

A Hybrid IMRT Technique for Treatment of Breast Cancer: A Dosimetric Study

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1. Introduction

Breast Cancer is the most common malignant neoplasm in women and the main cause of death among women worldwide. Nearly 1.2 million women are diagnosed with breast cancer all over the world every year, and 500,000 women die of it each year [1]. Therefore, the breast cancer remains the primary cause of cancer mortality in women after lung cancer. With the development of treatment strategies, an enhanced awareness of medical examination, and the popularity of breast cancer screening, the 5-year overall survival of breast cancer patients has improved in the last 30 years [1]. The 5-year, 10-year, and 15-year overall survival is 89%, 83%, and 78%, respectively. Analyses of randomized clinical trials have proven that breast-preserving surgery achieves survival equivalent to mastectomy in patients with early-stage breast cancer [2-4]. Adjuvant whole-breast irradiation is performed on these patients as the standard of care. In Bangladesh, the rate of breast cancer occurrence is estimated to be 22.5 per 100,000 females of all ages, compared to 124.8 per 100,000 females worldwide. For Bangladeshi women aged between 15-44 years, breast cancer has the highest rate of occurrence 19.3 per 100,000, compared to any other type of cancer [5]. Breast cancer can be treated using a multimodality approach of surgery, chemotherapy, radiotherapy and targeted therapy. The treatment options vary as per the stage and grading of the tumor. The most adopted treatment method for breast cancer patients is breast conservation surgery (BCS), or mastectomy followed by adjuvant radiotherapy. Adjuvant radiotherapy improves local control and improves overall survival [6].

The adjuvant radiotherapy of the left chest wall is commonly delivered by three dimensional conformal radiotherapy

(3DCRT) with field-in-field technique which have shown that increased cardiac morbidity and mortality in patients treated with radiotherapy for left-sided breast cancer compared to right-sided, due to the higher cardiac dose for the left-sided patients [7]. Cardiotoxicity is most frequently reported as decreased myocardial function or coronary artery disease (also reported as ischemic heart disease or decreased cardiac perfusion). However, less common toxicities can include myocardial infarction, congestive heart failure, pericarditis, arrhythmias, angina, or valve dysfunction [8]. However, many studies have demonstrated increased cardiac mortality and morbidity after breast radiotherapy [9]. Although many of the studies included in this review involved old treatment techniques, which probably delivered a higher dose to the heart than seen in modern radiotherapy clinics, the issue of cardiac morbidity and mortality after breast cancer treatment is still relevant [10]. Dose-response curves for cardiac mortality derived from two randomized trials of surgery with or without radiotherapy for early breast cancer show a strong correlation with the dose delivered and a lesser dependency on the volume of the heart irradiated, assuming homogeneous radio-sensitivity within the irradiated heart volume [11]. The avoidance of hot spots throughout the breast volume is difficult with external whole breast radiotherapy using conventional forward wedge planning [12]. For this reason, intensity-modulated radiotherapy (IMRT) is gradually replacing wedge planning [13].

The development IMRT provides excellent dose homogeneity throughout the breast volume that is impossible for 3D conformal radiotherapy. IMRT reduces the volume of OAR such as the heart and lung receiving high dose of radiation while improving the conformity and homogeneity of the tumor doses [14]. The

main disadvantage of IMRT is that the IMRT plans might be more susceptible to setup and motion uncertainties in breast cancer [15-19]. The possible solution to reduce the effects of geometrical uncertainties would be the use of a hybrid technique that incorporates a combination of glancing open fields and inverse-planned IMRT beams. The development of novel hybrid techniques that reduce normal tissue injury without compromising the radiation doses to the tumor in a short delivery time is now the subject of much interest in radiation therapy research. The Hybrid IMRT has the potential of lowering the radiation doses to the OAR while improving the conformity and homogeneity to the tumor with fewer monitor units (MUs) and a short delivery time compared with IMRT [20-27]. Mayo et al. found that the 4-field hybrid IMRT plan (combining 2 open tangents with tangential IMRT beams), with a quality comparable to that of forward-planned IMRT (FP-IMRT), could be achieved in substantially less planning time. Moreover, improvements in the uniformity of dose to the target volume and conformity may be achieved by adding 2 anterior oblique IMRT beams to the 4-field hybrid technique (6-field hybrid IMRT). They propounded that the 2-field tangent-only IMRT plans were more effective in reducing the high-dose exposure to lungs and heart [28]. Consequently, this study can be proposed to a new hybrid treatment technique that encompasses 2-non-modulated tangential fields as well as 2-IMRT. A dosimetric evaluation was done with regard to target coverage as well as organ-at-risks (OAR) doses. This study was performed in dosimetric evaluations to assess the extent of dose reduction to the heart, contralateral lung, ipsilateral lung and contralateral breast. The study was also expressed to significantly reduce hot spot regions within the breast tissue and less skin reaction.

2. Materials and Method

2.1 Patient Selection

More than eight patients with left breast carcinoma who underwent whole breast irradiation were selected for Hybrid-IMRT in the hospital between January 2018 and April 2018. Patients between 34

and 46 years old, with adequate function of the liver, kidney, heart, and hematopoietic system were considered eligible for the study. Patients with positive axillary or supraclavicular lymph nodes and distant metastasis was excluded from the study. All patients were immobilized in the supine position with the arm abducted (90° or greater) on the disease side. A computed tomography (CT) scan with 5 mm slice thickness was acquired for each patient, with coverage from the mandible to 4–6 cm below the inframammary fold to cover the entire lung volume. Imaging data were then transferred to the Eclipse treatment planning system (Eclipse 13.7) for delineation of targets and critical structures.

2.2 Delineation of Target Volumes and Organs at Risk

All patients were immobilized in the supine position on a AIO cover image breast board which increased patient comfort, and arm rests to allow for a comfortable but reproducible positioning of the arms above the head and out of the treatment fields. A CT scan with a slice thickness of 5 mm was acquired from each patient with coverage from the mandible to 4 to 6 cm below the inframammary fold to cover the entire lung volume. After CT scan, Digital Imaging and Communication in Medicine (DICOM) images were transferred to Eclipse treatment planning system (V13.7). The breast targets with other volume was delineated by the radiation oncologist with the following considerations. The CTV for the tumor bed was defined as the lumpectomy cavity (seroma) found on the CT scan image or the fibrous tissue under the surgical scar if no seroma could be found on the CT scan image. The normal tissue and OAR including healthy tissue, the lungs, the heart, the spinal cord, and the contralateral breast were contoured for dose calculation. The target delineation was performed based Radiation Therapy Oncology Group (RTOG) guidelines (Figure.2.1 and 2.2) The CTV whole breast was never closer than 5 mm to the skin. The body was delineated on the CT scans and Boolean operations were used to construct a modified body volume that operations were used to construct a modified volume that excluded breast CTV.

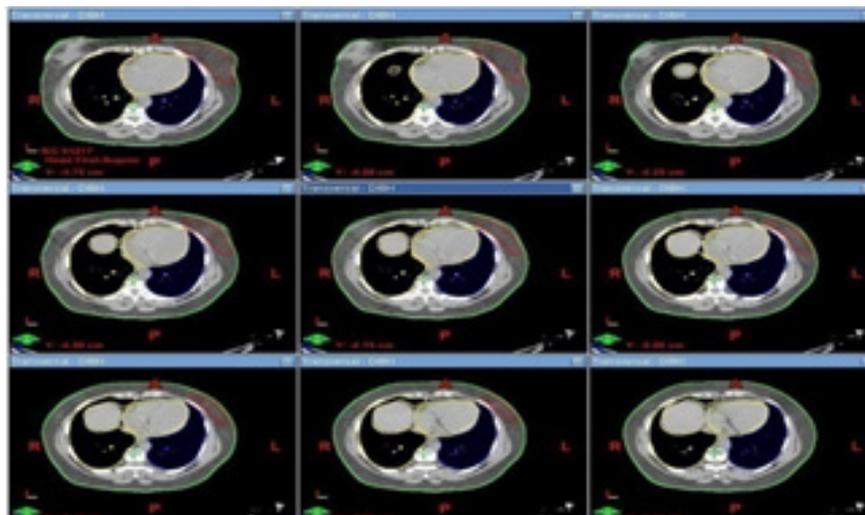


Figure 2.1: Illustration of Post Lumpectomy Target Delineation

2.3. Hybrid IMRT Approaches

The hybrid technique is a novel technique of radiotherapy in which typically combines 3DCRT fields (80% of the dose) and IMRT or VMAT fields (20% of the dose). In hybrid IMRT, isocenter is placed longitudinally in the middle of the breast field, on the chest wall or in lung. Potential advantages of this type of treatments

include a reduction in the volume of lung exposed to low doses. Hybrid-IMRT reduces treatment planning time, compared to full IMRT techniques, and minimizes the set of optimization constraints. Hybrid-IMRT significantly reduces hot spot regions within the breast tissue.

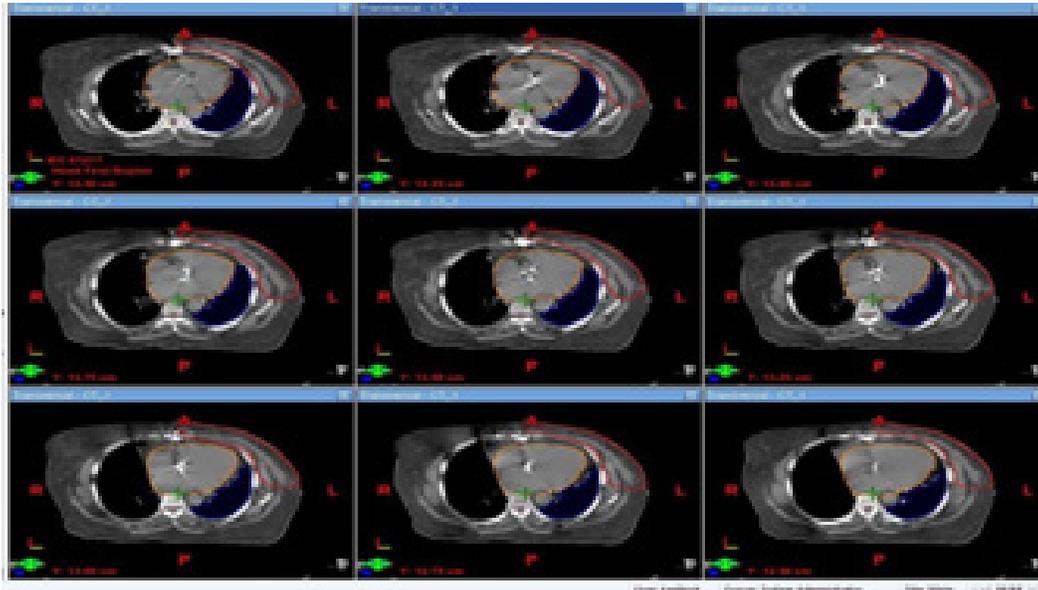


Figure 2.2: Illustration of Target, Left Lung and heart delineation

2.4 Prescribed dose and Fractionation

Standard WBRT consists of 45–50 Gy in 25–28 fractions of 1.8–2 Gy. Long-term data from multiple large randomized trials also demonstrate the non-inferiority of hypo-fractionated WBRT (HF-WBRT) consisting of 40.05–42.56 Gy in 15–16 fractions of 2.66–2.67 Gy for early stage breast cancer with equal or lesser acute and long-term toxicity. The prescription dose to the whole breast was 40.05 Gy in 15 fractions of 2.67 Gy in this study according to the RTOG-1005. The Boost dose of 10 Gy at 2 Gy per fraction was delivered to the tumor bed after delivery of 40.05 Gy using 6 MV Photon beams to the entire breast. Boosting to a total tumor bed dose greater than 50.05 Gy should be considered in patients with positive margins.

2.5 Hybrid-IMRT Treatment Planning Techniques

For each patient, CT scans were contoured by radiation oncologist and were carried out by medical physicist to ensure plan uniformity. Hybrid IMRT plan was executed, and the afflicted breast was exposed to 40.5 Gy in 15 fractions of 2.67 Gy to cover the PTV. All the treatment plans were generated using an Eclipse treatment planning system(V13.7). The treatment plans were planned to deliver with 6-MV photon beams on a 2300 C/D linear accelerator

that is mounted with a 120-leaf of Millennium multi-leaf collimator (MLC) (maximum leaf speed of 2.5 cm/s). While executing the plan on each patient, the same isocenter and tangential beams were applied. The hybrid technique consisted of a two-step process in which one step is 3DCRT and second step is IMRT. In the first planning step (3DCRT), two opposing 6 or 10 MV tangential fields [Figure.2.3] at one isocenter were added conforming the CTV whole breast. A margin of 3cm anteriorly was added. This ensures entire breast coverage in spite of breathing. The beam angles and beam weighting (usually minimal) were chosen to optimize coverage of the CTV whole breast, while minimizing exposure to the ipsilateral lung, heart and contralateral breast. Gantry angles ranged from 310° to 350° for the medial fields and from 110° to 125° for the lateral fields for patients treated on the left side. The fields extended 2 cm anteriorly of the chest to provide coverage of the “flash” region. All other plans were normalized to achieve isodose coverage of the breast tissue at least as good as the tangent plan. A portion of the total breast dose in 3DCRT, that is, 80%, was calculated to a reference point as per ICRU 50 and 62 guidelines, and weightings were used to provide an even distribution of dose across the whole breast.

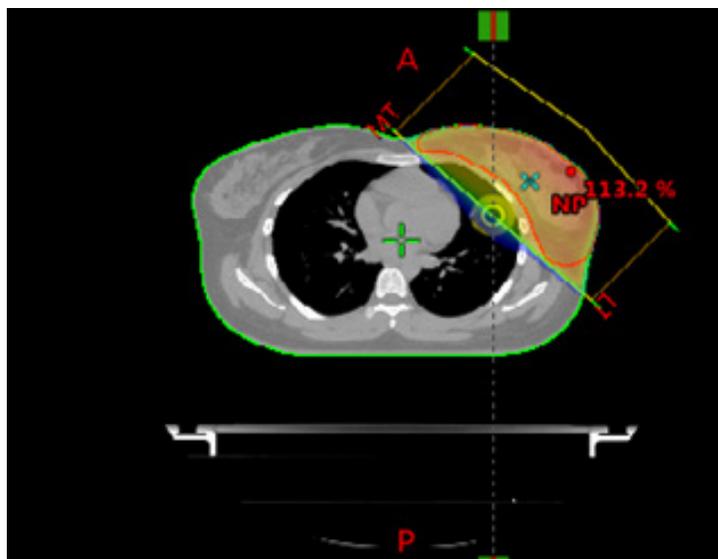


Figure 2.3: Illustration of 3DCRT of Hybrid IMRT

As the second step, two IMRT fields [Figure. 2.4] were added at the same isocenter; two tangential fields at the same gantry angle as the original two tangents and two fields angled to best access the boost cavity. The two non-tangential fields were dedicated to treat reflecting a conventional tangent plan. A portion of the total breast dose in IMRT, that is, 20%, was calculated to a reference point as per ICRU 83 guidelines, and weightings were used to provide an even distribution of dose across the whole breast. No additional fields or beam modifiers were used in this plan. A second IMRT plan was created at the same isocentre as the conventional plan and comprised of two fields; two tangential fields at the same gantry angle as the original two tangents and two fields angled to

best access the boost cavity. The two non-tangential fields were dedicated to treat the boost cavity by locking the jaws around the whole CTV-boost during the optimization process. The IMRT plan was optimized using a standard optimization template employing sliding window dynamic IMRT with Eclipse optimization software to achieve dose constraints and utilize avoidance volumes to reduce undesirable excess dose. A basic level of planning experience was simulated by limiting optimization calculations and use of avoidance structures to two. The plan was dosed with the remaining, that is, 20%, of the total breast dose and 10 Gy additionally for the boost cavity.

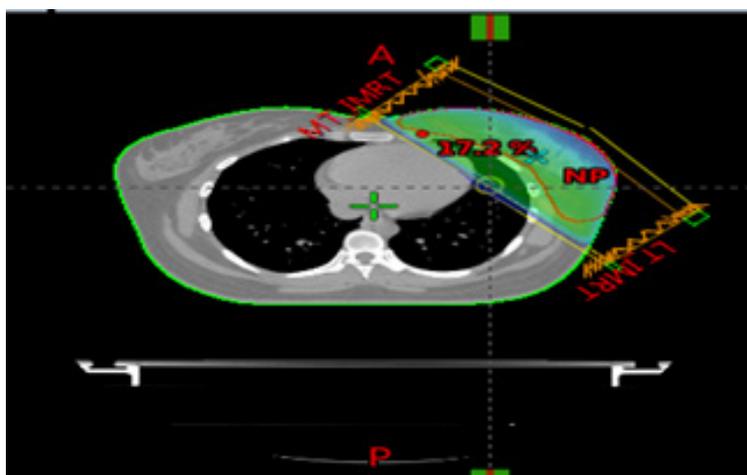


Figure.2.4: Illustration of IMRT of Hybrid IMRT

For the hybrid-IMRT treatment plan, 2 tangential IMRT fields and 3DCRT fields were integrated to a single treatment plan [Figure. 2.5]. The standard medial and lateral 3D-CRT beams with control points were created by adding a 2.5 cm expansion margin on the surface of the chest wall skin, and a 0.5 cm margin was added in

the other directions. Two IMRT beams had the same gantry angles as that of the tangential beams. The beam angles and field weights were chosen to optimize coverage of the CTV, while minimizing exposure to the left lung, heart and right breast. This study has followed QUANTEC and RTOG protocols.

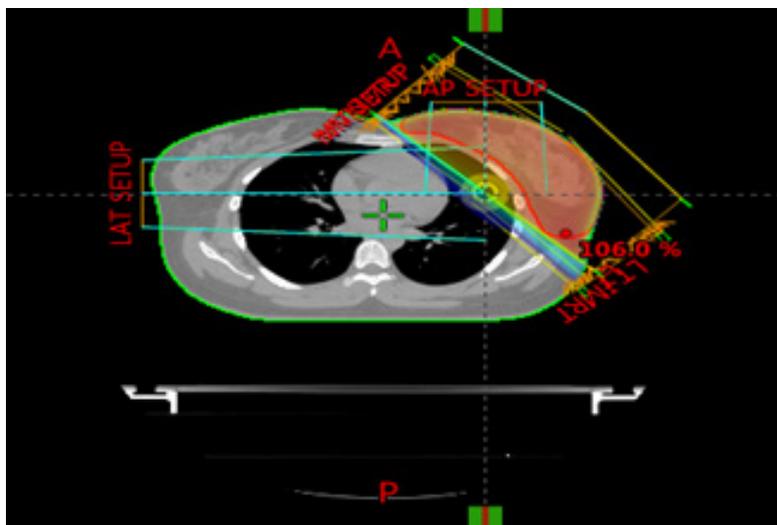


Figure.2.5: Illustration of Hybrid IMRT

3. Results and Discussion

3.1. Dose Analysis of Target Volume

Dose distribution color washes from the treatment modality of hybrid-IMRT for two representative patients in this paper. The patients were chosen for their dosimetric parameters most closely matched the mean value of the eight patient's data set. Figure 3.1 and 3.2 shows axial and frontal dose distributions with hybrid-

IMRT using by colour wash. Hybrid-IMRT achieved 95% coverage of the CTV_ whole breast. We found that hybrid-IMRT deliver fewer doses to the OAR and improve better dose coverage across the whole breast for all patients in this study. The mean volumes, averaged from the 8 patients, for CTV_ whole breast, heart, left lung and right lung were 1140 ± 104 , 526.4 ± 132 , 1050 ± 210 , and 1205 ± 205.7 (cm³), respectively.

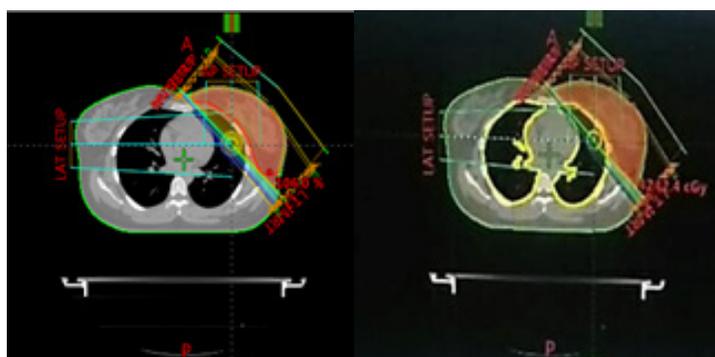


Figure. 3.1: Dose-color wash distributions for H-IMRT of two treatment plans

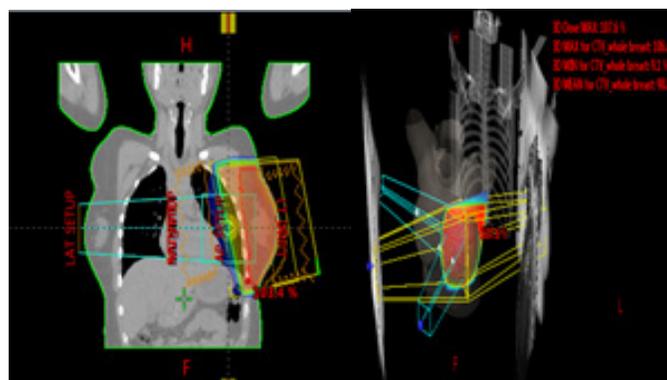


Figure. 3.2: Dose-color wash for H-IMRT of frontal view

3.2 Dose Analysis in OAR (Heart)

As shown in table 3.1 CT-simulation scans demonstrated significantly irradiated heart volume for hybrid-IMRT. Hybrid-IMRT also resulted in a significant reduction in the heart V5, V20 and V30 and mean heart dose. The mean dose to the entire heart

was smaller for the hybrid-IMRT plans according to protocol RTOG. Table 3.1 also shows that; heart V5 is 3.55% which value is significantly lower in the hybrid-IMRT plans compared to protocol RTOG.

Structure	Parameter	H-IMRT	Acceptable value	Ideal value
Heart mean dose	D mean(Gy)	(1.64 ± 0.55)	≤ 5Gy	≤ 4Gy
Volume Heart Volumetric Constraint (Left)	V5(%)	3.55 ± 2.65	V5 ≤ 35%;	V5 ≤ 30%;
	V20(%)	2.5 ± 0.55	V20Gy ≤ 30%;	V20 ≤ 25%;
	V30(%)	1.05 ± 0.65	V25Gy ≤ 5%;	V30Gy ≤ 5%;

Table.3.1: Dose characteristics of the Heart of H-IMRT including the mean dose for left-sided patients.

3.3 Dose Analysis in OAR (L-Lung and R-Lung)

The D-mean and V Gy (the volume of the organ receiving at least a given dose (Gy)), for the left and right lungs, spinal cord and esophagus in the hybrid-IMRT are shown in Table 3.2 The hybrid-IMRT plans produced the best results with low dose area to OAR

and better parameters of the contralateral lung and ipsilateral lung. The hybrid-IMRT plans contributed less percentage of ipsilateral lung receiving a radiation dose more than 20Gy (V20Gy) compared to protocol.

Structure	Parameter	H-IMR mean	Acceptable value	Ideal value
Ipsilateral Lung	D-mean (Gy)	7.5 ± 2.24	13	7
	V5Gy (%)	28% ± 4.5%	V5Gy ≤ 70%	V5Gy ≤ 65%
	V10Gy (%)	20.24% ± 5.6%	V10Gy ≤ 60%	V10Gy ≤ 50%
	V20Gy (%)	14.77% ± 6.9%	V20Gy ≤ 35%	V20Gy ≤ 30%
	V30 Gy (%)	11.98% ± 2.8%	V30Gy ≤ 66%	V30Gy ≤ 60%
Contralateral Lung	D-mean (Gy)	0.097		
	V5(%)	0.0%±0.0%	V5Gy ≤ 15%	V5Gy ≤ 10%

Table 3.2: Characteristics of dose directed to lung, Contralateral lung in hybrid-IMRT for left-sided patients.

3.4 Dose Analysis in OAR (R-Breast, Esophagus)

Table 3.3 presents the irradiation doses and volumes in the contralateral breast, esophagus and spinal cord of H-IMRT plans.

The hybrid-IMRT plans produced the best results with low dose area to OAR and better parameters of the contralateral breast and esophagus and spinal cord.

Structure	Parameter	H-IMR mean	Acceptable value	Ideal value
Contralateral Breast	D-mean (Gy)	0.5 ± 0.3		
	V5(%)	0.1% ± 0.2%	V4.1Gy ≤ 5%	V3Gy ≤ 5%
Esophagus	D-mean(Gy)	0.447±0.1		
Spinal cord	D-mean(Gy)	0.182 ±0.0		

Table.3.3 Dose characteristics of the right breast, esophagus and spinal cord of hybrid-IMRT including the mean dose for left-sided patients.

4. Discussion

The treatment of whole breast radiation therapy reduces risk of local recurrence and improves overall survival, but the problem of radiotherapy is the side effects on the heart, lung and contralateral breast. In this regard in our study was carried out to evaluate the

difference in dose distribution of hybrid IMRT of whole breast in early breast cancer patients underwent breast lumpectomy. This Study have shown that tangential beam of hybrid IMRT of the chest wall significantly reduces heart, lungs and contralateral breast in patients treated on the left side breast cancer. Regarding to heart

sparing; this current study showed that hybrid IMRT resulted in better heart sparing; mean dose of heart ($1.64 \pm 0.55\text{Gy}$), V5($3.55 \pm 2.65\%$), V20($2.5 \pm 0.55\%$), and V30($1.05 \pm 0.65\%$) were significantly lower according to protocols (RTOG-1304 and QUANTEC). In the current study 4 fields hybrid IMRT were used to optimize the plan [28]. This is in accordance with the results of Mayo et al. reported that The 6-field hybrid technique creates the most conformal dose distribution at the expense of more normal tissue receiving low dose. The results of the current study were also supported by OUYANG Shuyu et. al who compared with the Hybrid IMRT and IMRT: V13 of the ipsilateral lung decreased from 27.66% to 20.7%, V5 of the contralateral lung decreased from 8.01% to 2.25%, V10 and V20 of the heart decreased from 35.23% and 16.77% to 19.22% and 10.6% respectively, V5 and V10 of the contralateral breast decreased from 35% and 10.39% to 20.38% and 5.7% respectively, all with significant difference. V30 and V40 of the ipsilateral lung and V40 of the heart increased by 1.28%, 1.48%, and 2.48%, with significant difference. Regarding to lung sparing; in the current study hybrid IMRT resulted in better lung sparing according to protocols. This is in accordance with the results of OUYANG Shuyu et. al and Ahmad Amoush et. al the mean lung dose was significantly reduced with tangential hybrid IMRT compared to IMRT [23-24].

Ahmad Amoush et. al also reported that The advantages of the single-isocenter include elimination of isocentric errors due to couch and collimator rotations and reduction in treatment time. This study supports consideration of a single-isocenter four-field hybrid IMRT technique for patients undergoing breast and supraclavicular nodal irradiation. The similar results from this study have shown to evaluate the delivery time with H-IMRT technique. As regard to Contralateral breast dose; current study revealed significant reduction of CB mean dose with hybrid IMRT compared with protocols. This is in accordance with Mayo et al. the mean dose to the CB was significantly reduced with the tangential hybrid IMRT plans. Low irradiation dose in the healthy breast is an important cause of right breast cancer after radiotherapy. Gao et al. proved that healthy breast may suffer secondary cancer after radiotherapy of 2.9 Gy to 4.3 Gy [29]. In our study, the contralateral breast received at low dose of 0.5 ± 0.3 Gy. We proved that hybrid IMRT is also more flexible in terms of positioning repeatability. A hybrid IMRT plans not only reduce hot spots outside the target volume but also improve dose homogeneity within the target volume due to colour wash. According to literature of hybrid IMRT, it may benefit patients in good cardiopulmonary health as the hybrid technique not only improves the cosmetic outcome but also reduces the volume of healthy tissue receiving low-dose irradiation.

4. Conclusion

The objective of this study was to investigate the dosimetric characteristics of hybrid-IMRT technique to the left-side breast radiotherapy in the early stage of the breast Cancer. In the current study, the data shows that tangential beam hybrid-IMRT for left breast cancer patients offers the potential to significantly reduce dose-volume parameters of the ipsilateral lung, heart and contralateral breast compared to tangential beam 3-DCRT and IMRT of articles

with comparable target dose coverage. In this study, we proved that hybrid IMRT plans requiring less MUs can achieve dosimetric equivalence to full-IMRT. This hybrid IMRT is also more flexible in terms of positioning repeatability. In the case of hybrid IMRT, the dosimetric parameters equivalence are achieved to VMAT beams to the standard tangential conformal beams. In this manner, hybrid IMRT plans not only reduce hot spots outside the target volume but also improve dose homogeneity within the target volume. However, hybrid-IMRT technique was superior in terms of low dose volume of normal tissue, integral dose, and treatment time. In context of limiting mean and low dose to lung and heart, hybrid-IMRT is found to achieve good OAR sparing with acceptable PTV coverage for free breathing, left breast irradiation. So from the overall consideration we suggest to choose hybrid-IMRT which was suitable for the protection of heart in the left-sided breast cancer radiotherapy.

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