Iranian Journal of Medical Physics

ijmp.mums.ac.ir



Impacts of Increasing the Number of IMRT Beams on Heart's Dose Distribution in Left Breast Irradiation: Dosimetric Study

Mohammad Shahanawaj Ansari ^{1, 2*}, Mohammad Ziyauddin Khan¹, Sunil Dutt Sharma³

- 1. Dr.C.V.Raman University, Kota, Bilaspur (C.G.), India
- 2. Apollo Hospitals Bilaspur (C.G.), India
- 3. Bhabha Atomic Research Centre , Mumbai, India

ARTICLE INFO	A B S T R A C T
<i>Article type:</i> Original Paper	Introduction: The main objective of this study was to assess the impacts of an increasing the number of IMRT beams on cardiac dose distribution in left-sided breast irradiation so that we can reduce the heart's mean dose up to aligned up compared by a second back of the second
<i>Article history:</i> Received: Apr17, 2021 Accepted: Aug18, 2021	<i>Material and Methods:</i> For this study 107 female patients, diagnosed with left-sided breast cancer were selected retrospectively. In 107 patients, there were 52 patients of chest wall irradiation including supra- clavicular fossa, while 22 patients were of breast-conserving surgery excluding supra-clavicular fossa and
<i>Keywords:</i> Breast Cancer Optimization Heart Radiation Dose IMRT Radiotherapy	 internal mammary lymph nodes, and 33 patients were of chest-construing singley excitating suppra-clavicular hosts in the state of chest wall irradiation including internal mamma lymph nodes and supra-clavicular fossa. Exclusion criteria were previous history of left-sided breast radiat therapy, uncommon fractionated dose delivered in past, and indication of palliative radiation thera Intensity modulated radiotherapy plans were generated using 7, 9 and11 beams for each patient and prescribed dose was 40.05 Gy in 15 fractions (2.67 Gy /fraction) for the targets. <i>Results:</i> Heart: <i>V_{5Gy}(cc):</i> This was a low-dose volume of our study in which the 11-bIMRT technique yield better result as compared to 9- and 7-bIMRT. Maximum and minimum values of V₅ were found 539.60cc 9-bIMRT and 141.32cc in 11-bIMRT techniques respectively.<i>V_{25Gy}(cc):</i> The maximum value of V_{25Gy} v found 41.73cc in 7-bIMRT technique, while the lowest value was 0.29cc in 11-bIMRT. The IMRT technique with 11 beams showed comparatively better result on this parameter as well as 3-5cc volume of V_{25Gy} v spared. Mean dose (Gy): Maximum value of mean dose was found 8.51Gy in 7-bIMRT while it was 6.53 in 11-bIMRT technique. <i>Conclusion:</i> The study indicates that increasing the number of IMRT beams reduces heart's high-d volume and improves the quality of treatment plans. It is judicious to use 11-bIMRT technique in left-side breast irradiation as it produces clinically acceptable mean heart dose.

▶ Please cite this article as:

Ansari MS, Khan MZ, Sharma SD. Impacts of Increasing the Number of IMRT Beams on Heart's Dose Distribution in Left Breast Irradiation: Dosimetric Study. Iran J Med Phys 2022; 19: 145-153.10.22038/IJMP.2021.57104.1959.

Introduction

Breast cancer has been a common malignancy in women across the globe. However, it is a fast growing disease in female particularly in the developed world [1]. Radiotherapy (RT) plays an important role in the treatment of breast cancer especially in breastconserving therapy. It has been observed that breastconserving surgery (BCS) followed by adjuvant radiation therapy results as the same survival rate as radical breast surgery [2,3]. Nowadays, several techniques are available in radiotherapy for delivering dose safely and accurately to the targets with minimal damage of the surrounding normal organs. Recently introduced the accelerated partial breast irradiation (APBI) technique is an alternative treatment modality for selected cancer patients with early stage breast cancer. Moreover, Intensity-Modulated Radiotherapy (IMRT) has the advantage of dose conformity and homogeneity as compared with three-dimensional (3D-CRT) techniques with more sparing effects of organs at risk [4-10]. Half beam block (HBB)

technique is also a very useful method to spare the

underlying lung and heart while irradiating the left

breast. In this technique, the contra-lateral lung and opposite breast receive very less radiation dose which

is well within their tolerance value [11]. In many

cases, breast cancer requires multimodal treatment

e as such as surgery, chemotherapy followed by radiotherapy. Several randomized data in conjunction with meta-analysis have shown less recurrence and elevated long-term survival (5–10%) after adjuvant 3D-CRT in breast cancer patients [12–14]. However, apart from the beneficial effects of radiotherapy, irradiation may cause detrimental side effects on normal tissues. Normally, ipsilateral lung and heart with coronary vessels receive a large amount of radiation dose in left-sided breast RT. A large number of reputed journals have recently reported on the increasing rate of coronary contingency and cardiac

^{*}Corresponding Author: Tel: +91-99147147; Email: ansarisnz05@gmail.com

mortality as a result of cardiac radiation dose received in the left breast irradiation [15–17].

In order to reduce the dose to normal organs as low as possible, many modern techniques have been developed with the aim to increase conformity and homogeneity of dose to the tumor and simultaneously sparing the organs at risk [18–21]. Many literatures have been reported that post-operative radiotherapy (PORT) significantly reduces the rate of local recurrence and improve the long-term survival rate on the cost of morbidity of heart and ispi-lateral lung [22-25]. In left breast RT, heart is one of the most important organs which remains at risk, and causes the rise of contingency of cardiac mortality [26, 27]. It has been estimated that the rate ratio (RR) of cardiac mortality increased by 0.04 per gray (Gy) mean heart dose (MHD) in modern breast RT [28].

A case-control study for females who underwent breast irradiation in between 1958 and 2001 found that the rate of cardiac exigency has increased linearly with MHD by 7.4% per Gy, though heart doses were evaluated retrospectively. In contrary, more recent studies reported that the absolute cardiac risk after left breast RT has been decreased by using modern techniques, as well as the rate of radiation induced pneumonitis and pulmonary fibrosis are reported still low even regional lymph node-RT is performed [29-32]. The IMRT technique has been generally used for the treatment of various sites with a good sparing effect of normal tissues and more homogeneous dose distributions. IMRT is a new modality for whole breast irradiation and it is used to improve conformity and homogeneity of the targets as well as to reduce OAR doses. Many studies concluded that the differences between IMRT plans with increased number of fields were not statistically significant [33], however it significantly improves conformity index (CI) and homogeneity index (HI) of the plans. Moreover, it reduces high-dose volume of heart and lung. The demerit of IMRT is that the opposite lung also receives a small amount of dose and increases the low-dose volume of the heart as well. On the other hand, IMRT increases dose homogeneity inside the breast PTV and reduces the heart's high-dose volume. In order to compare minutely the IMRT delivery protocols and to study the impacts of increasing number of IMRT beams on heart dose-distribution, we have planned to take additional data for heart's dose-distribution like dose to 33% volume (D33%), dose to 50% volume (D50%), dose to 67% volume (D67%), and dose to 100% volume (D100%). These data are clinically significant while analyzing the treatment plans for the left-sided breast.

Objectives: The main objective of this study was to assess the impacts of increasing number of IMRT beams on cardiac dose-distribution in left-sided breast RT so that we can reduce the MHD up to clinically acceptable level.

Materials and Methods

Patients, target delineation and treatment planning

For this study, 107 patients were selected retrospectively with age ranging from 31 to 82 years with median age 57-years, diagnosed with left-sided breast cancer (including lobular and ductal carcinoma in situ) in our institution between June 15, 2019 and May 20, 2021. In this study,female patients aged 45-62 years at diagnosis, lobular and ductal/lobular carcinoma were diagnosed with stage II/III. It was observed that comedo, tubular, mucinous, and medullary carcinomas were less likely to find at an advanced stage. The histology of the breast- cancer patients under this study were differed in their grades point and clinical presentations.

Out of 107 patients, 52 patients were of chest wall (CW) irradiation including supra-clavicular fossa (SCF), while 22 patients were of breast-conserving surgery (BCS) excluding SCF and the internal mammary lymph nodes (IMLN). There were 33 patients with treatment of CW irradiation including IMLN and SCF. Exclusion criteria were the previous history of left-sided breast RT, uncommon fractionated dose delivered in the past, sign of palliative RT, partial breast RT and documented refusal of data collection for this study. The CT simulation was done for each patient in supine position with both arms positioned above the head, and a copper wire placed around the breast tissues just for marking purposes and getting help while contouring the planning target volume (PTV). Spiral CT images were taken from neck to lower border of diaphragm and then reconstructed for 1.5 mm slice thickness. PTV and organs at risk (OAR) such as heart, right breast; ipsiand contra-lateral lungs were contoured according to Radiation Therapy Oncology Group (RTOG) guidelines [34, 35].

All patients were treated in supine position with both arms above the head. Portal dosimetry was performed for each plan that clinically finalized and accepted for treatment before executing over the patient. The treatment techniques used here for generating plans were 7-beam IMRT (7-bIMRT), 9-beam IMRT (9-bIMRT) and 11-beam IMRT (11-bIMRT) with only 6MV photon. In case of regional lymph nodes (LN) irradiation, regions were recorded separately as axillaries, supra-clavicular and internal mammary nodes (IMN), with axillaries and supra-clavicular LN typically delineated up to levels 1-3 and level-4 respectively as per ESTRO consensus guideline, while IMN was extending caudally to the 4-5th rib [36]. For each patient, radiation doses of heart, lungs and opposite breast were recorded from RT plans.

In this study, 51 patients were treated with 11bIMRT, 37 patients with 9-bIMRT, and 19 patients with 7-bIMRT. Portal dosimetry was done for all plans before executing the treatment. For this study, three different IMRT plans were created separately by our medical physicist's team for each patient using 7, 9 and 11 beams. The eclipse planning system, version 11.0 (Varian Medical System, Palo, USA) was used to generate the plans. The beam angle of each modality is tabulated in (Table 1). Collimator angle was '0' degree in all plans. Beam isocenter was placed at a distance of 2.0-3.5 cm from the skin; the distance of the heart from the beam's isocenter and breast-PTV curvature are displayed in Fig.1 for a typical plan.

	6N	IV photon	
Beam No.	7-bIMRT	9-bIMRT	11-bIMRT
B1	0-5	0-5	0-5
B2	25	25-30	25
B3	75-80	80	60
B4	110	105	90
B5	130	120	115
B6	320	130	135
B7	300-305	300-305	150
B8		320	305
B9		355	325
B10			340
B11			350-355

Table 1. Gantry angle (in degree) in each treatment modality



Figure 1. Displaying the position of the beam's isocentre, curvature of PTV, the distance of heart from the isocenter , and the distance of isocentre from the skin in a typical treatment plan

Table 2. Details of maximum, minimum and mean value of D95% (Gy), Global maximum-dose , CI and HI for left-sided breast PTV

			Left	Breast-PTV			
	D	_{95%(} Gy)			Global ma	ax dose (%)	
	7-Beam	9-Beam	11-Beam		7-Beam	9-Beam	11-Beam
Max	38.62	39.24	39.58	Max	117.20	115.10	119.70
Min	37.07	38.06	38.04	Min	108.60	106.40	108.40
Mean	38.06	38.57	38.78	Mean	111.98	112.05	112.52
		HI			(CI	
	7-Beam	9-Beam	11-Beam		7-Beam	9-Beam	11-Beam
Max	1.23	1.18	1.15	Max	1.08	1.06	1.05
Min	1.13	1.11	1.08	Min	0.93	0.95	0.97
Mean	1.16	1.14	1.12	Mean	1.04	1.03	1.01
	Mean dose (Gy)						
			7-Beam	9-Beam	11-Beam		
		Max	43.62	42.08	42.27		
		Min	39.92	40.07	40.33		
		ρ	40.67	40.73	40.84		
	Max= Maximum, Min= Minimum, ρ= Mean of mean doses						
		CI= Confo	ormity index, HI=	Homogeneity	index		

Dose Reporting

Prescribed dose (PD) was 40.05 Gy in 15 fractions (2.67Gy/ fraction) for each patient. Each plan was optimized for achieving 95-100% dose coverage just to envelope the whole target. Inverse planning optimization was used for generating the plans in each technique. There was no specific reference constraint to any organs at risk in any case. We referred to QUANTEC-guidelines for dose constraints of OARs [37], and used almost uniform dose constraints in every plan optimization and did very minor adjustments in the priority of OARs and PTV during the process of optimization. All plans were analyzed first for the target's dose coverage using the parameters D_{95%}, mean dose, maximum dose, HI and CI, as tabulated in (Table 2). The index parameters like CI and HI were calculated as per RTOG definition.

For analyzing the cardiac dose-distribution and comparing these three IMRT delivery protocols , 10 parameters such as V_{5Gy} , V_{25Gy} , V_{30Gy} , $D_{33\%}$, $D_{50\%}$, $D_{67\%}$, $D_{100\%}$, D_{5cc} , D_{10cc} and MHD based on the literatures [38,39] were calculated as well as analyzed, and data of these parameters after optimization were tabulated in (Table 3). Monitor Units (MU) were also recorded, ranging from 1200 to 2100.

For evaluating the heart's low-dose volume, 5Gy dose was taken into consideration as the minimum dose and PTV dose- distribution was analyzed at 95% of the prescribed dose, as displayed in Fig.2.

The mean doses of right-breast, ipsi-and contralateral lungs were taken as another analyzing parameters, as well as mean of mean doses (ρ) were also evaluated just for ease of comparing the data; and the findings are tabulated in (Table 4).

Table 3. Analytical details of the heart's dose-distribution (max., min., mean value) in terms of different parameters used for this study in left-sided breast irradiation

	V _{5Gy} (cc)			V _{25Gy} (cc)			
	7-Beam	9-Beam	11-Beam	7-Beam	9-Beam	11-Beam	
Max. value	485.86	35.86 539.60		41.73	37.41	29.06	
Min. value	146.30	156.20	141.32	0.77	0.34	0.29	
Mean value	298.36	300.79	291.01	19.00	17.20	14.52	
	V _{30Gy} (cc)			D _{50%(} Gy)			
	7-Beam	9-Beam	11-Beam	7-Beam	9-Beam	11-Beam	
Max.value	29.97	17.82	17.90	7.96	8.16	8.25	
Min. value	0.03	0.05	0.02	4.10	4.20	4.08	
Mean value	8.76	8.19	6.11	5.55	5.59	5.53	
	D _{67%} (Gy)			D _{100%} (Gy)			
	7-Beam	9-Beam	11-Beam	7-Beam	9-Beam	11-Beam	
Max. value	6.28	6.57	6.62	3.30	3.31	3.14	
Min. value	3.30	3.27	3.26	1.10	0.63	0.36	
Mean value	4.58	4.61	4.63	1.85	1.82	1.70	
	D _{33%(} Gy)			$D_{5cc}(Gy)$			
	7-Beam	9-Beam	11-Beam	7-Beam	9-Beam	11-Beam	
Max. value	10.05	10.76	10.02	36.20	36.61	35.86	
Min. value	4.76	5.02	4.33	21.00	19.34	10.04	
Mean value	6.99	7.01	6.45	30.68	30.73	25.63	
	D _{10cc} (Gy)			Mean Dose(Gy)			
	7-Beam	9-Beam	11-Beam	7-Beam	9-Beam	11-Beam	
Max. value	32.68	34.08	32.87	8.51	7.81	6.53	
Min. value	14.67	14.80	12.32	4.72	4.82	3.78	
Mean value	27.61	27.42	23.55	6.74	6.61	4.92	

Max: Maximum, Min: Minimum, α = Mean of mean doses

Table 4. Details of mean-dose of contra-lateral breast, ipsi-and contra-lateral lungs

Contra-	lateral lung		Contra-lateral breast				Ipsi-lateral l	lung	
Mean I	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	2.40	2.43	2.42	2.78	2.73	2.65	17.03	16.86	16.57
Min	0.93	0.83	0.84	1.40	1.26	1.20	9.33	8.83	8.31
ρ	1.30	1.35	1.40	2.11	1.57	1.41	12.87	12.62	11.21



Figure 2.Displaying the dose-distribution (95% of PD) along with DVH in left-sided breast PTV for each treatment protocol.

Statistical analysis was performed using one-way ANOVA-test at confidence level of 95% for intercomparison of these three treatment techniques, and findings are tabulated in (Table 5). The p-value < 0.05 was considered for analyzing the data, and to test the significance of differences. We used one-way ANOVAtest along with normality-test for comparing the results of these three different IMRT treatment protocols which show major differences in MHD, V_{30Gy} and D_{10cc} of the heart.

Table 5. One-way ANOVA -test results for different parameters of cardiac dose-distribution at the confidence level of 95%.

$\alpha = 0.05$	
Parameters	P-Values
mean dose	0.031
V _{5Gy} (cc)	0.862
V _{25Gy} (cc)	0.365
V _{30Gy} (cc)	0.024
D33% (Gy)	0.595
D _{50%} (Gy)	0.748
D _{67%(} Gy)	0.779
D _{100%(} Gy)	0.808
D _{5cc} (Gy)	0.385
D _{10cc} (Gy)	0.043

Results

Heart dose analysis

 $V_{5Gy}(cc)$: This was the low-dose volume of this study in which 11-bIMRT technique yielded better result as compared to 9- and 7-bIMRT. Maximum and minimum values of V₅ were found 539.60cc in 9-bIMRT and 141.32cc in 11-bIMRT techniques respectively. Mean value of V_{5Gy} was also observed lowest in 11-bIMRT techniques, 291.01cc. No significant differences were observed among these three IMRT delivery techniques from the V_{5Gy} point of view.

 V_{25Gy} (*cc*): The mean value of V_{25Gy} in 7-bIMRT, 9bIMRT and 11-bIMRT were observed 19.00 cc, 17.20cc and 14.52cc respectively. The volume of 3-5cc was spared in 11-bIMRT technique as compared to others. The maximum value of V_{25Gy} was found 41.73cc in 7-bIMRT technique, while the lowest value was 0.29cc in 11bIMRT. The IMRT technique with 11 beams showed comparatively better results on this parameter as well as the technique reduced 3-5cc volume of V_{25Gy} .

 $V_{30Gy}(cc)$: This was the high-dose volume of our study, andfor this parameter 11-bIMRT technique produced significantly better outcomes. Maximum, minimum and mean value of V_{30Gy} were found 17.9(cc), 0.02(cc) and 6.11(cc) respectively in 11-bIMRT technique. The heart's volume 2.10-2.65cc was spared in 11-bIMRT as compared to 7-beam and 9-beam techniques. Maximum value of V_{30Gy} was 29.97cc found in 7-bIMRT while minimum value was 0.02cc in 11-bIMRT technique.

 $D_{33\%}$, $D_{50\%}$, $D_{67\%}$ and $D_{100\%}$ (Gy): The minor differences were observed among 7-bIMRT, 9-bIMRT and 11-bIMRT techniques. Maximum, minimum and mean values of these parameters are found almost equal in all these treatment modalities. In terms of $D_{33\%}$,IMRT technique with 11 beams showed a minor advantage over 7-bIMRT and 9-bIMRT. The maximum, minimum and mean values of $D_{33\%}$ were found 10.02Gy, 4.33Gy, and 6.45Gy respectively in these treatment modalities. The maximum, minimum and mean value of $D_{100\%}$ were observed 3.14 Gy, 0.36 Gy and 1.70 Gy respectively in 11bIMRT. All these three IMRT techniques produced no remarkable differences in terms of $D_{50\%}$ and $D_{67\%}$, but slight differences were observed in $D_{33\%}$ and $D_{100\%}$.

D_{5cc} (Gy): A significant difference was observed in mean dose of D_{5cc} parameter. In 11-bIMRT technique, the mean value of D_{5cc} was found 25.63 Gy which was the lowest among all these three treatment modalities. The maximum value of mean of D_{5cc} was 30.73 Gy found in 9bIMRT. The minimum values of D_{5cc} parameter in 7-, 9and 11-bIMRT techniques were recorded as 21.00 Gy, 19.34 Gy and 10.04Gy respectively. Minor differences were observed in the maximum value of D_{5cc} parameter among all these three treatment modalities. In 11-bIMRT technique, minimum value of D_{5cc} parameter was found less by 9-11Gy as compared to 7- and 9-bIMRT techniques. The difference of 11-bIMRT with the next greater value for minimum and mean values are 48% and 16%, respectively. Thus, 11-bIMRT technique showed slightly good results in terms of the minimum and meanvalue of D_{5cc} parameter.

 D_{10cc} (*Gy*) :There was a significant difference observed in the mean value of this parameter. The 11-bIMRT technique reduced the mean dose by 17% and the minimum dose by 19% as compared to others IMRT modalities. The mean values observed here were 27.61 Gy, 27.42 Gy, and 23.55 Gy in 7-, 9- and 11-bIMRT techniques respectively. The maximum value was 34.08 Gy found in 9-bIMRT technique. The minimum value was found 12.32 Gy in 11-bIMRT which was the lowest among all these three IMRT techniques. Thus, 11-bIMRT showed a major advantage over 7- and 9-bIMRT techniques in terms of D_{10cc} parameter.

Mean dose (Gy): Maximum value of the mean dose was found 8.51Gy in 7-bIMRT while it was 6.53Gy in 11-bIMRT technique. Mean of mean doses were 6.74 Gy, 6.61 Gy and 4.92 Gy found in 7-, 9-and 11-bIMRT techniques respectively. The minimum value of mean dose was 3.78Gy recorded in 11-bIMRT technique. The compelling advantages were observed in 11-bIMRT, that reduced the mean of mean doses by 37.0% , the maximum value of mean dose by 27.5% as compared to 7- and 9-bIMRT techniques.

Ipsi-lateral lung

Maximum value of the mean dose was 17.03 Gy found in 7-bIMRT while the minimum value was 8.31 Gy in 11bIMRT technique. The value of ρ was 11.21 Gy found the lowest in 11-bIMRT technique. In 7-and 9-bIMRT techniques, the value of ρ was found 12.87 Gy and 12.62 Gy respectively. The mean of the irradiated volume of V_{20cc}in 11-bIMRT technique was observed less by 17.00cc as compared to others. Thus, 11-bIMRT technique yielded comparatively better outcomes in terms of V_{20cc}. Maximum values were found almost the same in these three treatment techniques, but the value of ρ was recorded less by 14.80% in 11-bIMRT as compared to 7-bIMRT techniques , and less by 12.60% as compared to 9-bIMRT. Thus, 11-bIMRT showed a better performance in terms of reducing the mean dose of ipsi-lateral lung.

Contra-lateral breast

Maximum and minimum values of mean dose were 2.78Gy and 1.20Gy found in 7- and 11-bIMRT techniques respectively. The lowest value of mean of mean doses was 1.41Gy found in 11-bIMRT technique. In 7- and 9-bIMRT techniques, the values of ρ were recorded as 2.11Gy and 1.57 Gy respectively. There was no significant difference observed in the maximum value of the mean dose among these three techniques.

Contra-lateral lung

The lowest value of the minimum mean doses was 0.83 Gy found in 9-bIMRT while the maximum was 2.42 Gy in 11-bIMRT technique. The lowest value of ρ was 1.30 Gy observed in 7-bIMRT technique. In 9-and 11-bIMRT techniques, the values of ρ were found 1.35 Gy and 1.40Gy respectively. In terms of ρ of the contra-lateral lung, 7-bIMRT performed slightly better as compared to 9-and 11-bIMRT techniques.

Discussion

The study was designed to analyze the heart's dose distribution in left-sided breast RT accounting the increased number of IMRT beams, and how to improve the quality of IMRT plans using suitable number of beams. Our medical physicist team went through a number of studies on randomized controlled trials about IMRT in conservatively resected breast carcinoma. Some of these studies reported advantages in patients treated by IMRT modality with 4-7 beams mainly in terms of normal tissue sparing effect, toxicity and cosmesis [40–46]. This is well known fact that cardiovascular complications may appear over a period of time after irradiation and may cause death. Various studies reported about the risk of subsequent ischemic events which is proportional to MHD [47-49].

Normally, breast cancer survivors who undergo radiation therapy have a risk of long-term cardiac complications. Cardiac vascular damage in older women is a severe mortality threat than breast cancer itself [50]. In this study, significant differences were observed in cardiac dose distribution among three IMRT techniques, particularly in MHD. The IMRT technique with 11 beams yielded comparatively better outcomes in terms of reducing V_{25Gy} , V_{30Gy} and MHD doses. Many authors have shown the significant dosimetric advantages with lower dose to the heart, lungs and contra-lateral breast following deep inspiration breath-hold position (DIBH) irradiation in left reconstructed chest wall and regional nodes [51]. But, treatment with DIBH modality is a very cumbersome job and needs very advanced technique with very high cost. Moreover, patient needs to be coached for breath hold, and breathe through the nose during entire course of treatment. In contrast, IMRT is a free breath modality and comfortable for the patients. In 11-bIMRT modality heart's high-dose volume was found less than others. MHD was also reported significantly less in 11-bIMRT as compared to 7-and 9bIMRT techniques. Significant differences were observed in D_{5cc} and D_{10cc} among these three IMRT techniques, while differences were observed in the mean dose of opposite breast and contra-lateral lung. The target's dose coverage was found almost the same in these techniques.

When we increase the number of beams, the TPS has more degree of freedom to deliver the dose to targets in a defined manner. But the problem is that it (11-bIMRT) consumes more time as compared to others in the treatment which may cause discomfort to the patients. However, 11-bIMRT technique reduces MHD up to clinically acceptable levels equivalent to deep inspirational breath hold (DIBH).

The dose conformity to the target volume, accompanied by a higher number of beams, is often at the cost of slightly increased low-dose exposure to normal tissues surrounding the tumor. This may cause higher risk for the induction of second malignancies, and raise a question about using newer advanced treatment modalities [52]. Our study showed that heart's higher-dose volume largely spared and received 2-5Gy less dose in 11-bIMRT as compared to others. But on the other hand, it slightly increases cardiac low-dose volume which might be clinically not acceptable depending upon clinical condition of the patient. When we tried to reduce the heart's mean dose <4Gy in 11bIMRT plan, the global maximum dose was increased up to 119.7% and consequently the dose-heterogeneity in PTV was also increased. IMRT with 11 beams produced significantly good results in terms of reducing the dose to cardiac volume $V_{\rm 25Gy}$ and $V_{\rm 30Gy}.$ The patient's treatment time (dose delivery only) was recorded 6-10 minutes depending upon the number of MUs. The 11-bIMRT treatment modality remarkably reduced cardiac doses D_{5cc} and D_{10cc} while irradiating left-sided CW along with IMLN. It was noticed that increasing the number of beams in IMRT technique yielded significant advantages in reducing high-dose volume of the heart and enhanced the dose homogeneity in left breast-PTV. The technique of 7-bIMRT yielded slightly better results in case of contra-lateral lung dose. But, 11-bIMRT technique showed a good performance in reducing ipsilateral lung dose. The 11-bIMRT showed good results that reduced heart's mean of mean doses by 36.99% and it also reduced the mean dose of D_{10cc} by 17-19%. In this study, the heart's mean of mean-doses were analyzed for comparing and evaluating the data in an easy way so that a concrete conclusion can be extracted related to heart's dose distribution. We have studied the dose volume of 33%, 50%, 67% and 100% of the heart which are clinically significant parameters at the time of plan analysis. For analyzing the data minutely, we included the small volume -dose like D_{5cc} and D_{10cc} as they are clinically significant volumes that evaluate the heart's ventricle doses responsible for cardiac contingency in long-term survival. In addition to this, we collected the data for opposite breast and opposite lung for studying the spillage of doses in IMRT techniques. The study reported that 11-bIMRT performed well in terms of reducing the gross cardiac dose, especially when IMLN has to be treated along with CW. For studying dose conformity and homogeneity of breast-PTV, CI and HI were also included in data mining. In 11-bIMRT, the mean values of CI and HI were 1.01 and 1.12 respectively, indicating that 11-bIMRT technique provided a better target-coverage. The dose of D_{95%} was found almost same in all three techniques. The maximum value of global maximum dose was 119.70% found in 11-bIMRT while the lowest was 115.10% in 9-bIMRT.

Conclusion

Nowadays, IMRT technique is evolving as a fascinating treatment modality in left-sided breast irradiation. The performance of 11-bIMRT technique is better in terms of reducing heart's high-dose volume as well as MHD. The study revealed that increasing the number of IMRT beams has reduced the heart's high-dose volume and improved the quality of treatment plans. Further, more studies are needed to investigate the impacts of increasing the number of IMRT beams on the heart's dose distribution using more than 11 IMRT beams. However, it is judicious to use 11-bIMRT technique in left-sided breast RT as it produces clinically acceptable doses of MHD, V_{25Gy} , V_{30Gy} and D_{10cc} .

Acknowledgment

The authors are very much thankful to Dr.Manoj Nagpal as he supported and provided all facilities to accomplish this brilliant research work within the time frame.

References

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021 Feb 4. doi: 10.3322/caac.21660.
- 2. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, 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. New Engl J Med 2002; 347: 1233-41.

- Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347: 1227-32.
- Hille-Betz U, Vaske B, Bremer M, Soergel P, Kundu S et al. Late radiation side effects, cosmetic outcomes and pain in breast cancer patients after breastconserving surgery and three-dimensional conformal radiotherapy: risk-modifying factors. Strahlenther Onkol. 2016;192:8–16.
- Njeh CF, Saunders MW, Langton CM. Accelerated partial breast irradiation using external beam conformal radiation therapy: a review. Crit Rev Oncol Hematol 2012; 81: 1-20.
- Polgár C, Van Limbergen E, Pötter R, Kovács G, Polo A, Lyczek J, et al. Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). Radiother Oncol 2010; 94: 264-73.
- Coles CE, Brunt AM, Wheatley D, Mukesh MB, Yarnold JR. Breast radiotherapy: less is more? Clin Oncol (R Coll Radiol) 2013; 25: 127-34.
- Livi L, Meattini I, Marrazzo L, Simontacchi G, Pallotta S, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase-3 randomised controlled trial. Eur J Cancer 2015; 51: 451-63.
- Smith BD, Arthur DW, Buchholz TA, Haffty BG, Hahn CA, et al. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). J Am Coll Surg 2009; 209: 269-77.
- Arthur DW, Vicini FA. Accelerated partial breast irradiation as a part of breast conservation therapy. J Clin Oncol 2005; 23: 1726-35.
- 11. Ansari S, Kumar Satpathy S. Half Beam Block Technique in Breast Cancer and It's Dosimetric Analysis using different Algorithms. Iran J Med Phys 2017; 14: 66-74.
- 12. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effect of radiotherapy after breastconserving surgery on 10-year recurrence and 15-year breast cancer death. Meta-analysis of individual patient data for 10 801 women in 17 randomized
- Clarke M, Collins R, Davies C, Elphinstone P, Evans E, et al. 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 randomized trials. Lancet. 2005;366(9503):2087–106.
- Overgaard M, Jensen MB, Overgaard J, Hansen P, Rose C, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen. Danish breast Cancer cooperative group DBCG 82c randomized trial. Lancet. 1999;353(9165):1641–8.
- 15. Darby S, McGale P, Taylor C, Peto R. Long-term mortality from heart disease and lung cancer after

radiotherapy for early breast cancer. Prospective cohort study of about 300 000 women in US SEER cancer registries. Lancet Oncol. 2005;6(8):557–65.

- Sardaro A, Petruzzelli MF, D'Errico MP, Grimaldi L, Pili G. Radiation-induced cardiac damage in early left breast cancer patients. Risk factors, biological mechanisms, radiobiology, and dosimetric constraints. Radiother Oncol. 2012;103(2):133–42.
- Darby S, Ewertz M, McGale P, Bennet A, Blom-Goldman U, Brønnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med. 2013;368(11):987–98.
- Vicini F, Sharpe M, Kestin L, Martinez A. Optimizing breast cancer treatment efficacy with intensitymodulated radiotherapy. Int J Radiat Oncol Biol Phys. 2002;54:1336–44.
- Kestin L, Sharpe MB, Frazier R, Vicini F, et al. Intensity modulation to improve dose uniformity with tangential breast radiotherapy: initial clinical experience. Int J Radiat Oncol Biol Phys. 2000;48(5):1559–68.
- Ha B, Suh HS, Lee J, Lee KJ, Lee R, Moon BI. Longterm results of forward intensity-modulated radiation therapy for patients with early-stage breast cancer. Radiat Oncol J. 2013 Dec;31(4):191-8. DOI: 10.3857/roj.2013.31.4.191.
- Mukesh B, Barnett GC, Wilkinson JS, Moody AM, Wilson C, et al. Randomized controlled trial of intensity-modulated radiotherapy for early breast cancer. 5-year results confirm superior overall cosmesis. J Clin Oncol. 2013;31(36):4488–95.
- Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomized trials. Lancet. 2011;378(9804):1707–16.
- Hooning MJ, Botma A, Aleman BM, Baaijens MH, Bartelink H, et al. Long-term risk of cardiovascular disease in 10-year survivors of breast cancer. J Natl Cancer Inst. 2007;99(5): 365–75.
- 24. Henson KE, McGale P, Taylor C, Darby SC. Radiation-related mortality from heart disease and lung cancer more than 20 years after radiotherapy for breast cancer. Br J Cancer. 2013;108(1):179–82.
- Morgan EA, Kozono DE, Wang Q, Mery CM, Butrynski JE, et al. Cutaneous radiation-associated angiosarcoma of the breast: poor prognosis in a rare secondary malignancy. Ann Surg Oncol. 2012;19(12):3801–8.
- Paszat LF, Mackillop WJ, Groome PA, Schulze K, Holowaty E. Mortality from myocardial infarction following post lumpectomy radiotherapy for breast cancer: a population-based study in Ontario, Canada. Int J Radiat Oncol Biol Phys. 1999;43(4):755–62.
- Clarke M, Collins R, Darby S, Davies C, Elphinstone P, et al. 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 randomized trials. Lancet. 2005;366(9503):2087–106.

- Finazzi T, Nguyen VT, Zimmermann F., et al. Impact of patient and treatment characteristics on heart and lung dose in adjuvant radiotherapy for left-sided breast cancer. Radiat Oncol.2019; 14- 153. DOI:10.1186/s13014-019-1364-3.
- Taylor C, Correa C, Duane FK, et al. Estimating the Risks of Breast Cancer Radiotherapy: Evidence From Modern Radiation Doses to the Lungs and Heart and From Previous Randomized Trials. J Clin Oncol. 2017;35(15):1641–9. DOI:10.1200/JCO.2016.72.0722.
- Boero IJ, Paravati AJ, Triplett DP, Hwang L, Matsuno RK, Gillespie EF,et al. Modern Radiation Therapy and Cardiac Outcomes in Breast Cancer. Int J Radiat Oncol Biol Phys. 2016 Mar 15;94(4):700-8.
- Poortmans PM, Collette S, Kirkove C, Van Limbergen E, Budach V, Struikmans H, et al. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):317-27. DOI: 10.1056/NEJMoa1415369.
- Whelan TJ, Olivotto IA, Parulekar WR, Ackerman I, Chua BH, Nabid A, Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015 Jul 23;373(4):307-16. DOI: 10.1056/NEJMoa1415340.
- 33. Ayata HB, Güden M, Ceylan C, Kücük N, Engin K. Comparison of dose distributions and organs at risk (OAR) doses in conventional tangential technique (CTT) and IMRT plans with different numbers of beam in left-sided breast cancer. Rep Pract Oncol Radiother. 2011;16(3):95-102.
- 34. Nielsen M, Berg M, Pedersen A, Andersen K, Glavicic V, et al. Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer. National guidelines and contouring atlas by the Danish breast Cancer cooperative group. Acta Oncol (Stockholm, Sweden). 2013; 52(4):703–10.
- Radiation therapy oncology group (2009) Breast cancer atlas for radiation therapy planning: consensus definitions. http://www.rtog.org/CoreLab/ ontouringAtlases/BreastCancerAtlas.aspx.
- Offersen BV, Boersma LJ, Kirkove C, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. Radiother Oncol. 2015;114:3–10. DOI:org/10.1016/j. radonc.2014.11.030.
- García-Vicente F, Béjar MJ, Pérez L, Torres JJ. Clinical impact of the detector size effect in 3D-CRT. Radiother Oncol. 2005 Mar;74(3):315-22. DOI: 10.1016/j.radonc.2004.10.012.
- Marks L, Bentzen S, Deasy J, Kong F. Radiation dose volume effects in the lung. Int J Radiat Oncol Biol Phys. 2010;76:70–6. DOI:org/10.1016/j. ijrobp.2009.06.091.Radiation.
- Kwa SLS, Lebesque JV, Theuws JC, Marks LB. Radiation pneumonitis as a function of mean lung dose: an analysis of pooled data of 540 patients. Int J Radiat Oncol Biol Phys. 1998;42:1–9.
- Livi L, Meattini I, Marrazzo L, Simontacchi G, Pallotta S, Saieva C, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. Eur J Cancer. 2015 Mar;51(4):451-463. DOI: 10.1016/j.ejca.2014.12.013.
- 41. Meattini I, Saieva C, Marrazzo L, Di Brina L, Pallotta S, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy technique compared

to whole breast irradiation for patients aged 70 years or older: subgroup analysis from a randomized phase 3 trial. Breast Cancer Res Treat. 2015;153:539–547.

- 42. Pignol JP, Olivotto I, Rakovitch E, Gardner S, Sixel K et al. A multicenter randomized trial of breast intensitymodulated radiation therapy to reduce acute radiation dermatitis. J Clin Oncol. 2008;26:2085–2092.
- 43. Pignol JP, Truong P, Rakovitch E, Sattler MG, Whelan TJ. Ten years results of the Canadian breast intensity modulated radiation therapy (IMRT) randomized controlled trial. Radiother Oncol. 2016;121:414–419.
- 44. Mukesh MB, Qian W, Wilkinson JS, Dorling L, Barnett GC et al. Patient reported outcome measures (PROMs) following forward planned field-in field IMRT: results from the Cambridge Breast IMRT trial. Radiother Oncol. 2014;111:270–275.
- Livi L, Meattini I, Marrazzo L, Simontacchi G, Pallotta S et al. Accelerated partial breast irradiation using intensity- modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. Eur J Cancer. 2015;51:451–463.
- 46. Meattini I, Saieva C, Marrazzo L, Di Brina L, Pallotta S et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy technique compared to whole breast irradiation for patients aged 70 years or older: subgroup analysis from a randomized phase 3 trial. Breast Cancer Res Treat. 2015;153:539–547.
- Sardaro A, Petruzzelli MF, D'Errico MP, Grimaldi L, Pili G et al.Radiation-induced cardiac damage in early left breast cancer patients. Risk factors, biological mechanisms, radiobiology, and dosimetric constraints. Radiother Oncol. 2012;103(2):133–42.
- Darby S, Ewertz M, McGale P, Bennet A, Blom-Goldman U et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med. 2013;368(11):987–98.
- Mege A, Zioueche A, Pourel N, Chauvet B. Radiationrelated heart toxicity. Cancer Radiother. 2011;15 (6– 7):495–503.
- Laxmi S , Karol E , Ana B , Theresa M , Vera B , et al. Cardiovascular disease and breast Cancer: where these entities intersect. A Scientific Statement from the American Heart Association. Circulation. 2018;137:e30–66.
- 51. Dumane VA, Saksornchai K, Zhou Y, Hong L, Powell S. Reduction in low-dose to normal tissue with the addition of deep inspiration breath hold (DIBH) to tangential volumetric modulated arc therapy (TVMAT) in breast cancer patients with implant reconstruction receiving regional nodal irradiation. Radiat Oncol. 2018;13(1):187.
- 52. Dorr W, Herrmann T. Second primary tumors after radiotherapy for malignancies. Treatment-related parameters. Strahlenther Onkol. 2002;178(7):357–62.