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Physical and Biological aspects of 3-dimensional conformal and Intensity Modulated Radiotherapy techniques for Treating Left-Sided Breast Cancer

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Purpose: This study investigated the application of 3D Conformal Radiotherapy (3D-CRT) and Intensity-Modulated Radiotherapy (IMRT) for the treatment of left-sided breast cancer following breast-conserving surgery. These techniques are intended to eradicate residual tumor cells while minimizing radiation exposure to surrounding critical organs, particularly the heart and lungs. Owing to the anatomical proximity of the heart to the left breast, reducing long-term cardiopulmonary toxicity constituted a key objective of this study.

Methods: Sixteen female patients with left-sided breast cancer were treated following breast-conserving surgery. The study compared the performance of 3D conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) using both biological and dosimetric parameters. Biological metrics, including the equivalent uniform dose (EUD), tumor control probability (TCP), and normal tissue complication probability (NTCP), were calculated using MATLAB software. Dosimetric indices, such as the homogeneity index (HI) and conformity index (CI), along with dose-volume parameters derived from dose-volume histogram (DVH) analysis, were evaluated for the planning target volume (PTV: V95%, V107%, Dmax, Dmean, Dmin), the heart (V30%, Dmax, Dmean, Dmin), and both lungs (V20%, Dmax, Dmean, Dmin).

Results: IMRT achieved superior tumor control within the PTV, reflected by higher and more consistent TCP values. It also outperformed 3D-CRT in conformity and homogeneity indices, ensuring a more uniform and precise dose distribution. DVH analysis indicated that IMRT delivered higher minimum and mean doses to the PTV, although the difference in Dmax was not significant. Both techniques were safe for the heart; however, IMRT yielded a higher EUD, raising concern about potential cardiac risks. Lung protection was adequate with both approaches, though 3D-CRT demonstrated slightly lower and more stable NTCP values for the left lung.

Conclusions: IMRT provided superior accuracy and uniformity in dose delivery relative to 3D-CRT, which may translate into improved treatment efficacy and patient outcomes.

Keywords: Radiobiological evaluation, Dosimetric evaluation, left-sided breast cancer, Three dimensional conformal, Intensity-modulated radiation therapy.

Introduction

Breast cancer is the most common malignancy among women worldwide, accounting for approximately 22% of female cancers and 13% of cancer-related deaths [Mor S. et al., 2002]. Although predominantly affecting women, men may also develop the disease and are treated with similar protocols [World Health Organization, 2024]. Originating from abnormal cells in the ducts or lobules, breast cancer can progress to invasive tumors capable of metastasis to lymph nodes or distant organs [World Health Organization, 2024]. Advances in surgery, chemotherapy, radiotherapy, hormonal therapy, and immunotherapy have significantly improved survival rates, with over 84% of women living at least five years post-diagnosis [Zhou GX et al., 2011]. Despite this progress, the global burden remains substantial, with 2.3 million new cases and 670,000 deaths reported in 2022 [World Health Organization, 2024].

Radiation therapy (RT) is an integral part of breast-conserving treatment, as it can reduce the risk of local recurrence by up to 66% [Elzawawy S. et al., 2015]. For patients with left-sided breast cancer, however, RT planning poses unique challenges due to the close proximity of the heart and lungs to the treatment field, which increases the potential for radiation-induced toxicity. Traditionally, treatment plans have been evaluated using dose-volume (DV) parameters, but these metrics may not fully capture the biological effects of radiation. More recently, radiobiological models such as Tumor Control Probability (TCP), Normal Tissue Complication Probability (NTCP), and Equivalent Uniform Dose (EUD) have been introduced alongside DV parameters to provide more clinically relevant predictions of both tumor response and normal tissue toxicity [Ling and Li, 2005; Astudillo-Velázquez et al., 2015].

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Several studies have compared different RT techniques in breast cancer, including three-dimensional conformal radiotherapy (3D-CRT), field-in-field (FiF), and intensity-modulated radiotherapy (IMRT). 3D-CRT, based on CT imaging with shaped beams, has been widely used due to its simplicity and effectiveness [Saibishkumar EP *et al.*, 2008]. FiF is often regarded as a forward-planned form of IMRT, offering improved dose homogeneity compared to conventional tangential beams. In contrast, IMRT employs inverse planning and beam intensity modulation, enabling superior dose conformity and sparing of organs at risk (OARs) [Zhao H *et al.*, 2015]. However, IMRT may increase the volume of normal tissue receiving low doses of radiation, raising concerns about potential long-term complications [Darby SC, Ewertz M. *et al.*, 2013]. While multiple reports have evaluated these techniques in different populations, most studies relied predominantly on dosimetric indices, with limited integration of radiobiological modeling to predict clinical outcomes.

Given this background, the present study aims to compare 3D-CRT and IMRT in the management of left-sided breast cancer following surgery, with a dual focus on dosimetric and biological endpoints. By integrating EUD, TCP, and NTCP modeling into treatment evaluation, this work provides a more comprehensive assessment of therapeutic effectiveness and normal tissue risk. Furthermore, the analysis was conducted in an Egyptian patient cohort, representing a population that has been underrepresented in prior radiotherapy research. This contribution is expected to offer valuable insights for optimizing breast cancer treatment in similar clinical settings.

Material and methods

This retrospective study was approved by the Ethics Committee of the National Cancer Institute (NCI), Egypt, and included 16 female patients with left-sided breast cancer who had undergone breast-conserving surgery. Patients were randomly selected, varying in age and tumor size. All relevant clinical and imaging data were collected from existing medical records. CT scans were performed to define tumor volumes for treatment planning. Targets and volumes of interest were delineated according to Radiation Therapy Oncology Group (RTOG) guidelines [Rudra S. *et al.*, 2014].

Treatment Planning:

A 3D conformal plan (3D-CRT) was developed using the TPS, and optimal intensity-modulated radiotherapy (IMRT) plans were generated to maximize target coverage while minimizing dose to organs at risk (OARs).

All cases were treated using an Elekta Synergy linear accelerator with 6 MV photons, employing the step-and-shoot IMRT technique. An 80-leaf multileaf collimator (MLC) with 1 cm leaf width was used. Treatment planning was performed on Monaco TPS (Elekta, Sweden), and inverse planning optimization was carried out using the vendor-provided Monte Carlo-based algorithm.

For IMRT, five fields were applied per plan. For 3D-CRT, medial and lateral fields were used, with an average of three field-in-field segments for forward planning. The prescribed dose for all patients was 40.05 Gy delivered in 15 fractions (2.67 Gy per fraction), following hypofractionated clinical guidelines.

In Monaco TPS, plan optimization was performed using a combination of biological and dose–volume histogram (DVH)-based cost functions to model tumor control and normal tissue response. These included equivalent uniform dose (EUD), target penalty, parallel and series functions, quadratic underdose/overdose terms, DVH-based overdose/underdose constraints, and maximum dose objectives. Appropriate functions were selected and balanced during optimization to achieve target coverage while sparing organs at risk.

Table 1. Dose constraints employing during the treatment planning process [Giuseppe Carlo Iorio *et al.* (2017)].

OARs	Dose constraints
Ipsilateral lung (left lung)	V 5 < 42%
	V10 < 30%
	V20 < 20%
Contralateral lung (right lung)	V 5 < 5%
Heart	V 5 < 20%
	V10 < 15%
	V20 < 10%
	Dmean < 4 Gy

Dosimetric Evaluation

Dose–volume histograms (DVHs) were generated for the planning target volume (PTV) and all OARs to evaluate the treatment plans. Metrics included :(**PTV**: mean dose, Dmax, Dmin, D2%, D50%, D98%, V95%, V107%), (**Right lung**: mean dose, V20Gy), (**Left lung**: mean dose, V20Gy), (**Heart**: mean dose, V30Gy)

Homogeneity index (HI):

The HI measures the uniformity of dose distribution within the target volume (PTV). A lower the homogeneity index (HI) value indicates a more even dose, minimizing regions of overdose or underdose within the target [A. Shanei et al., 2020]

Conformity Index (CI):

The CI evaluates how well the prescribed dose conforms to the shape and size of the target volume (PTV). A conformity index (CI) value closer to 1 indicates that the dose precisely covers the target while sparing surrounding healthy tissues [Kareem A. El-Maraghy et al., 2019].

The homogeneity and conformity indexes were determined using equations (1) and (2), respectively.

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (1)$$

D2%, D98%, and D50% represent the doses received by 2%, 98%, and 50% of the target volume, respectively. [A. Shanei et al (2020)]

$$CI_{95\%} = \frac{V_{95\%}}{V_{PTV}} \quad (2)$$

Where $V_{95\%}$ represents the volume receiving at least 95% of the prescribed dose, while V_{PTV} denotes the total volume of the PTV. [Kareem A. El-Maraghy et al. (2019)].

These indices were calculated for all patients to quantitatively assess dose uniformity and coverage in both 3D-CRT and IMRT plans.

Lower HI indicates more uniform dose distribution, while CI closer to 1 indicates better conformity to the target [A. Shanei et al., 2020; Kareem A. El-Maraghy et al., 2019].

Radiobiological Evaluation

Cumulative DVHs were used to calculate Equivalent Uniform Dose (EUD), Tumor Control Probability (TCP), and Normal Tissue Complication Probability (NTCP) using MATLAB. Niemierko's model ["Niemierko, A. (1999). A generalized concept of equivalent uniform dose (EUD). Medical Physics, 26(6)"] was applied during optimization with parameters listed in Table 2, including dimensionless “a” parameters, TCD50, γ_{50} , and TD50. The MATLAB script was saved as eudmodel.m, with input DVHs as two-column cumulative matrices: first column = absolute/percentage dose; second column = corresponding volume.

Table 2. Biological parameters used to calculate from Niemierko's model [Niemierko, A. (1999). A generalized concept of equivalent uniform dose (EUD). Medical Physics, 26(6)].

Structures	a	γ_{50}	TCD50	TD50	α / β	References
Breast	-2.57	1.1	26.71		3.3	Mahmoudi Farshid et al., 2025.
Heart	3	3		18	1.8-2	Emami et al.
Lung	1	2		24.5	1.8-2	Emami et al.

Statistical analysis:

Statistical analyses were performed using Microsoft Excel. A paired Student's t-test was used to assess differences between 3D-CRT and IMRT plans. P-values < 0.05 were considered statistically significant. Confidence intervals (95% Confidence Interval of Difference) were included alongside p-values to provide a clearer and more rigorous statistical interpretation. Descriptive statistics included mean and standard deviation (SD), with data presented as mean $\pm$ SD. Bonferroni correction was applied to control the risk of type I error when performing multiple comparisons, ensuring that results marked as significant after adjustment reflect true and reliable differences. Absolute differences and percentage improvements were calculated to provide clinical meaning beyond statistical significance.

Results

Target volume

The results of the mean dose, EUD, TCP, CI, HI, and other dosimetric parameters for the 3D-CRT and IMRT plans are summarized in Table 3. The average mean dose (Gy) for 3D-CRT and IMRT plans was (38.43 ± 3.86) and (41.2 ± 0.64), respectively. However, this difference was not statistically significant after Bonferroni correction. Both EUD and TCP values were significantly higher for IMRT compared to 3D-CRT. The HI demonstrated improved dose homogeneity with IMRT, while the CI showed a trend toward better conformity that did not remain significant after correction. No significant differences were observed in V95% and V107%.

Table 3. EUD, TCP%, Max dose, Min dose, Mean Dose, CI, HI, V95%, and V107% for the target volume in 3D-CRT&IMRT "Significant values after Bonferroni correction are indicated"[Armstrong, R. A. (2014)].

parameter	3D±SD	IMRT±SD	p-value	Significant after Bonferroni	95% Confidence Interval of Difference	Notes
TCP%	81.7±4.1	86.9±1.3	0.0004	yes	3.09 to 7.31	Higher TCP with IMRT
EUD(Gy)	38.5±1.8	41.1±1.03	0.0002	yes	1.58 to 3.62	Higher EUD with IMRT
Min dose(Gy)	6.54±4.83	19.5±9.2	0.0002	yes	7.87 to 18.05	Significantly higher in IMRT
Max dose(Gy)	43.18±4.99	46.6±2.4	0.06	no	0.71 to 6.13	Slightly higher in IMRT
Mean dose(Gy)	38.43±3.86	41.2±0.64	0.02	no	0.85 to 4.69	higher with IMRT but not significant after correction
CI	0.88±0.07	0.94±0.05	0.02	no	0.018 to 0.102	higher with IMRT but not significant after correction
HI	0.4±0.23	0.2±0.12	0.002	yes	−0.327 to 0.07	significantly lower (better) with IMRT
V95%	1219 ±453 cc	1348±439 cc	0.17	no	−180.1 to 438.1 −180.1 to 438.1	was higher with IMRT but not significant
V107%	8.63±15.47 cc	185.17±201 cc	0.004	yes	77.76 to 275.32	significantly higher hotspots in IMRT

Table 4. Absolute Difference & % Improvement / Change of the target volume between the two techniques.

	Absolute Difference (IMRT–3D)	% Improvement / Change	Clinical Interpretation
TCP %	+5.20%	+6.4% relative increase	Improved tumor control probability with IMRT
EUD (Gy)	+2.60 Gy	+6.8% increase	Better tumor coverage with IMRT
Min dose (Gy)	+12.96 Gy	≈200% increase	Much higher minimum dose delivered with IMRT
Max dose (Gy)	+3.42 Gy	+7.9% increase	Slightly higher maximum dose
Mean dose (Gy)	+2.77 Gy	+7.2% increase	Higher average dose with IMRT
CI	+0.06	+6.8% increase	Improved coverage index with IMRT
HI	–0.20	–50% reduction	Lower heterogeneity (better) with IMRT
V95%	+129 cc	+10.6% increase	Higher target coverage with IMRT (not significant)
V107%	+176.54 cc	>20× increase	Much higher hotspots with IMRT

IMRT increased TCP by +5.2% compared to 3D-CRT. EUD improved by +2.6 Gy, the minimum dose was higher by +12.96 Gy, and the maximum dose increased by +3.42 Gy. The mean dose also rose by +2.77 Gy. The Coverage Index (CI) improved by +0.06, while the Homogeneity Index (HI) decreased by –0.20, indicating better dose homogeneity with IMRT. V95% increased by +129 cc, though this difference was not statistically significant. V107% increased by +176.54 cc, indicating higher hotspots with IMRT.

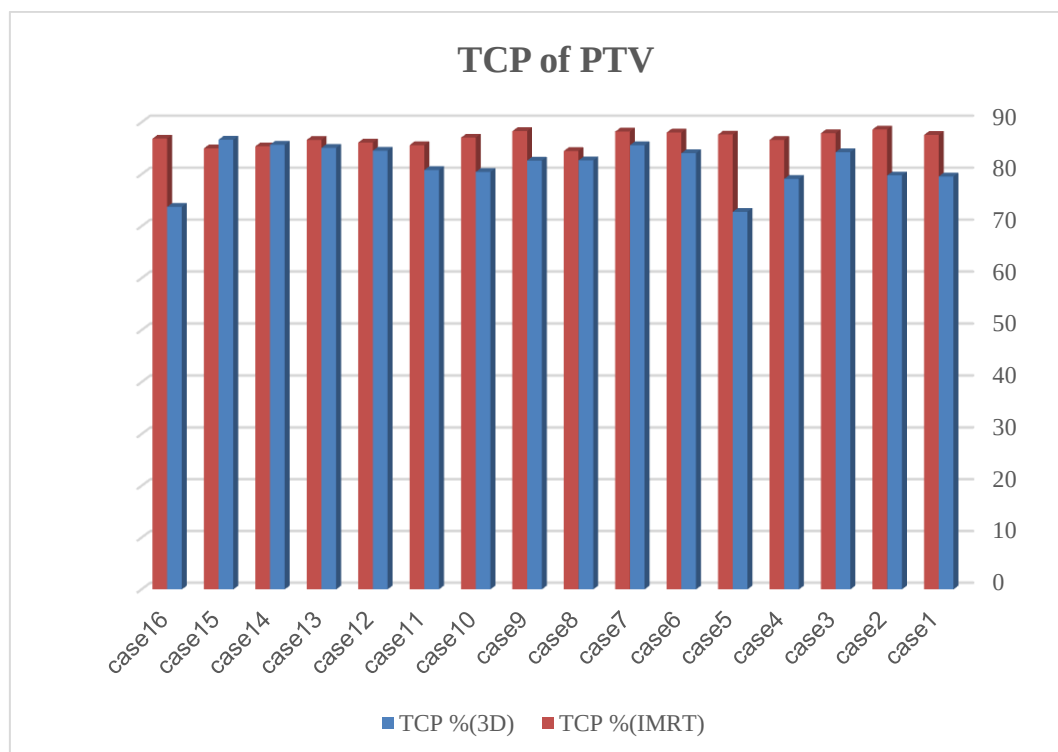


Fig. 1. Tumor Control Probability (TCP) of PTV. Comparison of TCP values for the planning target volume (PTV) between 3D-CRT and IMRT across 16 cases, showing consistently higher tumor control probability with IMRT.

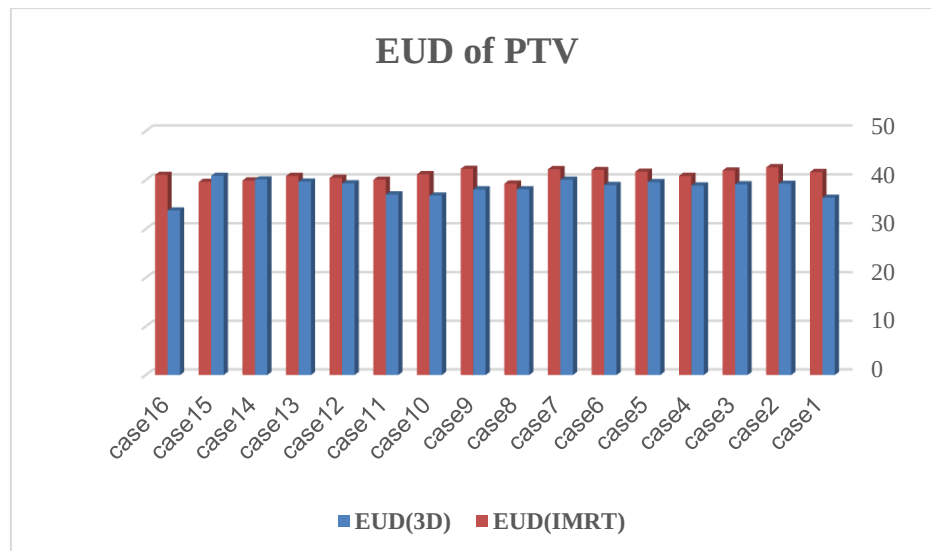


Fig. 2. Equivalent Uniform Dose (EUD) of PTV. Comparison of EUD values for the planning target volume (PTV) between 3D-CRT and IMRT across 16 cases, indicating higher dose uniformity with IMRT.

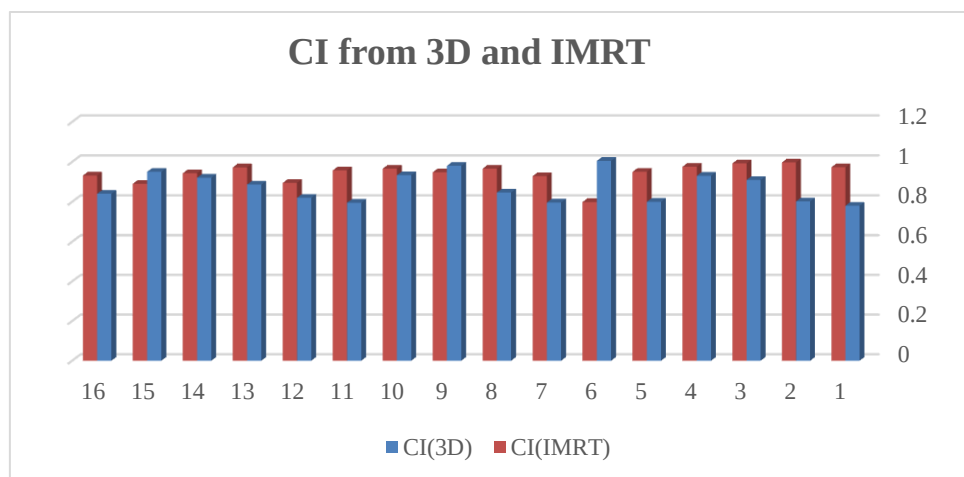


Fig. 3. Conformity Index. Comparison of conformity index (CI) values between 3D-CRT and IMRT treatment plans across all 16 patients, showing consistently higher conformity with IMRT.

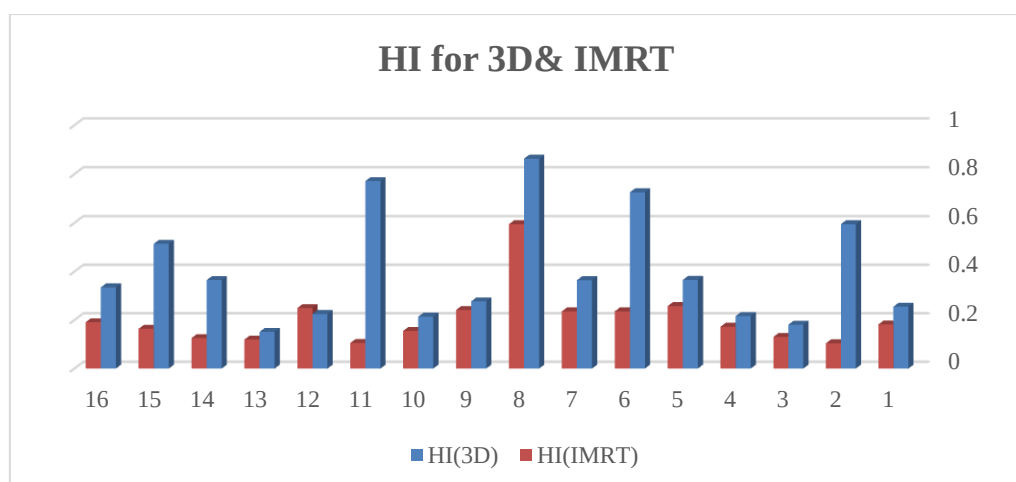


Fig. 4. Homogeneity Index. Comparison of homogeneity index values between 3D-CRT and IMRT plans, showing improved uniformity with IMRT.

Organs at Risk (OAR)

Tables 5 and 7 show the data for Equivalent Uniform Dose (EUD), Normal Tissue Complication Probability (NTCP), and V20Gy for both the left and right lungs, while Table 9 summarizes the results for the heart, including Mean Dose, EUD, and NTCP.

Table 5. Min dose, Max dose, Mean Dose, NTCP, EUD and V20Gy for the right lung in 3D& IMRT.
"Significant values after Bonferroni correction are indicated"[Armstrong, R. A. (2014)].

Parameter	3D $\pm$ SD	IMRT $\pm$ SD	p-value	95% Confidence Interval of Difference	Significant after Bonferroni
NTCP%	0	$6.03 \times 10^{-9} \pm 2.07 \times 10^{-8}$	Not applicable	Extremely low, clinically negligible	Not applicable
EUD	0.11 ± 0.05	0.92 ± 0.36	1.86×10^{-7}	$[0.6 - 1.0]^*$	Yes
V(20 Gy)%	0	0	0.05	–	No
Min dose (Gy)	0.11 ± 0.12	0.34 ± 0.08	1.28×10^{-5}	$[0.1 - 0.3]^*$	Yes
Max dose (Gy)	8.79 ± 9.61	10.7 ± 4.65	0.35	$[-1.5 - 5.3]^*$	No
Mean dose (Gy)	1.91 ± 2.5	1.99 ± 0.52	0.9	$[-0.9 - 1.1]^*$	No

Table 6. Absolute Difference & % Improvement / Change of the right lung between the two techniques.

Parameter	Absolute Difference (IMRT – 3D)	%Improvement / Change	Clinical Interpretation
NTCP %	$+6.03 \times 10^{-9}$	– (clinically negligible)	Extremely low values, clinically negligible (not applicable)
EUD (Gy)	+0.81	+736% increase	Significantly higher equivalent uniform dose with IMRT
V20 (%)	0	0% change	No difference between techniques
Min dose (Gy)	+0.23	+209% increase	Significantly higher minimum dose with IMRT
Max dose (Gy)	+1.91	+21.7% increase	Slightly higher maximum dose, not significant
Mean dose (Gy)	+0.08	+4.2% increase	No significant difference

NTCP increased slightly with IMRT ($+6.03 \times 10^{-9}$), but the values were extremely low and clinically negligible, making a meaningful statistical comparison impossible. EUD increased by +0.81 Gy, corresponding to a large relative percentage increase (+736%) due to the very low baseline 3D dose. However, the absolute increase remains modest in clinical terms. V20 showed no difference between the two techniques. The minimum dose increased by +0.23 Gy (~209% relative increase), reflecting the low baseline value, but this difference was statistically significant. The maximum dose increased slightly by +1.91 Gy (+21.7%), though this change was not statistically significant. The mean dose increased modestly by +0.08 Gy (+4.2%), with no significant difference between IMRT and 3D-CRT.

Table 7. Min dose, Max dose, Mean Dose, NTCP, EUD and V20Gy for the left lung in 3D-CRT&IMRT
"Significant values after Bonferroni correction are indicated"

Parameter	3D $\pm$ SD	IMRT $\pm$ SD	p-value	95% Confidence Interval of Difference	Significant after Bonferroni
NTCP%	0.001 ± 0.001	0.01 ± 0.02	0.04	$[0.0 - 0.018]^*$	No
EUD(Gy)	5.65 ± 1.49	6.73 ± 1.69	0.005	$[0.4 - 1.7]^*$	Yes
V (20 Gy) %	14.9 ± 3.86	16.6 ± 5.4	0.31	$[-1.7 - 5.1]^*$	No
Min dose (Gy)	0.31 ± 0.18	0.90 ± 0.24	4.39×10^{-6}	$[0.4 - 0.8]^*$	Yes
Max dose (Gy)	40.5 ± 6.68	42.36 ± 1.59	0.24	$[-1.6 - 5.3]^*$	No
Mean dose (Gy)	7.68 ± 2.37	9.55 ± 2.21	0.003	$[0.7 - 3.0]^*$	Yes

Table 8. Absolute Difference & % Improvement / Change of the left lung between the two techniques.

Parameter	Absolute Difference (IMRT – 3D)	% Improvement / Change	Clinical Interpretation
NTCP %	0.009	~9× increase	Slightly higher NTCP with IMRT (not significant)
EUD (Gy)	+1.08 Gy	+19.1% increase	Improved tumor coverage with IMRT
V20 (%)	1.70%	+11.4% increase	Slightly higher low-dose lung volume (not significant)
Min dose (Gy)	+0.59 Gy	~190% increase	Substantially higher minimum dose with IMRT
Max dose (Gy)	+1.86 Gy	+4.6% increase	Slightly higher maximum dose (not significant)
Mean dose (Gy)	+1.87 Gy	+24.3% increase	Higher average dose delivered with IMRT

IMRT resulted in a small increase in NTCP (+0.009), though this change was clinically negligible and not statistically significant. EUD improved by +1.08 Gy (+19.1%), indicating better tumor coverage with IMRT. V20 was slightly higher with IMRT (+1.7%), but the difference was not significant. The minimum dose increased substantially by +0.59 Gy (~190%), reflecting improved target coverage. The maximum dose increased slightly by +1.86 Gy (+4.6%), though this difference was not statistically significant. The mean dose increased by +1.87 Gy (+24.3%), showing a significantly higher average dose with IMRT. Table 9. Min dose, Max dose, Mean Dose, EUD, NTCP, and V30Gy for the heart in 3D-CRT&IMRT "Significant values after Bonferroni correction are indicated"[Armstrong, R. A. (2014)].

Table 9. Min dose, Max dose, Mean Dose, NTCP, EUD and V20Gy for the heart in 3D-CRT&IMRT "Significant values after Bonferroni correction are indicated"

parameter	3D ± SD	IMRT ± SD	p-value	95% Confidence Interval of Difference	Significant after Bonferroni
NTCP %	0.002 ± 0.009	0.007 ± 0.014	0.3	–0.005 to +0.015	No
EUD(Gy)	6.85 ± 3.33	8.86 ± 2.13	0.004	+0.72 to +3.30	Yes
V30 %	2.0 ± 1.9	1.3 ± 1.2	0.064	–1.45 to +0.05	No
Min dose (Gy)	0.41 ± 0.27	1.09 ± 2.13	0.00006	+0.42 to +0.94	Yes
Max dose (Gy)	39.06 ± 13.43	38.31 ± 3.34	0.5	–6.9 to +5.4	No
Mean dose (Gy)	3.01 ± 1.42	5.26 ± 1.95	0.000012	+1.27 to +3.23	Yes

Table 10. Absolute Difference (IMRT – 3D) & % Improvement / Change of the heart between the two techniques.

Parameter	Absolute Difference (IMRT – 3D)	%Improvement / Change	Clinical Interpretation
NTCP %	0.005	~2.5× increase	Slightly higher NTCP with IMRT (not significant)
EUD (Gy)	+2.01 Gy	+29.3% increase	Improved tumor coverage with IMRT (significant)
V30 (%)	–0.7%	–35% reduction	Lower high-dose lung volume with IMRT (not significant)
Min dose (Gy)	+0.68 Gy	~166% increase	Much higher minimum dose with IMRT (significant)
Max dose (Gy)	–0.75 Gy	–1.9% reduction	Slightly lower maximum dose with IMRT (not significant)
Mean dose (Gy)	+2.25 Gy	+74.8% increase	Substantially higher average dose with IMRT (significant)

NTCP showed a small increase of +0.005 with IMRT, but the values were extremely low and clinically negligible, with no significant difference. EUD improved by +2.01 Gy (+29.3%), reflecting significantly better tumor coverage with IMRT. V30 decreased by -0.7% (-35%), suggesting reduced high-dose heart exposure, although this difference was not statistically significant. The minimum dose increased by +0.68 Gy (~166%), indicating markedly improved minimum dose coverage with IMRT. The maximum dose was slightly lower by -0.75 Gy (-1.9%), with no significant difference. The mean dose increased substantially by +2.25 Gy (+74.8%), indicating a significant rise in overall dose delivery with IMRT.

Discussion

IMRT demonstrated superior tumor control probability (TCP) within the planning target volume compared to 3D-CRT (86.9% $\pm$ 1.3 vs. 81.7% $\pm$ 4.1, p = 0.0004). This improvement, coupled with reduced variability, reflects more consistent tumor control and can be attributed to IMRT's advanced modulation techniques. IMRT also provided a significantly higher minimum dose to the target (19.5 Gy $\pm$ 9.2 vs. 6.54 Gy $\pm$ 4.83, p = 0.0002), suggesting more adequate coverage of under-dosed regions. Although mean and maximum doses, as well as V95%, were slightly higher with IMRT, these differences did not remain significant after Bonferroni correction. A notable finding, however, was the significantly higher and more variable V107% in IMRT (185 $\pm$ 201 cc vs. 8.63 $\pm$ 15.47 cc, p = 0.004), indicating an increased risk of hot spots. This underscores the need for careful planning and dose verification to minimize overdosage while preserving the therapeutic advantage of IMRT.

Overall, the results demonstrate that IMRT provides measurable improvements in target coverage and dose homogeneity compared to 3D-CRT. Specifically, TCP increased by +5.2%, which may translate into a clinically relevant gain in tumor control. Similarly, the higher EUD (+2.6 Gy) and minimum dose (+12.96 Gy) suggest more adequate target coverage. The reduction in HI (-0.20) confirms improved homogeneity, a desirable feature for treatment quality. However, IMRT was also associated with higher hotspots (V107% +176.5 cc), raising concerns about potential toxicity. These findings indicate that while IMRT offers superior conformity and target coverage, careful planning is required to mitigate the risks of excessive dose escalation.

Heart Dose and NTCP:

Both techniques yielded very low NTCP values, confirming minimal risk of radiation-induced cardiac damage (3D-CRT: 0.002 $\pm$ 0.009; IMRT: 0.007 $\pm$ 0.014). However, IMRT increased the minimum and mean heart doses (Dmin: 1.09 $\pm$ 0.23 Gy vs. 0.41 $\pm$ 0.26 Gy; Dmean: 5.26 $\pm$ 1.95 Gy vs. 3.01 $\pm$ 1.42 Gy), likely due to the wider low-dose spread from multiple beam angles. While this raises concern about cumulative cardiac exposure, the more consistent maximum dose observed with IMRT (38.3 $\pm$ 3.3 Gy vs. 39.1 $\pm$ 13.4 Gy) suggests improved dose uniformity. Clinically, the trade-off appears acceptable, though patients with pre-existing cardiac conditions may require additional refinements to limit exposure.

Lung Dose and NTCP:

For the left lung, IMRT was associated with slightly higher EUD and mean dose (6.73 $\pm$ 1.69 Gy vs. 5.65 $\pm$ 1.49 Gy; 9.55 $\pm$ 2.21 Gy vs. 7.68 $\pm$ 2.37 Gy), as well as a significantly higher minimum dose (0.90 $\pm$ 0.24 Gy vs. 0.31 $\pm$ 0.18 Gy). These trends reflect IMRT's characteristic low-dose distribution across a wider area. NTCP remained low in absolute terms but was higher with IMRT (0.011 $\pm$ 0.017 vs. 0.0005 $\pm$ 0.0005), which may indicate a slightly increased risk of radiation pneumonitis in sensitive patients. Importantly, the maximum lung dose did not differ significantly, suggesting both techniques are comparable in controlling hotspots. Results for EUD, mean dose, and minimum dose remained significant after Bonferroni correction, while V20 and maximum dose differences were not significant.

For the right lung, both methods achieved excellent sparing, with V20% equal to 0%. IMRT delivered slightly higher EUD and minimum dose, but absolute values were clinically negligible, and NTCP remained essentially zero. These results confirm that IMRT's broader low-dose distribution does not compromise right lung safety while still improving target coverage.

Dosimetric Indices:

IMRT demonstrated superior conformity and homogeneity:

- Conformity Index (CI): Significantly improved with IMRT (0.94 $\pm$ 0.05 vs. 0.88 $\pm$ 0.07), indicating more precise dose shaping around the target.
- Homogeneity Index (HI): Lower and less variable with IMRT (0.20 $\pm$ 0.12 vs. 0.40 $\pm$ 0.23), reflecting more uniform dose distribution within the PTV.

These dosimetric advantages are crucial for reducing toxicity and ensuring reliable therapeutic delivery.

Summary of Key Parameters (from DVH Analysis)

Overall, IMRT provided improved target coverage, higher TCP, and better conformity and homogeneity compared with 3D-CRT. It achieved higher minimum and mean doses within the PTV, ensuring more complete tumor coverage. However, this came at the cost of higher low-dose exposure to the lungs and heart, with slightly elevated NTCP values, although the absolute risks remained low. The main drawback of IMRT was the significantly higher V107%, raising concern about hot spots and the potential for localized overdosage.

From a clinical perspective, IMRT offers clear advantages in complex anatomies such as large breasts or cases requiring boost volumes where improved conformity and cardiac sparing are particularly valuable. Nevertheless, careful plan evaluation and dose verification are essential to mitigate the risks of low-dose bath and hotspots.

Clinical Considerations

Although IMRT can increase radiation exposure to certain organs at risk, particularly the heart and lungs, it provides advantages in dose conformity, homogeneity, and tumor control. In this study, the increases in NTCP values for both the heart and lungs remained well below clinically significant thresholds. The low NTCP values observed in our cohort indicate that, for these patients, the small increases with IMRT are unlikely to result in meaningful clinical complications. While these benefits were observed in this cohort, outcomes may vary with different planning approaches or patient characteristics. Careful planning and individualized optimization remain essential, particularly for patients with pre existing cardiac or pulmonary conditions, to minimize treatment-related toxicity. Compared with 3D CRT, IMRT allows more precise tumor targeting and better sparing of healthy tissue, supporting improved consistency and clinical outcomes. Refining planning strategies continues to be important to maximize therapeutic benefit while ensuring long-term patient safety.

Limitations and Future Directions:

This study has several limitations. The relatively small sample size reduces the generalizability of the findings, and the absence of long-term follow-up data prevents firm conclusions regarding late toxicity or long-term tumor control. In addition, patient-specific variations in radiosensitivity were not considered, which may influence both TCP and NTCP outcomes. Furthermore, dose–volume histograms were based on a single CT scan and did not account for anatomical changes during treatment, which may affect the accuracy of radiobiological modeling.

Future studies should therefore include larger, more diverse patient populations and integrate markers of patient-specific radiosensitivity to refine outcome predictions. Long-term follow-up is essential to validate the dosimetric and short-term biological findings reported here. Adaptive planning techniques that accommodate anatomical changes during therapy could further enhance treatment precision and model accuracy, supporting more personalized radiotherapy strategies.

Comparison with Previous Studies:

Several previous studies have reported that IMRT can achieve better sparing of organs at risk compared to 3D-CRT, which seems inconsistent with some of our findings. For example, Mast *et al.* (2013) reported that IMRT significantly reduced cardiac doses in left-sided breast cancer. In their approach, 60% of the dose was delivered with two open tangential fields and the remaining 40% with four inversely planned IMRT fields, whereas in our study the entire dose was delivered using five IMRT fields. Similarly Selvaraj *et al.* (2007) reported lower cardiac and pulmonary doses with tangential field IMRT compared to 3D-CRT. However, their study employed a sliding window delivery technique, whereas our IMRT plans were delivered using a step-and-shoot approach with different beam arrangements, which may have contributed to differences in dose distribution. Furthermore Taheri *et al.* (2021) reported reductions in heart, LAD (Left Anterior Descending artery), and lung doses with IMRT in both conventional and hypofractionated regimens. Their study, however, used a different treatment planning system, applied another optimization algorithm, and included a greater number of beams than our study. Taken together, differences in treatment planning or delivery techniques, breathing approach (free breathing versus breath-hold), and patient anatomy likely contribute to the variability observed in IMRT dose distribution results.

Our results align partially with previous reports but highlight notable differences. Kazemzadeh *et al.* (2021) reported TCP values of 95–96% for hypofractionation regimens (40 Gy in 15 fractions) using the EUD model. In contrast, our EUD-based TCP values for a similar hypofractionated regimen (40.05 Gy in 15 fractions) were lower: 81.7% for 3D-CRT and 86.9% for IMRT. Although the same radiobiological model was applied, this discrepancy may be explained by differences in dose distribution inherent to the planning techniques, with IMRT providing more conformal coverage but also introducing potential hotspots.

Regarding NTCP values, our study found consistently low and clinically negligible cardiac risks across all hypofractionated regimens, in agreement with prior studies (e.g., Darby *et al.* 2013; Kazemzadeh *et al.* 2021), which also reported minimal heart NTCP in breast radiotherapy. Importantly, while our statistical analysis

showed no significant difference in cardiac NTCP between hypofractionation techniques, all hypofractionated regimens demonstrated significantly lower NTCP compared to conventional fractionation, reinforcing their safety advantage.

Taken together, these results suggest that while IMRT improves conformity and tumor coverage, its impact on radiobiological outcomes such as TCP and NTCP must be interpreted in the context of existing evidence. Direct comparison with established hypofractionated regimens (Darby 2013; Kazemzadeh 2021) underscores both the promise and the need for caution in generalizing results across different patient cohorts and planning methodologies.

Conclusion

This study demonstrates that IMRT achieves superior conformity and tumor control probability compared with 3D-CRT, while introducing a modest increase in mean cardiac and pulmonary doses in our cohort. Although the calculated NTCP values remain clinically negligible, these findings highlight the importance of careful treatment optimization to mitigate potential cardiopulmonary toxicity, particularly in patients with pre-existing comorbidities. However, when considering previously published studies, it becomes evident that the impact of IMRT on heart and lung doses is not uniform. Factors such as the use of deep-inspiration breath-hold, differences in beam arrangement or delivery techniques, and variations in patient anatomy or breast volume may significantly influence outcomes. Therefore, the slight increase in cardiac and pulmonary doses observed in our study should be interpreted within this context. The integration of advanced planning strategies and adaptive techniques remains essential to maximize the therapeutic ratio. To establish the long-term safety and efficacy of IMRT, larger prospective trials with extended follow-up are warranted.

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الجوانب الفيزيائية والبيولوجية لتقنيات العلاج الإشعاعي ثلاثي الأبعاد والمكثف (IMRT) في علاج سرطان الثدي الأيسر

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تُظهر هذه الدراسة أن تقنية العلاج الإشعاعي المعدّل الشدة (IMRT) تحقق دقة أعلى في استهداف الورم وتحكمًا أفضل في احتمالية السيطرة عليه مقارنة بتقنية العلاج الإشعاعي ثلاثي الأبعاد (D-CRT)، مع زيادة طفيفة في متوسط جرعات الإشعاع التي تتعرض لها عضلة القلب والرئتان. ورغم أن القيم المحسوبة لاحتمالية السمية الإشعاعية للأعضاء (NTCP) تبقى غير ذات أهمية سريرية، فإن النتائج تؤكد ضرورة تحسين خطط العلاج بعناية لتقليل أي مخاطر محتملة على القلب والرئتين، خاصة لدى المرضى الذين يعانون من أمراض مزمنة سابقة. كما تُشير مقارنة النتائج مع دراسات سابقة إلى أن تأثير تقنية IMRT على جرعات القلب والرئة ليس ثابتًا، إذ يمكن أن يتأثر بعوامل عدة مثل استخدام تقنية حبس النفس أثناء الشهيق العميق (DIBH)، واختلاف ترتيب الحزم أو أساليب التوصيل، وكذلك التباين في تشريح المريضة أو حجم الثدي. لذلك، يجب تفسير الزيادة الطفيفة في جرعات القلب والرئة التي لوحظت في هذه الدراسة في هذا الإطار. وتبقى الحاجة قائمة لاعتماد استراتيجيات تخطيط متقدمة وتقنيات علاج تكيفية بهدف تحقيق أفضل توازن علاجي وتعظيم النسبة العلاجية (Therapeutic ratio)، كما توصي الدراسة بإجراء تجارب مستقبلية أوسع ذات متابعة طويلة الأمد لتأكيد سلامة وكفاءة تقنية IMRT على المدى البعيد.