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Analysis of Dose-Distribution in Left-Lung and Heart as Increasing the Number of Beams in Left-Sided Breast Irradiation

Mohammad Shahnawaj Ansari [1,3*], Mohammad Ziyauddin Khan[1], Sunil Dutt Sharma[2], Neha Yadav [3,4], Mukesh Kumar Zope[5]

1. Dr. C.V. Raman University , Kota,Bilaspur, (C.G.),India
2. Bhabha Atomic Research Centre,Mumbai, India
3. Apollo Hospitals Bilaspur (C.G.), India
4. Applied Physics Department, Amity University Gwalior(M.P.),India
5. Indira Gandhi Institute of Medical Science,Patna,Bihar,India

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Introduction: Breast cancer has been a leading malignancy in women across the globe. In breast conserving treatment, radiation therapy plays an important role. This is clinically approved that breast conserving surgery followed by adjuvant radiation therapy produces as the same survival rate as radical breast RT. The aim of this study was to find out suitable number of IMRT fields to treat left-sided breast cancer and analyze the effects of increasing the number of fields in IMRT plans.

Material and Methods: We selected 105 patients retrospectively for this study diagnosed with left-sided breast cancer of age 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).

Results: 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).

Conclusion: The technique 7-bIMRT gives slightly better result in controlling low-dose volume of underlying lung and heart. 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.

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Introduction

There are various types of breast cancer, but the most common are ductal carcinoma in situ (DCIS) and invasive carcinoma. This is the most common malignancy which occurs frequently in females [1–6] and fast-growing disease in the world. In breast conserving treatment, radiation therapy (RT) plays a vital role. This is clinically approved that breast conserving surgery (BCS) followed by adjuvant radiation therapy produces as the same survival rate as radical breast surgery [7,8].

Many modern techniques have been developed within few decades to deliver dose with accuracy to the tumor with minimal damage of surrounding organs. Several studies recently reported that Intensity-Modulated Radiotherapy (IMRT) has advantage over 3D-CRT in terms of dose-conformity, homogeneity and sparing of normal organs [9-15]. IMRT needs an advanced computer program to calculate radiation dose accurately in three dimensions, based on the tumor's geometry and location. This technique modulates the intensity of the radiation beams around the breast-tumor, and spare normal organs in the surrounding of the tumor. The IMRT technique customizes the radiation dose as per exact 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 found useful in sparing heart and ipsi-lateral lung in left-sided breast irradiation. The major advantage of HBB is that contra-lateral lung and breast receive minimal dose [16]. Many clinical trials have been conducted in conjunction with adjuvant breast RT resulting smaller recurrence and higher long-term survival rate[17–19]. 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, radiotherapy for breast cancer has been a challenging and rapidly growing treatment modality. Regional

*Corresponding Author: Tel: +919914714716; Email: ansarisnz05@gmail.com

lymph node irradiation in younger trials with good target coverage shows reduction in long-term toxicity causing minor benefits in overall survival rate [20-22].

Many advance techniques have been developed recently in radiation therapy with aim to increase conformity and homogeneity of dose to tumor, and simultaneously sparing normal organs [23-28]. Various research papers showed that post-operative radiotherapy reduces the rate of local recurrence significantly. It also improves the long-term survival rate on the cost of morbidity of ispi-lateral lung [29,30]. Lung is a very important organ which remains at risk during breast RT which may cause rise of contingency of pneumonitis [31, 32].

The aim of this study was to find out suitable number of beams to treat left-breast, and to analyze the effects of increasing the number of IMRT beams on dose-distribution.

Materials and Methods

Patients, targets delineation and treatment planning

We selected 105 patients retrospectively for this study diagnosed with left-sided breast cancer age 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.

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 which help at the time of target 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.

We created three types of IMRT plans for each patient using7, 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 modality and it was tabulated in table 2.

Collimator angle was '0' degree in each plan. Beam and collimator angles remained unaltered in each technique. Beam isocenter was placed at depth 2-4cm from skin, demonstrated in figure1.

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

Table 2. Gantry angle (in degree) in each technique

7-Beam IMRT	9-Beam IMRT	11-Beam IMRT
5-10	5-10	5-10
25-30	25-30	20-25
80-85	80	50-55
100-105	100-105	90-95
125-130	120	115
315-320	130-135	135-140
300-305	305	150
….	320	300-305
….	350-355	325-330
….	….	340
….	….	350-355

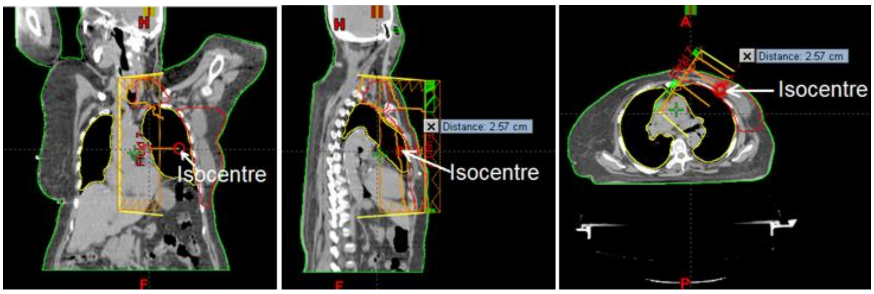

Figure 1. Displaying the position of beam's isocenter in coronal, sagittal and transverse plane.

Dose Reporting

The dose was prescribed 40.05Gy in 15 fractions (2.67Gy per fraction) for each patient considered under this study. Each plan was optimized with aim to achieve at least 95-100% dose coverage (of prescribed dose) to100% target's volume. Dose-constraints were almost same for OARs in each case. However, some extra precautions were taken during the plan optimization for reducing the mean-dose of underlying lung, and few minor adjustments were also done in 'Priority' of OARs and PTV.

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

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

In addition, $D_{100\%}$(Gy)of ipsi-lateral lung is also recorded and graphically displayed in figure2.

The parameters like mean, maximum, and minimum of 'mean doses'of contra-lateral lungs, contra-lateral breast and heart were also analyzed. These parameters were tabulated in table 5.

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.

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

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
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

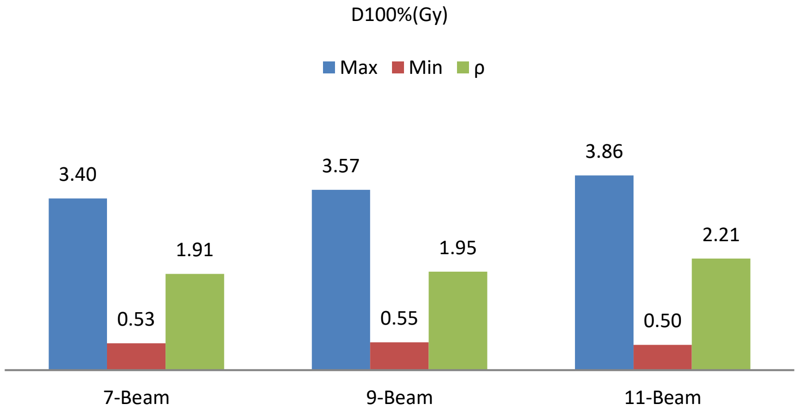

Figure 2. Displaying maximum, minimum and mean value of $D_{100\%}$ (Gy) of ipsilateral lung

Table 5. Details of mean dose of contra-lateral lung, contra-lateral breast and heart

Contra-lateral Lung				Contra-lateral Breast				Heart			
Mean Dose(Gy)				Mean Dose(Gy)				Mean Dose(Gy)			
	7-Beam	9-Beam	11-Beam		7-Beam	9-Beam	11-Beam		7-Beam	9-Beam	11-Beam
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

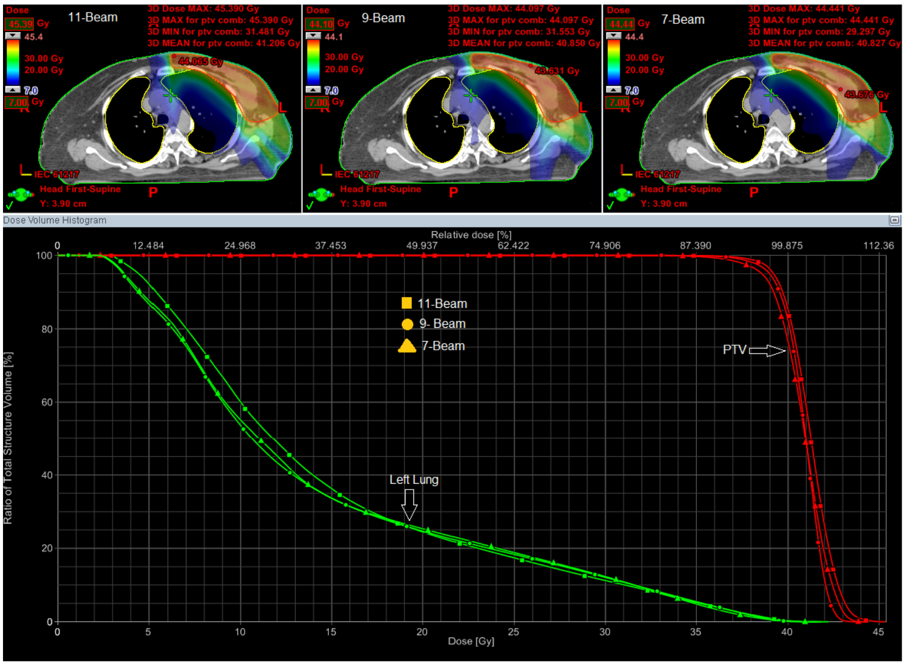

Figure 3. Dose distribution in each treatment modality along with DVH of PTV and left lung

Results

In this study, ispi-lateral lung, contra-lateral lung, contra-lateral breast, and heart were considered as OARs during the irradiation of 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 the parameters analyzed here, especially 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 was690.31cc in 11-bIMRT modality. Maximum value was1073.20ccrecorded 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}wererecorded as297.2cc, 45.25cc and 164.67cc respectively. The highest value of this parameter was 307.00cc founding 7-bIMRT plan. The highest-mean value of this parameter was181.70cc noted in 7-bIMRTtechnique. In 9-bIMRT plan, mean value was found 173.22cc. The minimum value of V_{20Gy}(cc) was 45.25cc recorded in 11-bIMRTtechnique.

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 founding 11-bIMRTplan. 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-bIMRTtechnique. 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-bIMRTyielded 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 in 11-bIMRT plan. Maximum and minimum values of mean-dose were found 16.86 Gy and 9.03 Gy respectively in 9-bIMRT plan. The technique11-bIMRT produces slightly good impacts in respect of ***mean-dose*** as compared to7-bIMRT and 9-bIMRT technique.

Heart Dose Analysis: Maximum values of mean doses were found approximately same in each technique. Heart's ***mean dose*** in 9-bIMRT and 11-bIMRT techniques were noted almost equal like 6.74Gy and 6.54Gy respectively while that of 7-bIMRTwas 8.82Gy. In 11-bIMRT technique, mean-dose was recorded less by 2.28Gy as compared to 9-bIMRT 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 results as compared to others.

Contra-lateral Lung Dose Analysis: IMRT technique with 9 beams showed comparatively better result in terms of mean dose. Maximum, minimum and mean-dose were found4.05 Gy, 0.86Gy and 2.79Gy respectively.

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 access the variation in dose-distribution in the treatment of left-breast on account of increasing the 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 [35-37], and it partially enhances cosmetic effects, too [38,39]. 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 doxorubic in 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 months of exposure to doses ≥ 8 Gy of radiation which can be lethal .

This can be divided into three phases (i) Latent period lasting up to 4 weeks, (ii) Exudative phase (3-8 weeks), and (iii) Acute pneumonitis phase between two and six months. The latter is an inflammatory reaction with intra-alveolar and septal edema accompanied by epithelial and endothelial desquamation. The 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 [40]. 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 [41].

In our 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. 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. But, the high-dose volume in 3D-CRT is reported wider as compared to IMRT. In this respect, the modality 11-bIMRT shows advantage over 3D-CRT.

The study shows that 11-bIMRT can 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) shows an advantage in 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

These days, IMRT modality is frequently used in left-sided breast irradiation to reduce mean-dose and high-dose volume of ipsi-lateral lung. The technique 7-bIMRTgives slightly better result in controlling low-dose volume of underlying lung and heart. However,11-bIMRT treatment technique provides relatively better results in reducing high-dose volume and mean-dose of left lung along with MHD. As the number of IMRT-beam increases, it translates into better outcomes in terms of reducing high-dose volume as well as mean-dose of left-lung. So, the study advises us to use ‘N’ number of IMRT fields such as 7≤ N ≤11 in left-sided breast RT.

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