left-sided breast cancer were considered under this study. Our medical physicist team surveyed 563 studies related to randomize controlled trials of IMRT in conservatively resected breast carcinoma. **Conclusion:** As the number of IMRT beams increases, it translates into better outcomes in terms of reducing high-dose volume as well as mean-dose of left lung. So, it is prudent to use 'N' number of IMRT fields such as $7 \leq N \leq 11$ in left breast RT.

Keywords: Breast Cancer, Beam, Irradiation, IMRT, Planning Target Volume.

INTRODUCTION

Breast cancer is of various types, but the most common is ductal carcinoma in situ (DCIS). This is the malignancy occurs frequently in females across the globe [Simonetto, C. *et al*., 2019- Haussmann, J. *et al*., 2019], and fast growing disease particularly in Africa and Asia. Radiation therapy (RT) plays a vital role in breast conserving treatment. This is clinically approved that breast conserving surgery (BCS) followed by adjuvant RT produces the same survival rate as radical breast surgery have [Veronesi, U. *et al*., 2002; Fisher, B. *et al*., 2002].

Many modern techniques have been developed within few decades for delivering dose to tumors with accuracy and precession causing minimal damage of surrounding normal organs. There are many studies reported recently about the advantage of Intensity-Modulated Radiotherapy (IMRT) showing the superiority over 3D-CRT in terms of dose conformity, homogeneity and sparing of normal tissues [Smith, B.D. *et al*., 2009; Njeh, C.F. *et al*., 2012]. The technique, IMRT, needs an advanced computer program to calculate radiation dose with accuracy in three dimensions, based on the tumor's geometry and location. IMRT modulates the intensity of the radiation beams around the breast tumor and spares normal tissues as well. It customizes the radiation dose as per geometrical shape of the tumor. In contrast, it increases integral dose to normal tissues, may cause second malignancy in long-term survivors. Half beam block (HBB) technique is also helpful in sparing heart and ipsi-lateral lung in left-sided breast RT.

The major advantage of this technique is that contra-lateral lung and breast receive less amount of dose [Ansari, S. *et al*., 2017]. Many clinical trials have been conducted in conjunction with adjuvant breast RT resulting smaller recurrence and higher long-term survival rate [EBCTCG, 2011; Overgaard, M. *et al*., 1999]. Though radiation therapy has beneficial effects, but it may cause side effects on surrounding normal tissue. In left-sided breast RT, not only heart, but left lung also receives significant radiation dose. However, RT for breast cancer has been a challenging treatment modality. The regional lymph nodes irradiation in younger-trials with good target coverage shows reduction in long-term toxicity yielding minor benefits in overall survival rate [Sardaro, A. *et al*., 2019- Darby, S.C. *et al*., 2005].

Many advance techniques have been developed recently in RT with aim to increase conformity and homogeneity of dose to tumor, and simultaneously sparing normal organs [Vicini, F.A. *et al*., 2002; 28. *et al*., 2019]. Many trials have reported that post-operative RT is able to reduce the rate of local recurrence significantly. It also improves the long-term survival rate on the cost of morbidity of ispi-lateral lung [Henson, K.E. *et al*., 2013; Morgan,

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E.A. *et al*., 2012]. Lungs are very important organ which remains at risk in breast- RT which may cause contingency of pneumonitis on receiving high dose [Paszat, L.F. *et al*., 1999; Clarke, M. *et al*., 2005].

Objectives

The aim of this study was to analyze the impacts of increasing number of IMRT-beams on left lung dose-distribution in left-sided breast irradiation.

MATERIALS AND METHODS

Patients, Targets Delineation and Treatment Planning

We selected 105 patients retrospectively for this study diagnosed with left-sided breast cancer aged ranging from 33 to 74 years. There were 52 cases of chest wall (CW) irradiation including SCF, 20 cases of BCS and 33 cases were of CW including supra-clavicular fossa (SCF) and internal mammary lymph nodes (IMLN). The treatment characteristics were recorded and tabulated in table (1).

Table1: Treatment characteristics of 105 patients

n=105 / treatment site	7b-IMRT	9b-IMRT	11b-IMRT	Median Age
CW+SCF, n = 52	0	10	42	57
BCS, n = 20	2	3	7	48
CW+SCF+IMLN, n = 33	0	4	29	54
CW= Chest Wall, SCF = Supra-Clavicular Fossa, IMLN = Internal Mammary Lymph Node				

CT simulation was done for each patient in supine position with both arms positioned above his head. A copper wire also placed around the breast tissue for marking purpose at the time of contouring. CT scans were taken from neck to lower abdomen, slice thickness of 3 mm. Planning target volume (PTV) as well as organs at risk (OARs) such as heart, ventricles, right breast, contra- and ipsi-lateral lungs were delineated as per Radiation Therapy Oncology Group (RTOG) guidelines for adjuvant radiotherapy of breast cancer[33, 34]. Portal dosimetry was performed of each plan before executing over patients.

Three types of IMRT plans were created for each patient using 7, 9 and 11beams. Each plan was generated using eclipse planning system, version 11.0 (Varian Medical System, Palo, USA). Beams were deployed at particular angle in each treatment modality, tabulated in table (2).

Table 2: IMRT-beam angle (in degree) in each technique

Beams No.	7-bIMRT	9-bIMRT	11-bIMRT
Field 1	5-10	5-10	5-10
Field 2	25-30	25-30	20-25
Field 3	80-85	80	50-55
Field 4	100-105	100-105	90-95
Field 5	125-130	120	115
Field 6	315-320	130-135	135-140
Field 7	300-305	305	150
Field 8	….	320	300-305
Field 9	….	350-355	325-330
Field 10	….	….	340
Field 11	….	….	350-355

Collimator angle was chosen as '0' degree in each plan for each patient. Beam and collimator angles remained unaltered in each technique. Beam isocenter was placed at depth 2-4cm from skin, demonstrated in figure (1).

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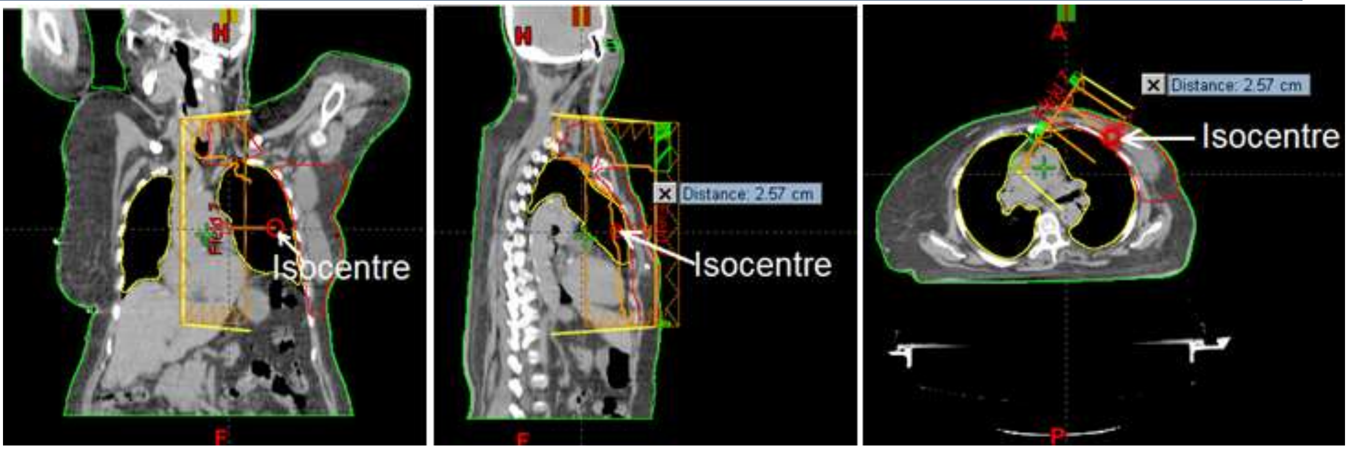

Figure1: Demonstrating the position of beam's isocentre in coronal, sagittal and transverse plane.

Dose Reporting

The dose was prescribed 40.05Gy in 15 fractions (2.67Gy per fraction) for every patient considered under this study. Each plan was optimized with aim to achieve at least 95-100% dose coverage (of prescribed dose) to 100% target's volume. Dose constraints were almost same for OARs in each case. However, some extra precautions were taken during optimization to reduce mean-dose of underlying lung and few minor adjustments were done in 'Priority' of OARs and PTV.

After completion the optimization, we analyzed each plan first for target's coverage ($D_{95\%}$), dose homogeneity, conformity of dose to targets and global maximum dose, tabulated in table (3).

Table 3: $D_{95\%}$, Global maximum dose, CI and HI for left-sided breast PTV

	$D_{95\%}$(Gy)				**Global max dose (%)**				**HI**				**CI**			
	7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT	
Max	38.60	39.24	39.57		117.20	115.56	115.43		1.22	1.18	1.16		1.09	1.06	1.05	
Min	37.07	38.06	38.04		108.62	107.57	107.40		1.13	1.11	1.08		0.94	0.95	0.98	
Mean	37.99	38.55	38.79		111.98	112.05	109.52		1.16	1.14	1.11		1.04	1.03	1.01	

Max = Maximum, Min = Minimum, HI = Homogeneity Index, CI = Conformity Index

For analyzing the ipsi-lateral lung dose distribution, we mainly consider six parameters such as V_{5Gy} (cc), V_{20Gy} (cc), V_{25Gy} (cc), $D_{50\%}$ (Gy), $D_{67\%}$ (Gy) and *mean-dose* , tabulated in table(4).

Table 4: Dose-distribution details of different parameters of ipsilateral lung.

Left Lung											
Mean Dose(Gy)				**V_{5Gy}(cc)**				**V_{20Gy}(cc)**			
	7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT
Max	17.03	16.86	16.97	Max	1068.60	1057.70	1073.20	Max	307.00	300.96	297.20
Min	9.33	8.83	8.74	Min	373.40	354.56	363.38	Min	74.53	58.69	45.25
ρ	12.87	12.62	11.52	ρ	638.76	687.59	690.31	ρ	181.70	173.27	164.67
V_{25Gy}(cc)				**$D_{50\%}$(Gy)**				**$D_{67\%}$ (Gy)**			
	7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT
Max	229.6	223.29	211.69	Max	12.51	11.98	11.75	Max	8.91	9.00	9.90

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Min	35.89	29.64	23.07	Min	6.95	6.58	6.30	Min	4.77	4.60	5.30
ρ	123.12	117.64	108.68	ρ	9.81	9.40	9.05	ρ	6.94	6.78	7.36
ρ: Mean of mean dose , Max : Maximum mean dose , Min: Minimum mean dose											

In addition, $D_{100\%}$ (Gy) of ipsi-lateral lung is also recorded and graphically displayed in figure (2).

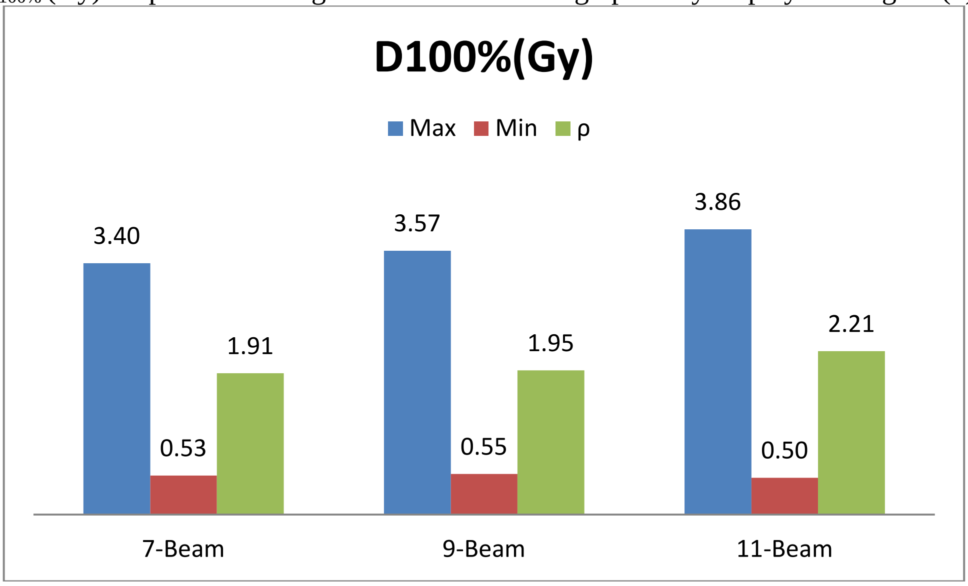

Figure 2: Displaying maximum, minimum and mean value of $D_{100\%}$(Gy) of ipsilateral lung

The parameters like mean, maximum, and minimum of ***'mean doses'*** of contra-lateral lungs, contra-lateral breast and heart were also analyzed, tabulated in table(4).

Table 4: Details of ***mean-dose*** of contra-lateral lung, contra-lateral breast and heart

Contra-lateral Lung Mean Dose(Gy)				**Contra-lateral Breast Mean Dose(Gy)**				**Heart Mean Dose(Gy)**			
	7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT		7-bIMRT	9-bIMRT	11-bIMRT
Max	4.28	4.05	4.81	Max	5.09	5.77	5.10	Max	10.47	10.32	10.83
Min	1.96	0.87	1.97	Min	1.40	1.26	1.70	Min	4.70	4.80	5.30
ρ	3.07	2.79	3.46	ρ	3.31	3.30	3.37	Mean	8.82	6.74	6.54
ρ: Mean of mean dose , Max : Maximum mean dose , Min: Minimum mean dose											

We have considered 7Gy as minimum dose to analyze dose dumping and low-dose volume of left lung. This is displayed in figure (3) along with DVH of ipsi-lateral lung and PTV.

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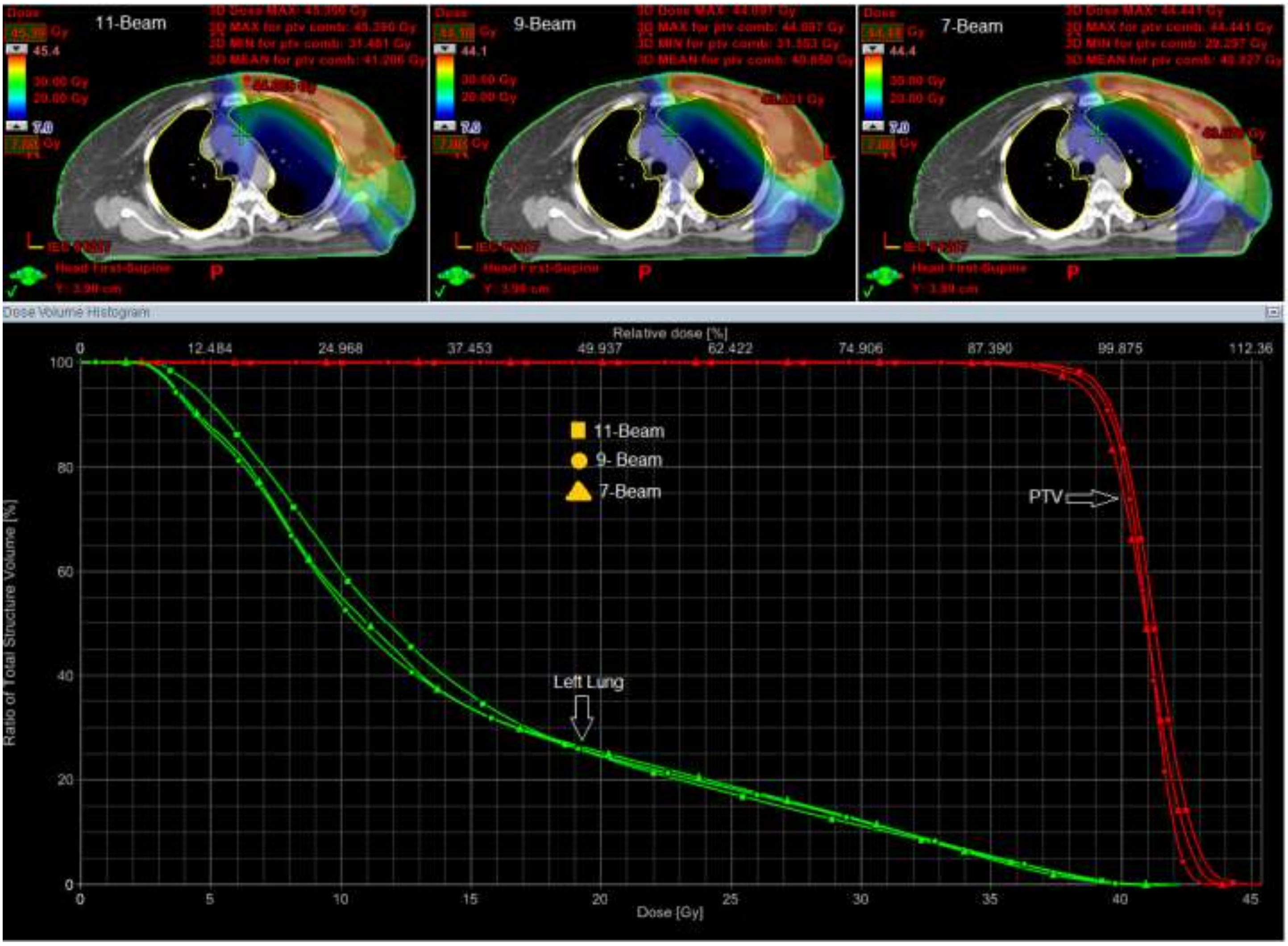

Figure 3: Dose distribution in each modality along with DVH of PTV and left lung.

RESULTS

In this study, ispi- and contra-lateral lungs, contra-lateral breast and heart were considered as OARs while irradiating left-sided breast. Our main objective was to analyze dose-distribution of left lung. Monitor Units (MUs) were also recorded and found almost same in these three modalities ranging from 1200 to 2000.

Left Lung Dose Analysis

Few major differences were observed in different parameters specifically in ***mean doses*** among these three techniques. The mean value of V_{20Gy} (cc) in 11-bIMRT technique was found less by 8-17cc as compared to 7-and 9-bIMRT technique. It was observed that 11-bIMRT technique yielded slightly better outcomes in terms of V_{20Gy} (cc).

V_{5Gy} (cc)

The lowest-mean value of this parameter was 638.76cc found in 7-bIMRT technique, whilst highest-mean value was 690.31cc in 11-bIMRT modality. Maximum value was 1073.20cc recorded in 11-bIMRT technique. The lowest-minimum value was 354.56 cc recorded in 9-bIMRT. Comparatively, 7-bIMRT technique showed slightly good result in reducing low-dose volume of 5Gy.

V_{20Gy} (cc)

In 11-bIMRT plan, maximum, minimum and mean value of parameter V_{20Gy} were recorded as 297.2cc, 45.25cc and 164.67cc respectively. The highest value of this parameter was 307.00cc found in 7-bIMRT plan. The highest-mean value of this parameter was 181.70cc noted in 7-bIMRT technique. In 9-bIMRT plan, mean value was found 173.22cc. The minimum value of V_{20Gy} (cc) was 45.25cc recorded in 11-bIMRT technique.

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V_{25Gy} (cc)

Maximum values of V_{25Gy} were recorded 229.6 cc, 223.29cc, and 211.69 cc in 7-, 9- and 11-bIMRT plans respectively. Lowest-mean value of this parameter was 108.68cc found in 11-bIMRT plan. Highest-mean value was 123.12 cc observed in 7-bIMRT. In 9-bIMRT, mean value of V_{25Gy} was 117.64cc while minimum value was 29.64cc. Lowest volume of this parameter was 23.07cc found in 11-bIMRT plan.

$D_{50\%}$ (Gy):

The lowest-mean value of $D_{50\%}$ was 9.05Gy found in 11-bIMRT plan. The highest maximum value was 12.51Gy observed in 7-bIMRT plan, while minimum value was 6.30Gy found in 11-bIMRT plan. In view of this parameter, no significant difference was noted among these three techniques. However, 11-bIMRT technique yielded comparatively good outcomes in term of reducing dose to 50% volume of left lung.

D67% (Gy)

The highest-mean value of $D_{67\%}$ was 7.36 Gy found in 11-bIMRT while lowest was 6.94 in 7-bIMRT technique. Maximum value of this parameter was 9.90Gy recorded in 11-bIMRT and lowest- minimum value was 4.60Gy observed in 9-bIMRTplan. Lowest value of maximum dose of $D_{67\%}$ was 8.91Gy found in 7-bIMRT technique, whilst minimum value was 4.77Gy. The modality 7-bIMRT yielded slightly better results as compared to 11-bIMRT in terms of reducing dose to $D_{67\%.}$

Mean Dose (Gy)

Highest value of mean dose was 17.03Gy recorded in 7-bIMRT plan. Lowest value of mean dose was 8.74Gy found in 11-bIMRT plan. Minimum value of mean doses was 11.52 observed in11-bIMRT plan. Maximum and minimum values of mean dose were found 16.86 Gy and 9.03 Gy respectively in 9-bIMRT plan. 11-bIMRT technique exhibited slightly good in respect of *mean dose* as compared to7- and 9-bIMRT technique.

Heart Dose Analysis

Maximum values of ***mean doses*** were found approximately equal in each technique. Heart's ***mean dose*** in 9-and 11-bIMRT techniques were noted almost same as 6.74Gy and 6.54Gy respectively while that of 7-bIMRT was 8.82Gy. In 11-bIMRT technique, mean dose was recorded less by 2.28Gy as compared to 9-and 7-bIMRT. It was observed that 11-bIMRT technique was able to reduce dose by 1.24 -1.70Gy to 5-10cc volume of the heart. In the view of heart's mean dose, 11-bIMRT technique yielded good result as compared to others.

Contra-lateral Lung Dose Analysis

The treatment modality 9-bIMRT yielded comparatively better outcomes in terms of mean-dose. Maximum, minimum and mean-dose were found 4.05 Gy, 0.87Gy and 2.79Gy respectively. Highest mean-dose was 4.8Gy found in 11-bIMRT while lowest mean-dose was observed 0.87Gy in 9-bIMRT technique. The highest value of ρ was 3.4Gy found in 11-bIMRT technique.

Contra-lateral Breast Dose Analysis

There was no significant difference found among these techniques in terms of contra-lateral breast dose. The mean dose was observed as 3.31Gy, 3.30Gy and 3.37Gy in 7-, 9- and 11-bIMRT techniques respectively.

PTV Dose Analysis

The maximum values of $D_{95\%}$ were found as 38.62Gy, 39.24Gy and 39.58Gy in 7-,9- and 11-bIMRT techniques respectively. Highest mean dose was recorded as 38.78Gy in 11-bIMRT plan, whilst minimum mean-dose was 38.06Gy in 7-bIMRT plan. Lowest global maximum dose was found 115.10% in 9-bIMRT plan.

DISCUSSION

The study was designed to analyze the variation in dose of left lung on account of increasing number of beams in IMRT modality. For this purpose, patients diagnosed with left-sided breast cancer were considered under this study. Our medical physicist team surveyed 563 studies related to randomize controlled trials of IMRT in conservatively resected breast carcinoma. Many studies reported multiple benefits of IMRT modality particularly in terms of normal tissue sparing effect and toxicity [Livi, L. *et al*., 2015; Pignol, J.P. *et al*., 2016], and it partially enhances cosmetic effects, too [Mukesh, M.B. *et al*., 2014; Meattini, I. *et al*., 2015]. Several studies showed that surviving rate in breast cancer is increasing nowadays on account of early detection, social awareness and modern approach of treatment modality. Moreover, the toxicity of different kind of agents like doxorubicine and trastuzumab, plays influential role in patient's surviving rate. In left-sided breast irradiation, the important organs which remain at risk (OARs) are left lung and heart. Clinically, it is observed that acute radiation pneumonitis may be evolved in patients within six

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months of exposure to doses ≥ 8 Gy of radiation which can be lethal.

This may be divided into three phases (i) Latent period (ii) Exudative phase and (iii) Acute pneumonitic phase between two and six months. Actually the acute pneumonitis phase is an inflammatory reaction with intra-alveolar and septal edema. It is observed that primary response of the lung to irradiation is an increase in micro-vascular permeability. Pulmonary fibrosis is a late effect of irradiation, which is clinically and experimentally proved. While fibrosis may not be entirely separate from early pneumonitis.

Several studies reported that the risk of subsequent ischemic events is proportional to ***mean-dose*** of the heart [Sardaro, A. *et al*., 2012- Mege, A. *et al*., 2011]. Normally, breast cancer survivors who underwent radiation therapy have risk of pneumonitis and long-term cardiac complications. Cardiac vascular damage may be severe mortality threat rather than breast cancer in elderly women [Mehta, L.S. *et al*., 2018].

In this study, when number of beams increases from 7 to 11, the volume of V_{20Gy} (cc) and V_{25Gy} (cc) of ipsi-lateral lung gradually decreases. But, the value of $D_{50\,\%}$ (Gy) of ipsi-lateral lung slightly increases. The modality 9-bIMRT yields comparatively better result in reducing the dose to 2/3rd volume of ipsi-lateral lung, and resultantly it reduces the risk of pneumonitis.

Minor differences were observed in mean dose and maximum dose of contra-lateral lung. PTV dose coverage was found almost same in these three treatment modalities. The modality of treatment named Deep Inspiration Breath Hold (DIBH) in irradiation of left reconstructed chest wall and regional nodes shows significant advantages in reducing dose to ipsi-lateral lung and underlying heart [Dumane, V.A. *et al*., 2018]. The IMRT treatment modality with 11 beams provided almost as the same result as DIBH in terms of left lung dose and mean heart dose (MHD).

The dose conformity of PTV with higher number of beams is slightly increased low-dose exposure of normal tissues around the tumor. This may enhance slightly the risk of second malignancies, and raise a question on using newer methods compared to conventional 3D-CRT [Dörr, W. *et al*., 2002]. But, the high-dose volume in 3D-CRT is reported bigger as compared to IMRT. In this respect, the treatment modality 11-bIMRT shows advantages over 3D-CRT.

The study showed that 11-bIMRT is able to reduce the dose of volumes V_{20Gy} (cc) and V_{25Gy} (cc) up to clinically acceptable level, and it also reduces the mean-dose of left lung. Hence, increasing number of IMRT beams (7-11 beams) showed an advantage in terms of reducing mean-dose , volume of V_{20Gy}(cc) and V_{25Gy}(cc) of ipsilateral lung. The technique 7-bIMRT is able to reduce low dose volume of underlying lung.

CONCLUSION

The IMRT modality is frequently used nowadays in left-sided breast irradiation as to reduce mean-dose and high-dose volume of ipsilateral lung. The treatment technique 11-bIMRT produces comparatively better results in reducing high-dose volume and mean-dose of left lung along with MHD. As the number of IMRT beams increases from 7 to 11, it translates into better outcomes in terms of reducing high-dose volume as well as mean-dose of left lung and reduces the left lung's dose up to clinically acceptable level. The technique 11-bIMRT is able to reduce the left lung's dose almost equal to DIBH treatment modality. So, it is prudent to use 'N' number of IMRT fields such as 7≤ N ≤11 in left breast RT.

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