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Intensity-Modulated Radiation Therapy (IMRT) Versus Rapidarc in the Treatment of Carcinoma Left Breast – Finding the Optimal Radiation Therapy Technique

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Introduction: This study aimed to evaluate the dosimetric variations and treatment efficacy between intensity-modulated radiotherapy (IMRT) and double-arc RapidArc for irradiation of carcinoma left breast, focusing on adequate target coverage, sparing of organs at risk (OARs), delivered monitor units (MUs) per fraction, and treatment delivery time.

Material and Methods: This prospective, observational study was conducted on 30 patients with carcinoma left breast. All these patients were treated with adjuvant radiation therapy. We generated two plans for each of these patients: IMRT and double-arc RapidArc technique. The target volume and OARs were analyzed using dose-volume histograms (DVHs). The average MUs and the treatment time were used as markers to assess the efficacy of treatment delivery.

Results: The planning target volume parameters such as homogeneity and conformity index were similar for all the plans with both techniques. With IMRT, statistically significantly better sparing of I/L lung, heart, C/L breast, C/L lung, and esophagus were achieved as compared to RapidArc. We found that RapidArc resulted in significantly lower MUs (535.05 ± 105.42) than IMRT (913.57 ± 129.35). Treatment delivery time was statistically shorter with RapidArc as compared to IMRT (p=0.001).

Conclusion: This study concluded that both IMRT and RapidArc plans have similar target coverage in terms of homogeneity and conformality indexes. Better OARs sparing was noticed with IMRT while RapidArc enabled higher efficacy with lower MUs and shorter treatment delivery time. However, further studies are needed to establish these dosimetric advantages being translated to improvements in the clinical outcomes of these patients.

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Introduction

Globally, breast cancer is the most common malignancy among women. It is an area of interest for the medical fraternity around the world as a consequence of its increasing incidence [1]. The incidence of breast cancer worldwide has been estimated to be 2.3 million new cases, constituting 11.7% of all cancer cases [2]. As per the Globocan 2020 data in India, breast cancer is responsible for 13.5% of all cancer cases and 10.6% of all deaths [3]. Radiation therapy (RT) plays an essential role in the multidisciplinary management of breast cancer. The effectiveness of RT following breast-conserving surgery for breast cancer has been demonstrated by The Early Breast Cancer Trialists' Collaborative Group. The results revealed that the addition of radiation reduces the 10-year locoregional recurrence from 25% to 8% as well as an absolute reduction in all-cause mortality of 3.8% - 5.4% at 15 years [4]. A large meta-analysis on patients with four or more positive nodes who have been treated with mastectomy and adjuvant RT observed a reduction in locoregional recurrence by 19% and a reduction in breast cancer mortality by 9% [5]. Long-term survival for these women has emphasized addressing the late side effects of the treatments. It has been seen that the intensity of radiation-induced side effects is a function of the tissue irradiated. The late toxicities as sequelae of breast RT are progressively being recognized among patients with left-sided disease [6], making it a challenging scenario.

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Intensity-modulated radiation therapy (IMRT) is a standard radiation technique that has the potential to deliver highly conformal dose distribution to the target while reducing the dose to the OARs [7]. Nonetheless, IMRT has its disadvantages in terms of a longer and more laborious treatment planning process and treatment time. In the last few years, there has been a surge in more sophisticated radiation technologies. RapidArc is an advanced rotational RT technique to deliver radiation using a continuous gantry motion with varying dose rate, speed and dynamically moving multi-leaf collimators [8]. The majority of the studies have shown the shortening of the treatment time and a reduction in the number of MUs as the unique finding of the RapidArc technique in left-sided breast cancer patients. Furthermore, RapidArc achieves better dose coverage for the target volume with improved or almost similar target conformality to IMRT. However, the literature is quite variable in the dosimetric results [8-10]. Majumdar et al [9]. Published the results of three different plans, 3-DCRT, IMRT, and RapidArc for left-sided breast cancer patients. The authors concluded that RapidArc was superior to IMRT in terms of target volume coverage and high-dose volumes in OARs but failed to show similar results in low-dose volumes. However, RapidArc is not a sure-shot solution for all cases. In clinical practice, each case needs to be evaluated individually and the most appropriate radiation technique should be chosen. Keeping this in mind, the present study was conducted to evaluate the dosimetric variations and treatment efficacy between IMRT plans and RapidArc plans for irradiation of carcinoma left breast, focusing on adequate target coverage, sparing of OARs, delivered MUs per fraction and treatment delivery time.

Materials and Methods

Patient characteristics

This study was conducted on thirty histopathologically proven carcinoma left breast patients who were undergoing RT or had recently completed radiation treatment. This study was approved by the Institutional Review Committee. These patients' clinical details and radiation treatment plans were retrieved and re-planned with both IMRT and RapidArc techniques. All these patients have undergone surgery either in the form of mastectomy or breast-conserving surgery and were planned for adjuvant RT. All these patients had received RT to the axillary and supraclavicular lymph nodes as well. The RT prescription dose to the planning target volume (PTV) was 50.4 Gy, delivered in 28 fractions. Patients with a previous history of malignancy or metastatic disease were excluded from this study.

Position and Simulation

All patients were immobilized using a vacuum bag in the supine position with both arms raised above the head. A thermoplastic cast was used to immobilize and reproduce the same position daily. A bolus of thickness 1-1.5 cm was often used in post-mastectomy cases. All patients underwent planning computed tomography (CT) imaging (Philips Brillance 64) at a slice thickness of 3 mm from above the cricoid cartilage to the xiphisternum. These images were transferred from the CT scan to the treatment planning system (TPS, Eclipse version 13.5).

Target volume delineation

The target volume and surrounding critical organs were outlined by the consultant radiation oncologist on the axial slices of the planning CT scan. The clinical target volume (CTV) was contoured as per the Radiation Therapy Oncology Group (RTOG) breast cancer atlas guidelines (RTOG) for the intact breast and chest wall [11].

Anatomical borders for breast contouring: Gross tumor volume of the lumpectomy cavity included seroma and surgical clips, if present. The CTV of the breast was defined as the complete CT apparent glandular breast tissue. The cranial border was taken at the insertion of the second rib, the caudal border was the disappearance of CT-apparent breast tissue, the anterior border was the skin, the posterior border was the pectoralis muscles, the medial border by the junction of the sternum and rib, and the lateral border was the mid-axillary line excluding latissimus dorsi muscle.

Anatomical borders for chest wall contouring: The cranial border was defined as the inferior border of the clavicular head, the caudal border being the disappearance of the CT-apparent contralateral (C/L) breast, the anterior border was the skin of the chest wall, the posterior border included pectoral muscles, chest wall muscles, and ribs, the lateral border at the mid-axillary line excluding latissimus dorsi muscle, and medial border as defined by the junction of sternum and rib. The medial end of the mastectomy scar was included in all cases. Regional nodal CTV was contoured to target the axillary and supraclavicular lymph node regions.

OARs delineation

The structures identified as OARs were the ipsilateral lung (I/L lung), opposite breast (C/L breast) and opposite lung (C/L lung), heart, and esophagus. These structures were contoured on the CT image of each slice. The entire lung was contoured in the lung window except for the hilar region, trachea, and the main bronchus by the auto segmentation tool and manually edited by the physician as needed. The heart was contoured beginning from the level of the inferior aspect of the pulmonary artery up to the apex of the heart [12].

Planning Techniques

For both IMRT and RapidArc planning, we have used Eclipse computerized 3D Treatment Planning System (TPS) version 13.5 was used for all the IMRT and RapidArc planning. The dose was prescribed to the isocenter. The IMRT plans were generated using 7-10, non-coplanar fields of 6 MV photons using a dynamic or sliding window technique. The RapidArc plans were generated using two complementary coplanar arcs of 360^0 of 6 MV energy photons, sharing the same isocenter.

Plan optimization

To achieve the aim of RT, that is, delivering highly conformal target coverage with normal tissue sparing, plans were optimized to achieve:

For CTV, the aim was to achieve the prescribed dose which meant not to exceed the maximal dose of 110% and 100% of the prescribed dose should be covering 95% of the CTV volume.

The dose constraints of the OARs were as follows: I/L lung – V20 ≤ 30%, mean heart dose < 26 Gy and V25<10%, mean esophagus dose < 34 Gy and V35 <50% as per the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) guidelines [13].

Plan Evaluation Parameters used

All the patients were planned by the same medical physicist in an attempt to minimize the effect of inter-operator variability on the planning process. The following parameters were employed for plan evaluation:

CTV coverage

The representative dose distribution and DVHs were generated to evaluate the dose to the CTV for IMRT and RapidArc treatment plans according to the ICRU 83 [14]. The CTV coverage was analysed as per the following parameters:

a) $D_{2\%}$ and $D_{98\%}$ parameters were used as representative markers for maximum and minimum doses. The mean dose (D_{mean}) was also reported.

b) Cold spot ($V_{95\%}$) and Hot spot ($V_{107\%}$) in the CTV were documented.

c) The homogeneity index (HI) was calculated as a measure of dose coverage to the target. HI = $(D_{2\%} - D_{98\%}) \times 100 / D_p$, where $D_{2\%}$ is the dose to the 2% of the PTV and $D_{98\%}$ is the dose to the 98% of the PTV; D_p is the prescription dose. This equation indicates that a lower HI value means a more homogeneous dose to the target.

d) The conformality index (CI) was calculated as a ratio of the product of the percentage of the PTV covered by the 95% isodose volume and the proportion of the 95% isodose volume covered by the PTV. It was a measure of target conformality. The CI varied from 0 to 1, where 1 was taken as the ideal value denoting the better conformity of the CTV [15].

OARs sparing

For all patients, DVHs for OARs (I/L lung, mean dose to the right lung, heart, mean dose to right breast, and esophagus) were calculated and compared. V_5, V_{10}, V_{20}, V_{25}, V_{45}, V_{50} values were reported for all OARs.

MUs and treatment delivery time

The number of MUs per fraction required for each plan was reported along with treatment delivery time.

Statistical analysis

Paired t-test was used for comparing the dosimetric differences between IMRT and RapidArc. p-value < 0.05 was considered statistically significant. All analysis was performed using SPSS version 21.0 (SPSS, IL, Chicago, USA).

Results

IMRT and RapidArc plans were done for each patient (a total of 60 plans). All treatment plans were evaluated using DVHs. Various dosimetric indices were recorded for all patients.

Planning target volume (PTV) coverage, Homogeneity index, and Conformity index

The calculated PTV varied from $347cc^3$ to $1735cc^3$. D2% and D98% of the PTV coverage were found to be similar for both IMRT and RapidArc techniques. The dose homogeneity calculated in terms of HI and CI was nearly similar in both techniques (Table 1).

Table 1. The PTV parameters, Homogeneity index, and Conformity index of both the techniques
(n=30, arithmetic mean)

Parameters	IMRT (mean±SD)	RapidArc (mean±SD)	p-value
D2% (Gy)	52.35±0.43	52.24±0.41	0.146
D98% (Gy)	49.21±0.37	49.28±0.33	0.422
HI	0.060±0.02	0.062±0.01	0.412
CI	0.997±0.01	0.999±0.01	0.124

PTV – Planning target volume; D2% - Dose received by 2% of PTV; D98% - Dose received by 98% of PTV; HI – homogeneity index; CI – conformity index

Figure 1 and 2 shows the dose distribution in an axial, sagittal, and coronal views demonstrating both techniques for the single patient.

Figure 3 shows the DVH for PTV and OARs comparing the two plans

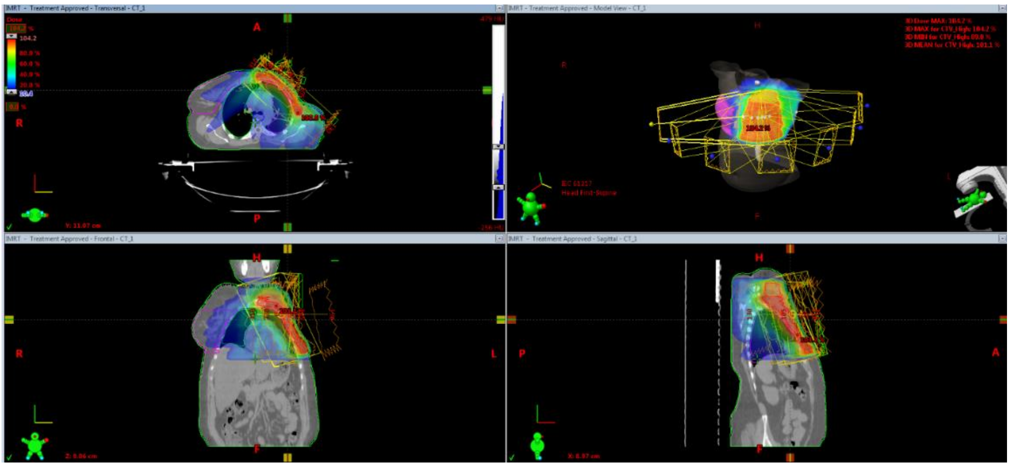

Figure 1. Shows the dose distribution in axial, sagittal, and coronal views by IMRT in a single patient

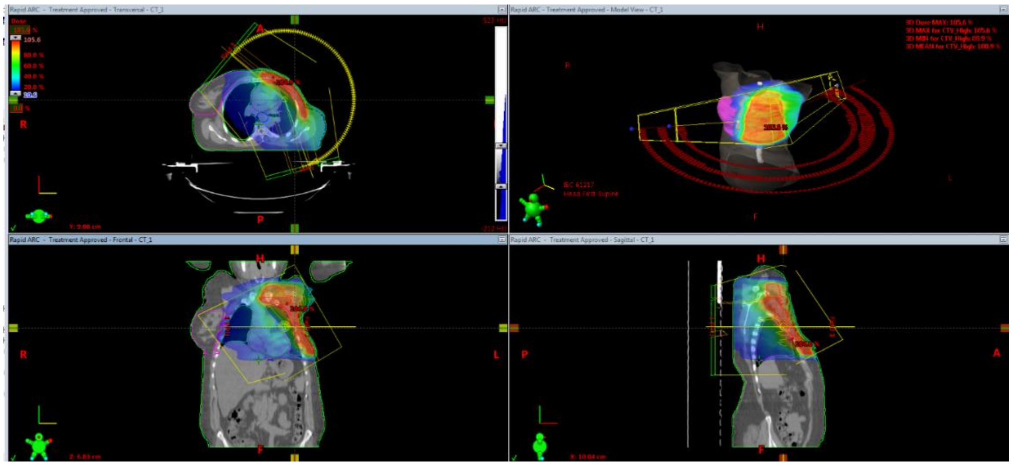

Figure 2. shows the dose distribution in axial, sagittal, and coronal views by RapidArc in a single patient

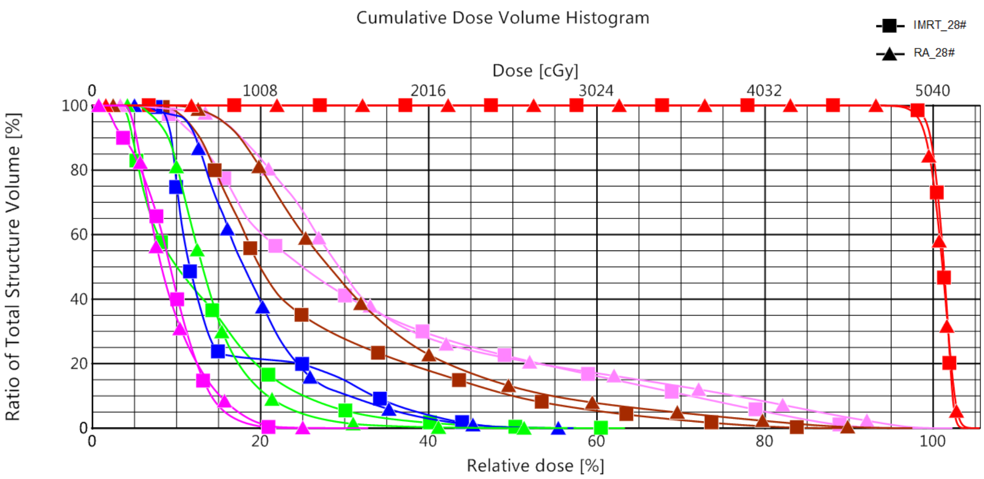

Figure 3 DVH comparison between IMRT and RapidArc. The PTVs are in red, I/L lung in magenta, C/L lung in light green, heart in brown, C/L breast in pink, and esophagus in blue

Dosimetric results for OARs

The dose to the OARs was within the tolerance limits for both plans as per recommended by RTOG (Radiation Therapy Oncology Group) guidelines. The sparing of the I/L lung was slightly better with IMRT technique in terms of V5, V10, V20, and D_{mean} when compared to the RapidArc technique. The IMRT plans gave a slightly lower mean dose to C/L lung and heart at lower doses in terms of V5, V10, and D_{mean}.

Table 2. Dosimetric comparison of OARs with IMRT technique versus RapidArc technique

Organs at risk (OARs)	Parameters	Techniques		p-value
		IMRT (mean±SD)	RapidArc (mean±SD)	
I/L Lung	V_{5Gy} (%)	95.85 ±3.94	99.24 ±1.54	0.000
	V_{10Gy} (%)	66.25 ±7.87	76.92 ±10.40	0.000
	V_{20Gy} (%)	30.09 ±1.57	32.08 ±2.90	0.002
	D_{mean}	17.24 ±0.90	18.58 ±1.90	0.000
C/L Lung	D_{mean}	5.97 ±0.64	6.86 ±0.78	0.000
Heart	V_{5Gy} (%)	92.84 ±8.27	98.32 ±3.53	0.001
	V_{10Gy} (%)	59.32 ±13.89	67.71 ±14.89	0.028
	V_{20Gy} (%)	19.44 ±3.89	21.12 ±4.67	0.135
	V_{25Gy} (%)	10.46 ±2.23	11.82 ±2.64	0.036
	D_{mean}	13.10 ±1.35	15.25 ±1.31	0.000
C/L Breast	D_{mean}	3.95 ±1.04	5.00 ±1.10	0.000
Esophagus	V_{10Gy} (%)	35.21 ±13.38	45.10 ±16.73	0.014

Contrary to this, at higher doses (V20, V25) the difference between the two techniques was not significant. No statistically significant difference was seen between the plans with respect to C/L breast and esophagus (Table 2).

Total MU and Delivery time

The average MUs required to deliver a dose of 200 cGy per fraction was 913.57±SD MU for the IMRT plans as compared to 535.05±SD MU for the RapidArc plans. Delivery time was defined as the beam on time at the beginning of radiation treatment to beam turn-off time after the last field being irradiated while the patient is being treated. This treatment delivery time was greater for IMRT when compared to RapidArc (Table 3).

Table 3. Difference of MUs and delivery time between IMRT vs. RapidArc technique

	IMRT	RapidArc	p-value
MUs	913.57±129.35	535.05±105.42	0.001
Delivery time (s)	3.58±0.34	2.34±0.12	0.001

All values displayed as the mean ± standard deviation

Discussion

The present study addressed a misty issue of comparing IMRT with the RapidArc technique for left-sided breast cancer following radical mastectomy or breast-conservation surgery. Incorporating leading-edge technology in radiation oncology has resulted in precise treatment delivery for oncological patients [16]. Among these technological advancements, IMRT is a technique in which the radiation beam's intensity is modulated by dividing each beam into a number of beamlets, thereby delivering a high dose to the tumor site while minimizing the doses to surrounding OARs [17]. However, IMRT has certain drawbacks such as a time-consuming planning process, increased integral dose, and higher monitor units. To overcome these limitations, arc therapy was introduced which has the ability to deliver the radiation dose at 360^0 beam angles continuously as the machine rotates around the patient [17].

Dosimetric studies comparing IMRT and RapidArc techniques have been published for various tumor sites. Though the results of these studies are quite conflicting. Initially, there was a presumption that VMAT is equivalent to IMRT. However, the results by Badakhshi et al. were quite different in that the authors reported VMAT to be inferior to IMRT and 3D-CRT for carcinoma breast patients with regard to coverage of the target volume and OARs, particularly at the low dose level [18]. Contrary to this, a dosimetric study on 35 patients of left-sided breast cancer patients reported VMAT as a better technology in terms of the target volume and high-dose irradiation but reverse is noted in low-dose irradiation [9]. It has been highlighted that the supremacy offered by RapidArc is the use of lower MUs and shorter treatment delivery time [19,20]. In other sites such as carcinoma cervix, various studies have favoured the RapidArc technique with regard to dose distribution in PTV and OARs while clinical results were similar for both plans [17,21,22]. Conversely, Guy et al. published a comparable conformity index of VMAT to IMRT with no improvements in OARs sparing for VMAT [23].

It has been reported that IMRT utilizes a finite number of beams resulting in missing optimal beam angles. In contrast, VMAT utilizes all possible beam angles during the optimization process hence, anticipating a better plan with RapidArc than IMRT [24]. RapidArc plans have been shown to accomplish better PTV conformation than IMRT plans. In a recent study by Halder S et al. the impact of a hybrid treatment planning approach for carcinoma left breast patients were reviewed and compared to alternative treatment options. The three treatment planning techniques i.e. field-in-field, IMRT, and hybrid IMRT were evaluated. The authors recommended hybrid treatment plans as they result in superior and similar PTV dose coverage and OAR sparing compared to field-in-field and IMRT plans. Moreover, hybrid IMRT plans showed lower MUs and beam on time, as well as fewer low-dose volumes in comparison to IMRT [25]. However, our findings suggested that both the techniques, IMRT and RapidArc were similar in terms of homogeneity and conformity indexes.

In the treatment of breast cancer with RT, the underlying lung tissue inevitably receives higher doses from the radiation fields resulting in radiation pneumonitis [26]. An association between intermediate-dose volume parameters V20, V30, and mean lung dose has been identified to correlate with grade 2 or higher acute radiation pneumonitis [27]. Our results showed that the mean lung dose, low-dose, and high-dose lung volumes, including V_{5Gy}, V_{10Gy}, V_{20Gy} of the total lung, were significantly reduced with the IMRT plan compared to the RapidArc plan. With IMRT, these dose volumes of the irradiated left lung were 95.85 ± 3.94, 66.25 ± 7.87, and 30.09 ± 1.57, respectively and 99.24 ± 1.54, 76.92 ± 10.40, and 32.08 ± 2.90, respectively for the RapidArc arm. These values are quite close to findings by Majumdar SKD et al. where the low-dose volume V_{5Gy} and V_{10Gy} of the irradiated lung were 82.14±9.27 and 58.45±6.05, respectively for IMRT while 83.96±6.99 and 45.00±6.58, respectively for the VMAT technique. Hence, the authors concluded that VMAT was inferior to IMRT when low-dose irradiation was considered [9]. This could be mainly attributed to different beam arrangements from different angles by IMRT, ultimately reducing the dose to I/L as well as C/L lung tissue.

The incidence of coronary artery disease as a result of radiation therapy has been following an increasing trend, running alongside advancements in oncologic treatment [28]. Cheng et al. have reported an absolute increase in the risk of coronary heart disease and cardiac death as a result of breast cancer treatment with RT [29]. Contemplating this high incidence of cardiac disease, it is of utmost importance to pay attention to the exposure of the heart in left-sided breast cancer irradiation. We found that IMRT was superior with regard to mean dose and low-dose values (V_{5Gy}, V_{10Gy}) to the heart as compared to VMAT. This suggests that normal tissues receive substantially higher low-volume doses with RapidArc plans.

Another challenge that long-term breast cancer survivors face following radiation to the breast is the risk of developing second cancer in the C/L breast [30]. Therefore, it is of paramount importance to reduce the scattered dose to the C/L breast. In this aspect, our observation was that IMRT was more effective in reducing the dose to the C/L breast as compared to the RapidArc plan. We could find work by Hu et al. to find the better radiation technique in terms of dose to C/L breast among other parameters well mentioned in other studies as well. The VMAT plans showed a lower maximum dose to the C/L breast compared to target-segmented planning and 9-field IMRT [31]. We report an interesting finding that the IMRT plans exhibited higher monitor units with longer treatment delivery time than RapidArc plans; possibly, due to the use of multiple beams. Keeping a shorter beam delivery time and MUs might translate to a reduction in the intrafraction motion of the patient. This could subsequently reduce the likelihood of developing secondary carcinogenesis [32]. Yet, this finding is quite variable in the literature. Sedeh et al [33]. have reported IMRT treatment delivery to be faster than RapidArc in terms of mean MUs used (382 vs 707). The limitation of the present study is the small sample size and primarily it is a dosimetric analysis with a lack of correlation of dosimetric parameters with clinical parameters.

Conclusion

Our findings enrich the existing data by favouring the IMRT technique for treating patients with carcinoma breast. The IMRT technique stood the test of time with regard to equivalent target coverage and significantly reduced doses to OARs including ipsilateral lung (I/L lung), heart, opposite breast (C/L breast), opposite lung (C/L lung), and esophagus in comparison to RapidArc technique. However, the RapidArc plans required fewer MUs which translated to shorter treatment delivery times. There is a need to conduct further studies to discover a conqueror regarding radiation techniques in the fight against breast cancer.

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