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Dosimetric Comparison of Various Treatment Techniques for Post-Mastectomy Breast Radiotherapy: Evaluation of a Novel Hybrid IMRT Approach in Nepal

Bidyapati Jha[a,b], Hari Prasad Lamichhane[b], Raju Prasad Srivastav*[c]

[a]Department of Radiation Oncology, Bhaktapur Cancer Hospital, Dudhpati, Bhaktapur, Nepal

[b]Central Department of Physics, T.U., Kirtipur, Kathmandu, Nepal

[c]Department of Radiation Oncology, Ghent University Hospital, Corneel Heymanslaan, Ghent, Belgium

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ABSTRACT

Background: Radiotherapy is integral to breast cancer treatment and is a crucial adjuvant therapy alongside a combination of surgery and chemotherapy in Nepal. The study was designed to assess the impact of hybrid intensity-modulated radiotherapy (h-IMRT) on tumor response, determine its role in improving overall survival, and compare different radiotherapy techniques, including field-in-field (FiF), intensity-modulated radiotherapy (IMRT), with h-IMRT.

Methods: Twenty-five left-sided breast cancer patients were included for plan evaluation in terms of planning target volume (PTV) coverage and organ at risk (OAR) irradiation. Patients who underwent modified radical mastectomy were planned in Eclipse 13.6 treatment planning system (TPS) for 40.05 Gy in 15 fractions, using FiF, IMRT, and h-IMRT separately. The PTV included the left chest wall, axillary nodes, and supraclavicular nodes.

Results: The D_{mean} (mean dose) within the PTV was lowest in IMRT and increased by 1.52% in the h-IMRT plan. The study showed that the lowest D_{mean} for the heart was in the h-IMRT plan, while it increased by 45% in the FiF plan. The V_{20} and V_{10} of the heart as good indicators of the heart risk were minimal in the h-IMRT plan compared to FiF and IMRT. The lung volume receiving a dose equal to or greater than 20 Gy (V_{20}) was also minimal in the h-IMRT plan compared to IMRT and FiF.

Conclusion: The h-IMRT treatment plan for left-sided breast cancer provides better PTV dose coverage and OAR sparing compared to FiF and IMRT plans. The h-IMRT plan also reduces monitor unit (MU) count.

INTRODUCTION

Breast cancer is the most widespread cancer among women worldwide, constituting 24.2% of all malignancies, according to GLOBOCAN statistics.[1,2] It is also the most common cancer in females in Nepal and other Asian countries. Compared to the developed world, most breast cancer patients in Nepal present with advanced stages, primarily due to limited screening facilities, lack of awareness, and financial constraints.[3] Given the higher stages of cancer, multimodal therapy is the standard treatment. Modified radical mastectomy (MRM) is the treatment of choice for the majority of breast cancer cases.[3] Numerous trials have shown that adjuvant radiotherapy improves local control and long-term survival in node-positive patients after MRM.[4,5]

***Address for correspondence:**
Dr. Raju Prasad Srivastav,
Department of Radiation Oncology, Ghent University Hospital, Corneel Heymanslaan, Ghent, Belgium
Email: rajupsrivasstava@gmail.com

Initially, the conventional two open-field tangential (2OFT) photon beam technique was used in radiotherapy. However, this method led to late toxicities due to non-uniform dose distributions across the target, exposure to healthy tissue, and limitations in dose escalation to the tumor. In left breast cancer patients, this technique resulted in higher doses to organs at risk (OAR), including the heart and bilateral lungs. It has been shown that the 2D technique moderately increases the risk of cardiac toxicities and morbidity in left breast treatments. To minimize these side effects, various advanced radiotherapy techniques have been developed.

The three-dimensional conformal radiation therapy (3D-CRT) technique is widely used in radiotherapy today. This method utilizes information from computed tomography (CT) scans to define the target region. The CT scans are transferred to a computer-based treatment planning workstation, where the 3D-CRT plan is created. Radiation beams in 3D-CRT are shaped to conform to the tumor, thereby reducing radiation exposure to normal tissue. The development of multi-leaf collimators (MLCs) has made it possible to match the treatment field to the shape of the tumor. The use of MLCs has become a valuable asset in improving the quality of care during radiotherapy. However, normal tissue toxicity remains a major concern for individual patients.

Field-in-field (FiF) and 3D-CRT are common radiotherapy techniques used in Nepal to treat breast cancer. In the FiF technique, beam orientations are similar to 3D-CRT, but additional fields with manually created apertures are used for blocking instead of wedges. This approach helps improve dose homogeneity and results in better cosmetic outcomes for the treated breast and chest wall. Several studies[6–8] have shown that the FiF technique leads to a more favorable dose distribution in post-surgical radiotherapy for breast cancer compared to two-dimensional treatment. Another frequently used technique is intensity-modulated radiation therapy (IMRT), which allows modulation of the intensity of individual radiation beams. Both forward-planned IMRT and inverse-planned IMRT improve target coverage and reduce the dose to OARs, although this technique requires longer treatment times. Selvaraj *et al.*[9] reported that IMRT provided better dose uniformity and reduced the volume of hot spots.

A new treatment planning technique is needed for breast cancer treatment to reduce the dose to OARs, shorten treatment time, and improve target coverage. Mayo *et al.*[10] proposed the concept of h-IMRT plans, which combine conventional and IMRT beams. Several studies have demonstrated the superiority of h-IMRT in whole breast treatment.[11,12]

The h-IMRT plan is a combination of FiF and IMRT with varying weightings for breast or chest wall irradiation. The objective of this work is to test several weight combinations in order to identify the best solution for the patient. The purpose of h-IMRT technique is to achieve better PTV coverage and optimal dose constraints for OAR and to improve conformity and homogeneity indexes. The study was designed to assess the impact of h-IMRT on tumor response and overall survival rates and to compare quality of life after applying FiF, IMRT, and h-IMRT.

METHODS

Patient selection

The study was conducted from February 2023 to April 2024 at the Radiation Oncology Department, Bhaktapur Cancer Hospital (BCH). Patients were retrospectively selected, including 25 female patients with left-sided breast cancer who had undergone modified radical mastectomy. Eligible patients were aged between 35 and 65 years and were staged according to the department's TNM classification protocol.

Simulation

All the patients were positioned on the breast board in a supine position with both arms raised above the head. CT imaging was performed with a 3-mm slice thickness using a Siemens CT scanner (Siemens Somatom Definition Flash, Germany). Images were acquired from the mandible to the 4th lumbar vertebra during normal breathing. Radiopaque markers were placed on the patient's skin to facilitate coordinate transformations for 3D planning and subsequent plan implementation.

Planning system and radiotherapy machine

The Digital Imaging and Communications in Medicine (DICOM) images were transferred to Eclipse treatment planning system (TPS; v15.6, Varian Medical Systems, Palo Alto, CA). The clinical target volume (CTV), planning target volume (PTV), and organs at risk (OARs)—including the ipsilateral lung, contralateral lung, contralateral breast, and heart— were contoured by the radiation oncologist.

A Varian linear accelerator (Varian Medical Systems, Palo Alto, CA) integrated with the TPS was installed in 2019. The Clinac iX linear accelerator, equipped with a Millennium 60-pairs, multi-leaf collimator (MLC), was used for treatment. The leaf width of the MLC was 0.5 cm at the isocenter.

Treatment planning technique

FiF planning: The FiF treatment plan involves 2 main tangent fields along with a small subfield directed towards the PTV. The gantry angle was individually optimized depending on the patient's anatomy. The MLCs were adjusted to create subfields to shield the hotspot region of the target. The subfields had significantly less weight compared to the main fields.

IMRT planning: IMRT plans included 4 to 6 beam angles, ranging from 305° to 130° of gantry angle. The angles of the collimator and the positions of the jaws for all the fields were adjusted before dose optimization. The Anisotropic Analytical Algorithm (AAA) was used for the final dose calculation with a grid size of 2.5 mm.

Hybrid planning: Hybrid plans consist of a combination of FiF and IMRT beams with different weightings. The dose was calculated with FiF/IMRT ratios of 70/30, 60/40, and 50/50, and all plans were normalized to the prescribed dose.

Dosimetric evaluation tools

A dose-volume histogram (DVH) was generated for the planning target volume (PTV) and organs at risk (OARs) for each patient during treatment planning. The $D_{98\%}$, $D_{95\%}$, $D_{2\%}$ and Dmax were evaluated for the PTV. D98% indicates the minimum dose received by 98% of the PTV volume, while D2% represents the maximum dose received by 2% of the PTV. $D_{50\%}$ applies the dose received by 50% of the target volume. The treatment plans were evaluated by analyzing the conformity index (CI) and the homogeneity index (HI) as defined in ICRU-83.[13]

The HI is defined as the difference between the doses received by 2% and 98% of the PTV, divided by the dose received by 50% of the PTV (HI = $[D_{2\%} - D_{98\%}] / D_{50\%}$). An HI value of zero indicates that the dose distribution is nearly homogeneous, which is considered an ideal value. The CI is presented as the ratio of the treated volume (TV) to the PTV (CI = TV prescribed / PTV total), with an ideal CI value of 1.

Statistical analysis

SPSS 25 (IBM Corp., Armonk, NY) was used for data analysis. Since the data followed a normal distribution, continuous variables are presented as mean ± standard deviation. A t-test was applied for the statistical comparison of various treatment techniques. The FiF, IMRT, and h-IMRT plan parameters were tested for statistical significance using a t-test, and the significance level of <0.05 was set. A One-way ANOVA test was performed to compare the means of more than 2 groups. The Bonferroni post hoc test was performed to identify which groups differed significantly from each other. Data distribution was visualized using box plots, which display the minimum, first quartile (Q1), median, third quartile (Q3), and maximum values.

RESULTS

Table 1 shows baseline characteristics for all study participants. The average PTV and heart volume were 544.92 ± 115.66 cc and 495.31 ± 72.15 cc. The median age of the patients was 48.44 ± 8.57 years. The average left lung volume was 909.35 ± 106.82 cc.

Table 1. The Patients' Baseline Characteristics (Tumor Staging, PTV, and OAR Volume Characteristics)

Variable	
Age, mean ± SD	48.44 ± 8.57
TNM, N (%)	
Type 1 (cT2N3M0)	52%
Type 2 (ypT0N0M0)	21%
Type 3 (pT3N0M0)	27%
PTV Volume, mean ± SD	544.92 ± 115.66
Heart volume, mean ± SD	495.31 ± 72.15
Left lung volume, mean ± SD	909.35 ± 106.82
Right lung volume, mean ± SD	1117.23 ± 129.56
Total Lung volume, mean ± SD	2026.55 ± 217.44
Contralateral Breast volume, mean ± SD	684.54 ± 58.83

OARs, organs at risk; PTV, planning target volume; SD, standard deviation; TNM, tumor, node, metastasis.

Figure 1 displays the prescribed dose distribution (95% isodose line) in transverse, frontal, and sagittal views for: (a) FiF (field-in-field), (b) IMRT (intensity-modulated radiation therapy), (c) hybrid (50% FiF + 50% IMRT), and (d) hybrid (70% FiF + 30% IMRT) techniques.

Table 2 presents the dosimetric parameters, MU calculations, CI, and HI for the PTV. The maximum dose point (D_{max}) was highest in FiF at 44.21 ± 0.57 Gy and 42.84 ± 0.64 Gy in the hybrid technique (70% + 30%). The mean dose (D_{mean}) was 41.91 ± 0.62 Gy in the hybrid technique (70% + 30%). The $D_{95\%}$ was 40.21 ± 1.01 Gy in the hybrid technique (70% + 30%), which represents a significant improvement over FiF (38.56 ± 0.68 Gy). The CI (0.975 ± 0.01) and HI (0.059 ± 0.02) showed the best performance in the hybrid (70% + 30%) plans. The hybrid plans (70% + 30%) were found to be more homogeneous than the other plans. The monitor units (MUs) were higher in IMRT (1208 ± 162.89) and significantly dropped to 971.20 ± 99.20 for the h-IMRT plan.

The P value calculated for a one-way ANOVA is presented in Table 2. The test compared the groups FiF, IMRT, and h-IMRT, showing no significant difference overall. However, pairwise comparisons revealed significant differences in D_{max} (IMRT vs h-IMRT) and $D_{95\%}$ (FiF vs h-IMRT).

After conducting a one-way ANOVA to examine differences among the three groups, the Bonferroni post-hoc test was performed to identify specific pairwise differences.

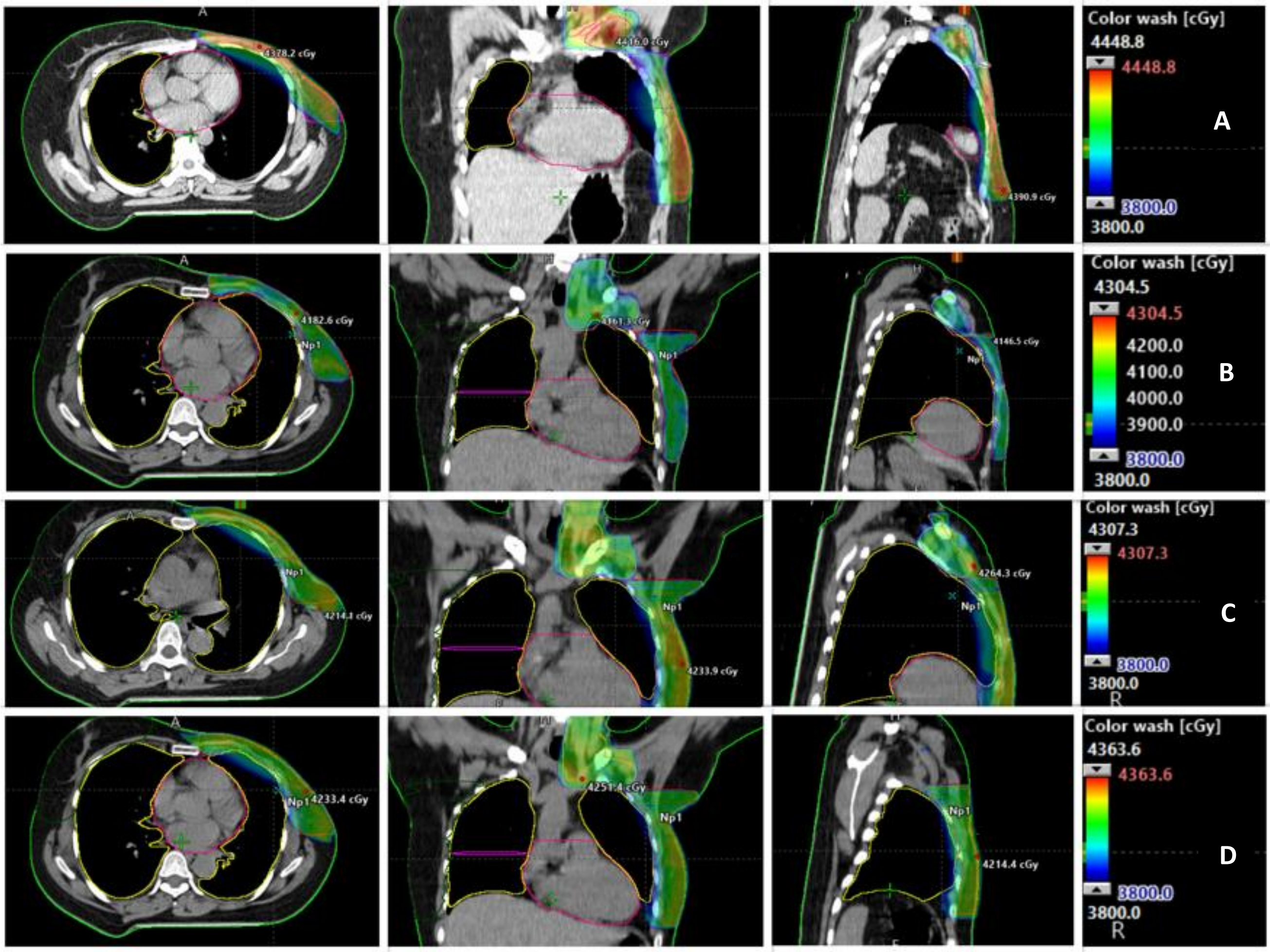

Figure 1. Screenshots of Dose Distribution in Color Wash. A, field-in-field (FiF); B, intensity-modulated radiation therapy (IMRT); C, hybrid (50% + 50%); D, hybrid (70% + 30%)

Table 2. Statistical Significance Results of PTV Dose Distribution, MU, CI and HI for FiF, IMRT, and h-IMRT

Dose metrics	FiF	IMRT	h-IMRT (hybrid 70/30)	ANOVA P value	Post hoc P FiF vs IMRT	Post hoc P FiF vs h-IMRT	Post hoc P IMRT vs h-IMRT
$D_{95\%}$(Gy)	38.6 ± 0.7	40.6 ± 1.0	40.2 ± 1.0	0.0021	Yes	Yes	No
D_{max} (Gy)	44.2 ± 0.6	43.8 ± 0.8	42.8 ± 0.6	0.2804	No	Yes	Yes
D_{mean} (Gy)	41.5 ± 0.4	40.4 ± 0.4	41.9 ± 0.6	0.00008	Yes	Yes	No
MU	609 ± 33	1208 ± 163	971 ± 99	0.0254	No	Yes	Yes
CI	0.94 ± 0.01	0.92 ± 0.02	0.98 ± 0.01	0.0088	Yes	Yes	Yes
HI	0.13 ± 0.02	0.12 ± 0.03	0.06 ± 0.02	0.0355	No	Yes	Yes

ANOVA, analysis of variance; CI, conformity index; Dmax, maximum dose; Dmean, mean dose; D95%, dose received by 95% of the volume; FiF, field-in-field; Gy, Gray; HI, homogeneity index; h-IMRT, hybrid intensity-modulated radiation therapy; IMRT, intensity-modulated radiation therapy; MU, monitor unit; PTV, planning target volume.

The analysis revealed no significant differences in $D_{95\%}$ or D_{mean} between IMRT and h-IMRT, whereas both FiF vs. IMRT and FiF vs h-IMRT showed significant differences for these parameters. Similarly, monitor units (MU) and heterogeneity index (HI) exhibited no significant differences across groups, while the conformity index (CI) was significantly different in all group comparisons.

Figure 2 shows the variation of conformity and homogeneity index across the planning techniques in our research in the form of box plots. A box plot visually represents the distribution of data, displaying key statistical measures including the minimum, first quartile (Q1), median (Q2), third quartile (Q3), and maximum values. Based on the plots, it becomes clear that the data for the h-IMRT plans is the most balanced with respect to both the CI and the HI since they have a lower variability among the data points as opposed to the other techniques where a higher degree of variability is observed. The h-IMRT plans demonstrated superior dose homogeneity (0.059 ± 0.02) compared to other treatment techniques. Table 3 shows the statistical significance of dosimetric parameters. The h-IMRT technique demonstrated significantly lower D_{max} values compared to both FiF and IMRT approaches. Furthermore, h-IMRT plans showed substantially improved conformity, with CI values significantly higher than conventional techniques (P=0.002).

Table 3 shows the distribution of OARs in FiF, IMRT, and h-IMRT. The mean dose to the ipsilateral lung was 19.4% and 38.1% lower in h-IMRT compared to FiF and IMRT, respectively. The dose to the contralateral breast was lower in the h-IMRT plan. The $V_{10\%}$ dose to the heart was significantly higher in FiF and 56.7% lower in the hybrid plan. The mean dose to the heart was also lower in the hybrid technique. The mean dose to the contralateral lung was the lowest in the hybrid plan.

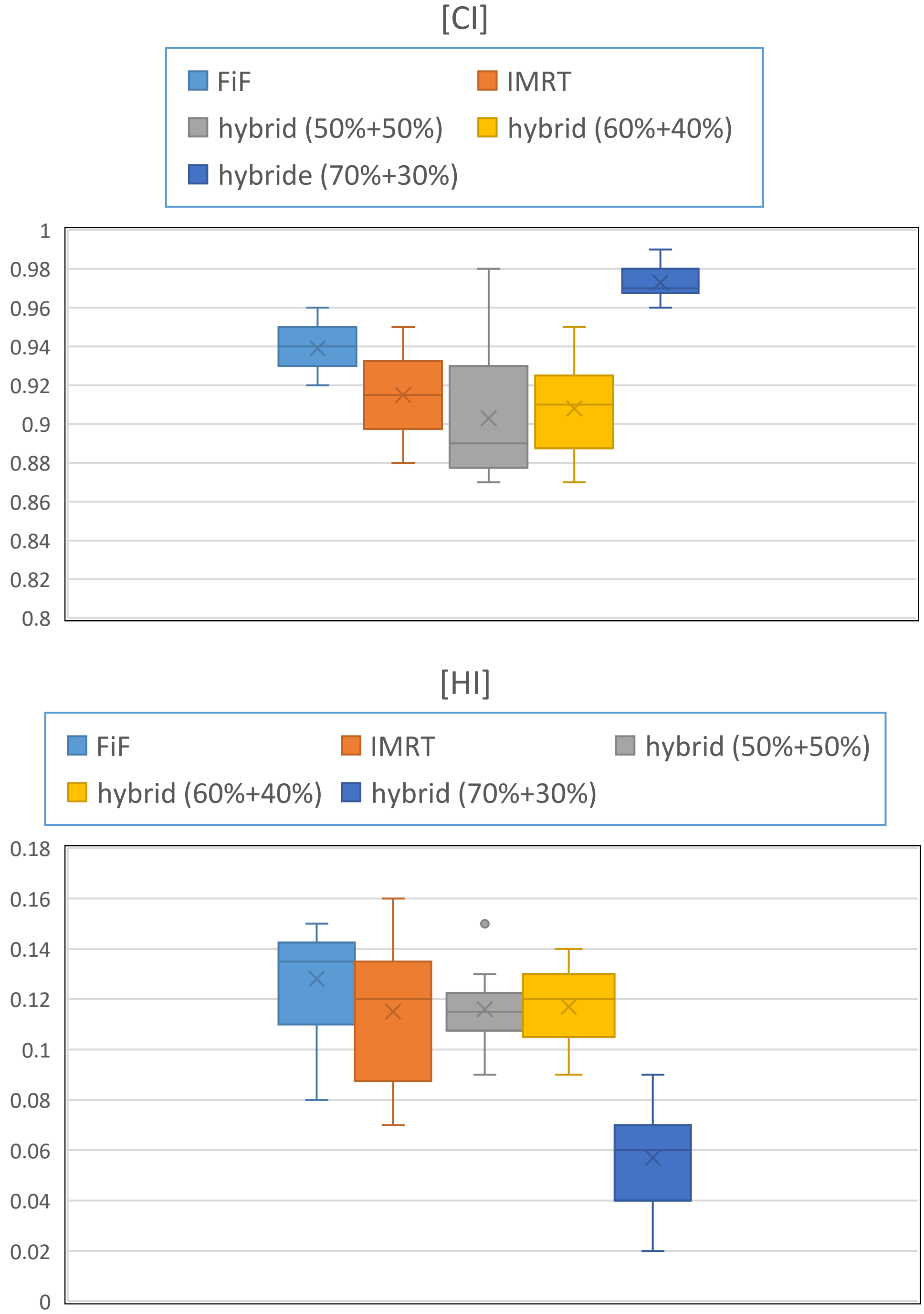

Figure 2. Box Plots Comparing Dose CI and HI Distributions Among FiF, IMRT, and h-IMRT Treatment Plans. CI, conformity index; FiF, field-in-field; HI, homogeneity index; h-IMRT, hybrid intensity-modulated radiation therapy; IMRT, intensity-modulated radiation therapy.

Table 3. Dose Distribution Summary of OAR in Various Treatment Techniques

Parameters	Variables	FiF	IMRT	h-IMRT	FiF vs h-IMRT P value	IMRT vs h-IMRT P value
Left lung (ipsilateral)	V_{30}	18.06 ± 2.36	16.97 ± 3.22	15.61 ± 2.09	0.02	0.51*
	V_{20}	32.92 ±4.21	24.93 ± 3.88	22.85 ± 3.51	0.04	0.40*
	V_{10}	44.66 ± 3.56	57.79 ± 4.21	34.03 ± 3.66	0.11*	0.01
	V_5	43.95 ± 4.91	85.05 ± 4.39	53.7 ± 4.02	0.32*	0.03
	D_{mean}	11.93 ± 1.29	13.80 ± 1.32	9.99 ± 0.89	0.05	0.02
Heart	V_{30}	7.49 ± 2.12	7.71 ± 2.74	4.62 ± 1.12	0.03	0.01
	V_{20}	13.22 ± 2.86	10.61 ± 3.82	7.22 ± 1.38	0.01	0.02
	V_{10}	19.2 ± 3.62	14.11 ± 4.12	10.9 ± 2.27	0.02	0.05
	D_{mean}	4.54 ± 0.56	6.18 ± 0.22	3.11 ± 0.13	0.06*	0.01
Right lung (contralateral)	D_{mean}	5.62 ± 0.32	6.11± 0.92	1.28 ± 0.45	0.02	0.04
Contralateral breast	D_{mean}	3.22 ± 0.22	4.83 ± 0.16	1.66 ± 0.06	0.03	0.02

DISCUSSION

Planning and dosimetric techniques such as 3DCRT, IMRT, and VMAT in breast cancer have been evaluated in a large number of studies. The results have often sparked discussions on the use of these advanced techniques in radiotherapy practice. Johansen *et al.*[14] recommended VMAT over IMRT and 3D-CRT in post-mastectomy breast cases to achieve a lower dose to OARs and improved PTV coverage, CI, and HI.

The primary aim of the hybrid technique is to reduce the radiation dose to the heart, lung, and contralateral breast to avoid radiation-induced secondary cancers and long-term effects (e.g., heart failure and lung pneumonia). The D_{mean} inside the PTV was the lowest in IMRT and increased by 1.52% in the h-IMRT planning. The dose coverage, $D_{95\%}$ (Gy), increased from 38.56 Gy in FiF to 40.26 Gy in h-IMRT.

Nakamura *et al.*[17] studied the plan quality and robustness of dose distributions against setup and motion uncertainties. They found that hybrid IMRT achieved better robustness against these uncertainties compared to full IMRT.

Fogliata *et al.*[18] studied dosimetric differences for the involved OARs among 3D-CRT plans with FiF and 2 VMAT plans (VMAT full and VMAT tang) for breast cancer. They confirmed that full VMAT delivered a noticeably higher mean dose to the OARs compared with VMAT tang. The h-IMRT plan in our study achieved better CI and HI for the PTV.

Research shows that the incidence of major coronary events increases by 7.4% for every additional 1 Gy added to the standard heart dose.[18-20] Our study showed that the lowest D_{mean} for the heart was in the h-IMRT plan, which increased by 45% in the FiF plan. The $V_{20\%}$ and $V_{10\%}$ of the heart are good indicators of heart risk and are minimal in the h-IMRT plan compared to FiF and IMRT.

Lung complications are the second major group of complications in breast cancer treatment. Patients who undergo radiotherapy may develop radiation pneumonitis, which can subsequently lead to irradiated lung fibrosis. Respiratory deficiency is a functional result of this complication. The volume of the lung receiving a dose equal to or greater than 20 Gy (V_{20}) is a significant indicator in minimizing the probability of complications. The study confirmed that the ipsilateral lung V_{20} was minimal in the h-IMRT plan compared to IMRT and FiF.

Another important point to consider is the dose for the contralateral breast, especially in the treatment of younger patients. Stovall et al.[21] reported an increased long-term risk of developing secondary contralateral breast cancer. The study showed that the hybrid plan delivered the lowest dose to the contralateral breast.

Ding *et al.*[20] studied the robustness of multi-field IMRT and VMAT plans for 7-field hybrid IMRT and 2-arc VMAT techniques. They confirmed that the 7F-H-IMRT plans showed a greater robustness than the 2A-VMAT plans. A higher D_{mean} of CTV Boost was found in 7F-H-IMRT plans. Racka *et al.*[21] evaluated 3D-CRT and hybrid techniques for left-sided breast cancer treatment. Previous studies have demonstrated that hybrid techniques provide significantly improved target coverage, with PTV V95% > 98% (P<0.001). Our h-IMRT results showed comparable dosimetric quality, achieving $D_{95\%}$ = 40.21 ± 1.0 Gy (P=0.002).

High monitor units and prolonged treatments can result in increased out-of-field leakage doses and scattered radiation to normal tissue, potentially raising the incidence of radiation-induced malignancies. Hall et al.[22] found that the rate of radiation-induced malignancy increased from 1% in 3D-CRT to 1.75% in IMRT. The study showed that the IMRT plan had the highest number of monitor units, which decreased by 24.4% in the h-IMRT plan.

This study has several limitations that should be considered when interpreting the results. First, the relatively small sample size may limit the generalizability of our findings. Second, individual anatomical variations between patients could significantly influence dose distribution patterns. Third, while we have analyzed short-term dosimetric outcomes, the long-term clinical implications, particularly regarding radiation-induced secondary malignancies, require further investigation through extended follow-up studies. Another limitation was the treatment planning system algorithm, which was based on the Anisotropic Analytical Algorithm (AAA). This algorithm may also introduce uncertainty in dose calculation for non-homogeneous regions. Srivastava *et al.*[23] reported mean relative differences of 1.1% ± 1.2% (AXBw vs AXBm) and 2.0% ± 1.2% (AXBm vs. AAA) in their comparative dosimetric analysis.

CONCLUSION

The study found that h-IMRT was superior to both FiF and IMRT techniques in terms of target dose coverage and OAR sparing for left-sided breast cancer. In the hybrid plans, the combination of 70% FiF and 30% IMRT resulted in better outcomes compared to the other approaches. The h-IMRT technique demonstrates clinically favorable dosimetric outcomes for left breast cancer radiotherapy, suggesting its potential for routine clinical implementation, because it provides better PTV dose coverage and OAR sparing compared to FiF and IMRT, and hybrid plans. The h-IMRT plan also reduces MU count and has a smaller low-dose volume compared to the IMRT plan.

ETHICAL CONSIDERATIONS

Not applicable.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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