

Comparative Analysis of Dosimetry: IMRT versus 3DCRT in Left-Sided Breast Cancer Patients with Considering Some Organs in Out - of – Field Borders

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Purpose: The local management approach for node-positive breast cancer has undergone substantial evolution. Consequently, there exists a pressing need to enhance our treatment strategies by placing greater emphasis on planning and dosimetric factors, given the availability of more conformal techniques and delineation criteria, achieving optimal goals of radiotherapy treatment. The primary aim of this article is to discuss how the extent of regional nodal coverage influences the choice between IMRT and 3D radiation therapy for patients.

Patients and Methods: A total of 15 patients diagnosed with left breast cancer with disease involved lymph nodes were included in this study. Delivering the recommended dose required the use of a linear accelerator (LINAC) with photon beams energy of 6 mega voltage (6MV). Each patient had full breast radiation using two planning procedures: intensity-modulated radiotherapy (IMRT) and three-dimensional radiotherapy (3D conformal). Following the guidelines set forth by the Radiation Therapy Oncology Group (RTOG), the planned treatment coverage was carefully designed to fall between 95% and 107% of the recommended dose. Additionally, Dose Volume Histograms (DVHs) were generated the dose distribution within these anatomical contours.

Results and Conclusion: The DVH parameters were subjected to a comparative analysis, focusing on the doses absorbed by both Organs at Risk (OARs) and the Planning Target Volume (PTV). The findings suggest that low doses in IMRT plan might raise the risk of adverse oncological outcomes or potentially result in an increased incidence of subsequent malignancies. Consequently, the adoption of inverse IMRT remains limited, and the decision to opt for this therapy should be reserved for situations where it is genuinely necessary to uphold a satisfactory quality of life. Additionally, this approach helps in reducing the likelihood of developing thyroid problems and mitigates the risk of injuries to the supraclavicular area and the proximal head of the humerus bone.

Keywords: radiotherapy, LINAC, RTOG, breast cancer, photon exposure and secondary cancer risk

Introduction

Breast cancer is the leading cause of death in women worldwide. It accounts for 15.3% of global cancer cases and leads to 7% of cancer-related fatalities. In Egypt, breast cancer is the most commonly diagnosed malignancy among females. In the year 2020, the recorded incidence rate reached 32.4%, resulting in 22,038 newly reported cases and 9148 documented fatalities.^{1–3}

A significant proportion of cancer patients in developing nations presents with advanced disease due to an array of factors, including insufficient public awareness and limited accessibility to healthcare facilities, resulting in delayed diagnoses.^{4,5}

In contrast to less economically developed nations, survival rates for breast cancer have shown improvement in industrialized countries over the last two decades. This progress has resulted in a greater number of women experiencing successful therapeutic outcomes. The majority of women diagnosed with early-stage breast cancer typically undergo surgical excision, often accompanied by adjuvant treatments to minimize the likelihood of disease recurrence. These adjuvant treatment options include the use of radiotherapy, hormonal therapy, chemotherapy and targeted treatments.⁶ Radiotherapy stands as a critical method of treating tumors through the transmission of ionizing radiation energy into the tissues it passes through.

Radiation therapy is a frequently utilized tool in the management of breast cancer at almost every stage.

Whether in the adjuvant setting to reduce the risk of recurrence in patients with involved lymph nodes or sizable tumors, or in advanced stages to alleviate symptoms caused by distant metastasis.⁷⁻¹⁴

Radiation therapy has made substantial progress in recent years, advancing from simple 2-dimensional radiotherapy to more sophisticated 3-dimensional conformal radiotherapy (3DCRT).¹⁵ While 2-dimensional radiation therapy with x-ray planning has yielded impressive outcomes, it falls short in certain aspects. Specifically, it lacks the capability to accumulate detailed dose-volume histogram (DVH) data and to accurately illustrate intricate structures of critical organs, such as the left anterior descending artery (LAD) and the chambers of the heart. Furthermore, achieving improved homogeneity through more advanced compensation techniques is not attainable. In many anatomical regions, such as the head and neck, central prostate, lungs, and the nervous system, 3DCRT has been found to be inferior to intensity-modulated radiation therapy (IMRT).¹⁶

The objective of IMRT is to deliver the highest feasible dose to the intended target while minimizing radiation exposure to critical organs. This is achieved through the modulation of intensity, by breaking the single radiation beam into minute beamlets using multi-leaf collimators.

During adjuvant breast radiotherapy, radiation oncologists express concern regarding the exposure of the lungs or the heart to radiation, especially considering that certain chemotherapeutic and targeted agents utilized in breast cancer management, such as Anthracyclines or HER2 targeted agents, can induce cardiotoxicity. IMRT represents an advanced form of high-precision radiotherapy. It precisely delivers radiation doses to a malignant tumor or specific regions within the tumor. IMRT achieves this by finely modulating or controlling the intensity of the radiation beam across numerous small volumes. This technique enables a more precise conformation of the radiation dose to match the three-dimensional (3-D) shape of the tumor. Additionally, IMRT facilitates the concentration of higher radiation doses on the tumor while concurrently minimizing the dose exposure to adjacent critical normal structures.¹⁷

Utilizing IMRT, radiation dose can be customized to precisely align with the geometric attributes of the breast tumor. However, with IMRT there is a concern regarding the potential for an increased risk of second cancers in individuals who survive over the long term. This heightened risk arises from IMRT's ability to elevate the cumulative dose delivered to normal, healthy tissue. Based on the results of several randomized clinical trials, hypo-fractionated whole-breast irradiation using 3DCRT has become the standard of care following breast conservative surgeries, after successfully demonstrating equivalent impact on disease control and toxicity compared to conventional fractionation, with the added advantage of shortened treatment duration. This study aims to conduct a comparative analysis of dosimetric variations between 3DCRT and IMRT in the treatment of left-sided breast cancer patients with disease involved lymph nodes. The primary objective is to identify which modality provides the highest dose to the target volume while minimizing radiation exposure to organs at risk (OARs).¹⁸⁻²¹

Women diagnosed with node-positive disease have a reduced risk of loco-regional recurrence (LRR) and breast cancer-related mortality when subjected to post-mastectomy radiation therapy (PMRT). This approach has now established itself as the standard of care, particularly for women presenting with four or more positive lymph nodes.

Women with higher risk LRR are expected to derive significant advantages from PMRT, as the survival benefits could be directly related to the reduction in LRR. Nevertheless, uncertainties persist regarding the utilization of PMRT in lower-risk groups. This includes individuals with up to three positive lymph nodes and those diagnosed with node-negative conditions, where the appropriate utilization of PMRT remains a topic of discussion.²²⁻³⁰

Patients and Methodology

Patients

Between January 1st, 2020, and March 30th, 2022, a total of 15 female patients were enrolled from the Alexandria center of radiotherapy (Armed Forces Medical Complex's oncology center). These patients had been diagnosed with histopathologically confirmed breast cancer and their ages ranged from 21 to 65. The study's protocol had obtained approval from Alexandria University, and all the procedures undertaken adhered to the guidelines set forth in the 1983 revision of the 1975 Helsinki Declaration.

(Approval of the Research Ethics Committee of the Medical Research Institute (Ethics code: IORG0008812))

Methodology

A multidisciplinary team comprises various medical specialists, such as medical physicists, oncologists, technologists, and therapists. Each of these professionals plays a vital role in the radiation process, which unfolds through significant steps as outlined below:

Step 1: Scanning and Simulation of Patients in the CT Room

The collaboration between the physicist and technician becomes evident in this stage, involving the preparation and establishment of patient positioning. This is accomplished by utilizing a breast board designed for immobilization. Each patient is positioned in a supine stance, secured to the treatment couch. The patient's arms are externally rotated, abducted, and extended over her head, resting on arm supports.

We noticed that post-surgery, raising the arm above the head and maintaining that position can be difficult and uncomfortable. To address this, the patient's left arm was positioned at a 90-degree angle, with the hand resting on the handle of the arm support. Additionally, a head support was placed under the patient's head to enhance both safety and comfort during the treatment sessions. The patient's head was positioned in a manner so that it faced the opposite breast.

From the patient's mandibular border (mid-neck) to their sternal border (lower chest), encompassing the upper abdomen above the diaphragm, slices were taken. Wires were used to mark surgical scars, breast boundaries and lead markers (2mm lead balls). Since ensuring consistent positioning for each treatment is crucial; durable ink markings are applied to the patient's skin, representing a reference position adjusted using laser-assisted Astor Red alignment. Typically, three-minute ink dots are created through pinpoint ink application, as illustrated in [Figure 1](#). For position assessment, a screening view was captured. During this procedure, patients underwent a non-contrast computerized tomography (CT) scan using a Siemens (SOMATOM scope).³¹ CT simulator, with the images acquired at 3 mm intervals. The images obtained from the CT scanner are transferred to the treatment planning system (TPS) via software (Syngo Multi-Modality, The workplace VE52A, the AG Siemens, Germany).³² Subsequently, these images are imported into the contouring workstation through the local area network system called Digital Imaging and Communications in Medicine (DICOM).

The planning target volume (PTV) and the vital volumes of structures at risk (OARs) are acquired and contoured in accordance with the recommendations of the American Society for Radiation Oncology (ASTRO) and/or the Radiation Therapy Oncology Group (RTOG).

Step 2: Contouring and Designing Plans in the Planning Room

The heart, the left side of lungs, the spinal cord, head of the humerus bone, head of the clavicle, thyroid gland, and right breast were the organs at risk (OARs) with critical volumes. The Radiation Therapy Oncology Group (RTOG) was used to obtain and contour the planning target volume (PTV) breast cancer atlas recommendations.³³ The complete left breast and the supraclavicular nodes were incorporated into the clinical target volume (CTV). Radiation oncology was performed at the Monaco contouring workstation (Elekta company, Inc., the state of Maryland Heights, the United States of America) to define the tumor and additional organs that were at risk on the CT image slices and create the PTV (outlining the contour of the body to the designated target volume to correct for treatment setting up variations and the internal organs movement but not exceeding the external body contour). This PTV took into account the clinical target volume (CTV) in addition to a margin of 0.5–1.0 cm avoidance with a 0.3 cm protection area around the skin.³⁴

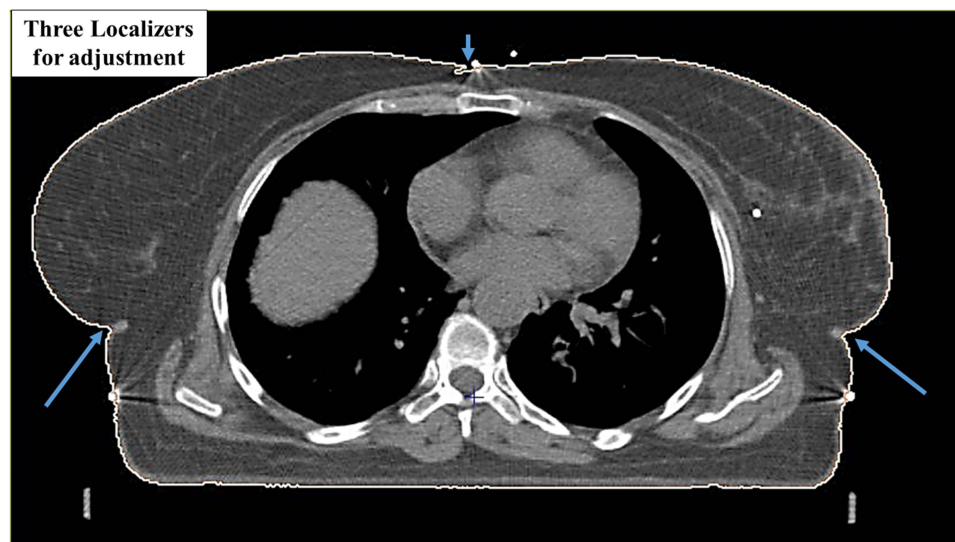


Figure 1 Position of the Markers. The blue arrows represent the three localizers for adjustment.

By using the HD Versa Medical Linear accelerator (LINAC) with a 150-millennium multi-leaf collimator (MLC) and a 6-MV beam, the patients received treatment using the 3DCRT or IMRT procedures with a dose of 50 Gy administered in 25 fractions at a rate of 2 Gy each, administered once day for five days a week.

For calculation in 3D-Conformal RT, the collapsed cone technique has been used.^{35,36} A small part of the lung and the whole breast were included in the irradiated volume when the dose was administered using the two opposed tangential beams technique.

And the nodal area underwent radiation via a direct field anterior-posterior (AP) with a gantry tilted up to 15° to spare the spinal cord and esophagus. In order to prevent junction area overdosing, consideration had been given to how geometrically the SCF field and the breast medial field matched each other.

To cover the wire contouring the breast using two tangential fields applied with the weighted small segments technique (Field in Field) with the MLCs in order to decrease the hot spots and the maximal dose, three fields were created using a mono-isocenter point, as shown in [Figure 2a](#) and [b](#). Tools to improve dosage coverage include plan normalization and equilibrium between field's weightings. The junction (the same point between the ending of the SCF field and the beginning of tangential fields) between the two tangential fields (medial and lateral) and third direct field AP and the coverage were be appeared after calculation process as shown in [Figure 3a](#) and [b](#).

The heart was taken into account using the beam's eye views, and all MLCs were set up to shield a portion of the lung, preserving both organs at the lowest dose possible.

In IMRT, the total PTV was irradiated using the center of the PTV as the sum of two radiation prescriptions, namely the supraclavicular area and the whole breast area, using IMRT 6 MV and only 5 fields (dynamic multi-leaf DMLC) using The Monte Carlo Algorithm.^{37–39} Static with tangential field setup, allowed field arrangement to minimize the exposure to OARs, with 5 fields with different angles of the gantry according to the Digital Reconstructed Radiograph (DRR), It was developed using a method known as inverse planned optimization, and the technique of Monte Carlo was employed for computation using a 6 MV photons beams. The beam configuration or decision-making, as indicated in [Figure 4a](#) and [b](#), was made at the physicist's choice for carrying out the optimal strategy. For each field in each plan, a (DRR) was collected to confirm the patients' position. Using cost-function constraints, the plans were optimized to cover the entire PTV while preserving the organs that were at hazard such as the left lung, the heart, the thyroid gland, the spinal cord, and the heads of clavicle bone and the humerus bone.

The cost functions choices were the target penalty, and maximum dose for the PTV, the cost functions were parallel and serial for the heart and the left lung, and the cost functions were maximum dose, the conformality and quadratic overdose for the patient skin, if we had higher doses than constraints of any organ of the OARs, we could add another

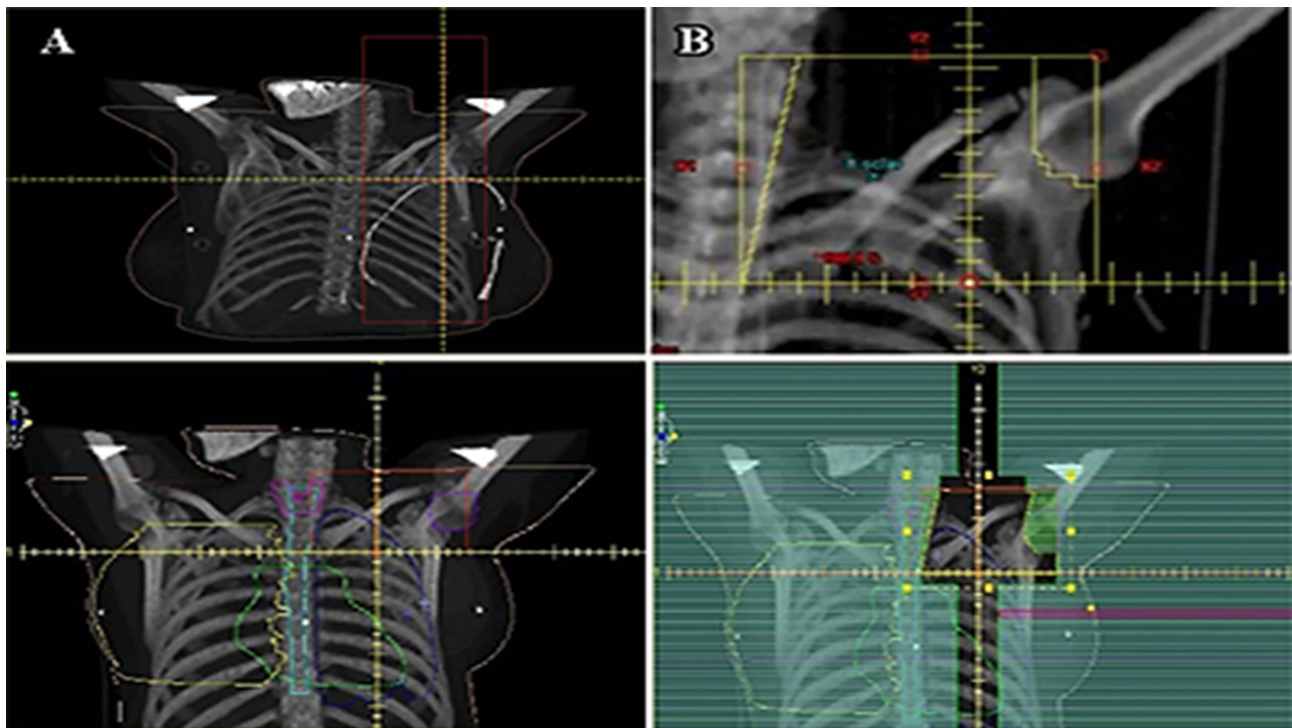


Figure 2 (A) Mono-isocenter point position and Wire contouring; (B) DRR of direct beam of S.C with MLC boundaries.

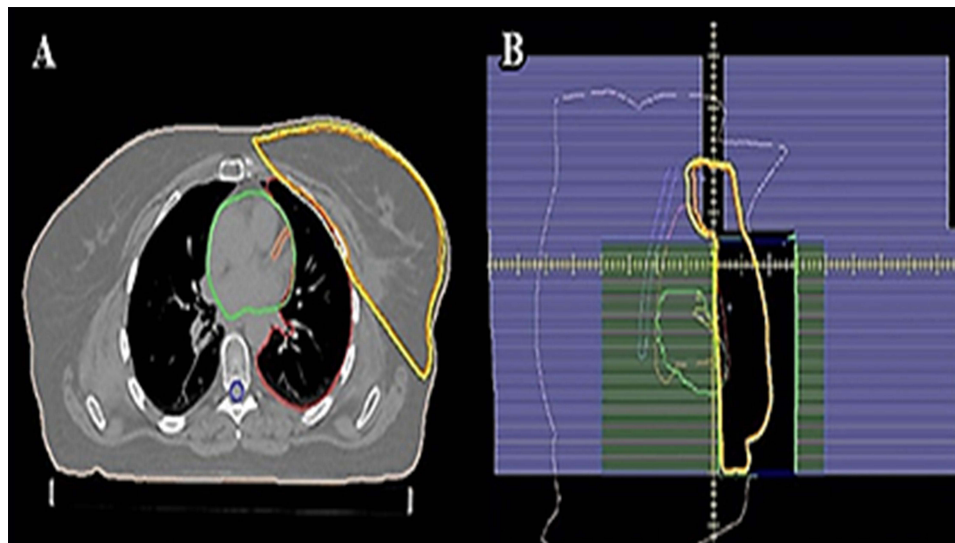


Figure 3 In the case of 3D conformal; the coverage of the distribution of the three-field: (A) the Coverage of tangential beams; (B) the Junction between the SC beam and tangential beams.

cost functions to these organs to achieve our goal which was the PTV coverage within range 95% - 107% and minimum doses to the OARs.

The priority was assigned to the PTV and Organ at Risk (OAR), which was raised gradually as considered necessary until an appropriate compromise between obtaining good coverage and avoiding OARs had been established.

The process of optimization was completed. The main goal was to limit the maximum dose below 107% and achieve coverage for 95% of the PTV with the prescription dose, as shown in Figure 4c and d.

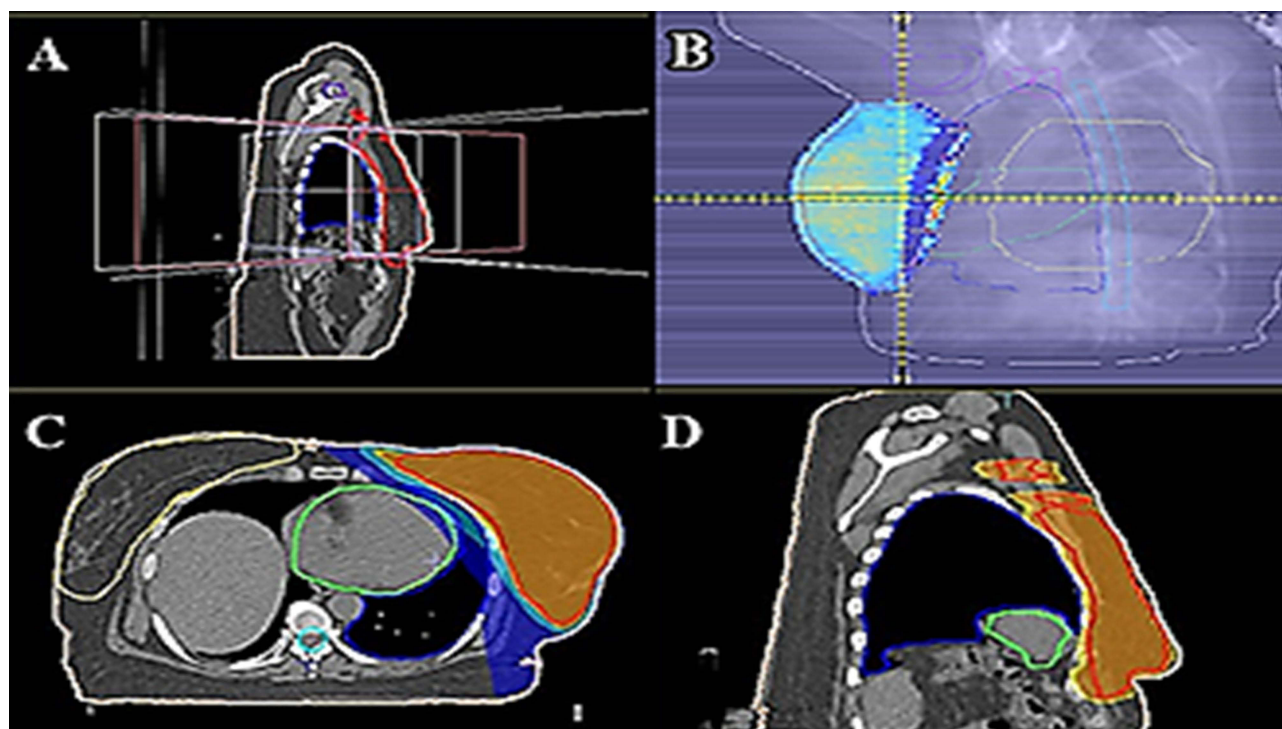


Figure 4 In IMRT technique; (A) Beams Arrangement; (B) DMLC of lateral beam; (C) The Coverage of whole breast; (D) The Total PTV coverage.

Step 3: Choosing the Optimum Plan and Treatment of Patients in Treatment Room

Following a series of plan trials, the most optimal plan among the two techniques was selected, which exhibits improved coverage of the Planning Target Volume (PTV) while ensuring robust protection of the Organs at Risk (OARs). Once finalized, the plans are exported to the MOSAIQ software, preparing them for implementation on the HD Versa linear accelerator.⁴⁰

Dosimetric Analysis

The following objectives were considered when evaluating the collected data using isodose distributions and dose volume charts for each organ in 3DCRT technique and IMRT technique from each plan: The PTV receives the minimal dose coverage of ninety- five percentage of prescribed dose and the maximal dose of 107% of that dose. Each plan's normalization adhered to the ICRU recommendation indicated in Report No. 50. To normalize the data, it was set at 100% using the ICRU point. The determined organs at risk (OAR) and PTV parameters are shown in Table 1 through 5 and Figure 5a–f through 10 a –c. According to RTOG, the organs that are most at risk when radiation is applied to the left breast in order to treat breast cancer include the left side of lungs, the heart, the contralateral breast, and the spinal cord in the lower cervical and dorsal region. The thyroid gland, the head of humerus bone, and the clavicular head bone were among the additional organs at risk that were taken into account in the present study, as shown in Figure 6a, b and Figure 7. Table 1 shows the data collected in this practical work for the PTV of all patients, including the D-min, D-max, D-mean, V95%, V107%, and the global max. Table 2 through 5, on the other hand, show the information gathered for several parameters for the organs at risk that were taken into consideration in this work.

In the current study, Data were fed to the computer and analyzed; Statistical analysis of data was carried out using IBM SPSS Version 22 software package.⁴¹ The normal or non-normal distribution was examined before running any statistical test to compare the PTV or organs at risk. The Paired *t*-test was used for normal distribution and Wilcoxon *z*-test for non-normal distribution. The Kolmogorov–Smirnov (K.S) test verified distribution normality. Range, mean, standard deviation, median, and interquartile range (IQR) were used to characterize quantitative data. Results were considered significant at 5%.

Table 1 Different Values of Doses Delivered to the (PTV) and Some Percentages of Coverage Volumes

Parameter	Data Analysis	3D	IMRT	Test of sig.	P	Sig.
Min Dose(cGy)	Mean± SD	2143.3 ± 1267.7	2682.4 ± 1178.6	t=-1.515	0.049*	S
	Median (IQR, Range)	1965.7 (2078.1, 3801.6)	2907.0 (2081.6, 3407.1)			
Max Dose(cGy)	Mean± SD	5429.1± 70.5	5481.8± 56.2	t=-2.197	0.045*	S
	Median (IQR, Range)	5446.4 (139.9, 213.9)	5481.0 (70.5, 198.60)			
Mean Dose(cGy)	Mean± SD	5053.8± 50.3	5065.4±11.3	z=-0.604	0.556	NS
	Median (IQR, Range)	5034.5 (66.1, 171.1)	5072.3 (44.1, 168)			
V95(%)	Mean± SD	96.2± 1.7	97.9± 1.7	t=-3.137	0.007*	S
	Median (IQR, Range)	96.6 (1.9, 5.9)	98.7 (3.2, 4.9)			
V107(%)	Mean± SD	1.5 ± 2.6	0.9 ± 2.7	t= 0.657	0.145	NS
	Median (IQR, Range)	0.2 (1.6, 8.8)	0.2 (0.2, 10.7)			
Global max(%)	Mean± SD	108.4± 1.1	109.3± 1.1	t=-2.168	0.04*	S
	Median (IQR, Range)	108.5 (2.7, 3.2)	109.4 (1.5, 3.9)			

Notes: t: Paired t- test in case of normal distribution, Z: Wilcoxon test in case of non-normal distribution, Mean dose: 50% of the volume receives the dose, V95: volume covered with 95% of 50 Gy, S: Significant, NS: Not significant, p: p value for comparing between 3D and IMRT and *: Statistically significant at $p \leq 0.05$.

Abbreviations: IQR, Inter quartile range; SD, Standard deviation.

Discussion

The core objectives of radiation therapy include delivering the prescribed dose to the target volume as uniformly as possible, while also striving to limit or minimize any impact on the adjacent healthy tissues. Medical imaging has

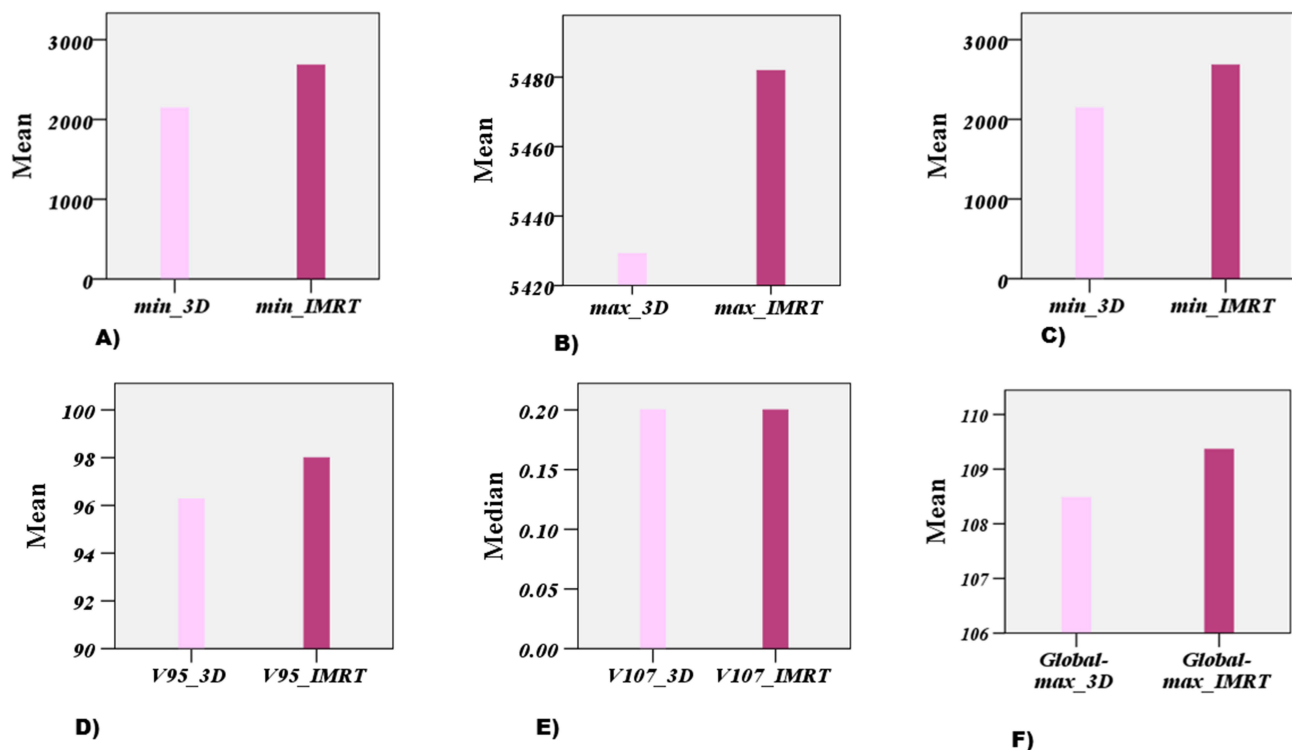


Figure 5 (A–F) Comparison between the different doses and different volumes in the two techniques for PTV (SC nodes plus whole breast). (A) Minimum dose of PTV. (B) Maximum dose of PTV. (C) Mean dose of PTV. (D) Volume of PTV covered by 95% of prescribed dose. (E) Volume of PTV covered by 107% of prescribed dose. (F) Global max of PTV.

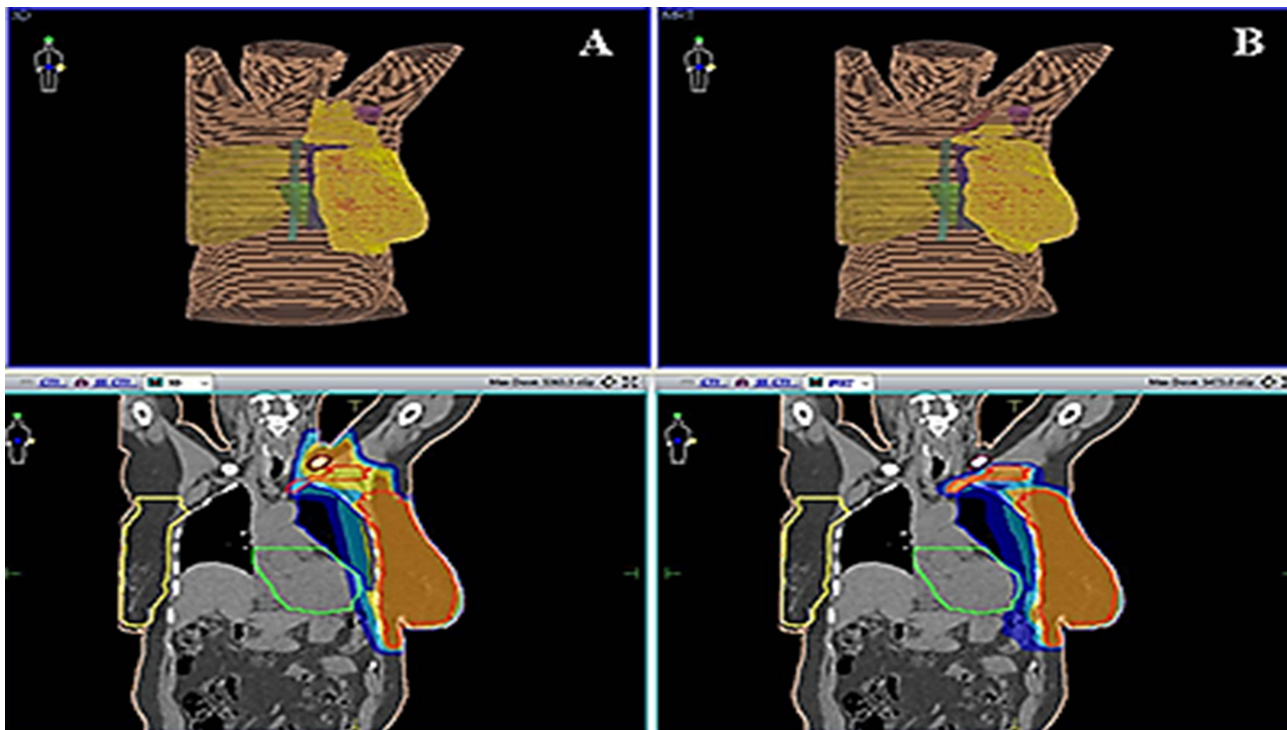


Figure 6 Three-dimensional and coronal comparison between two techniques: (A) In case of 3D conformal technique; (B) In case of IMRT technique.

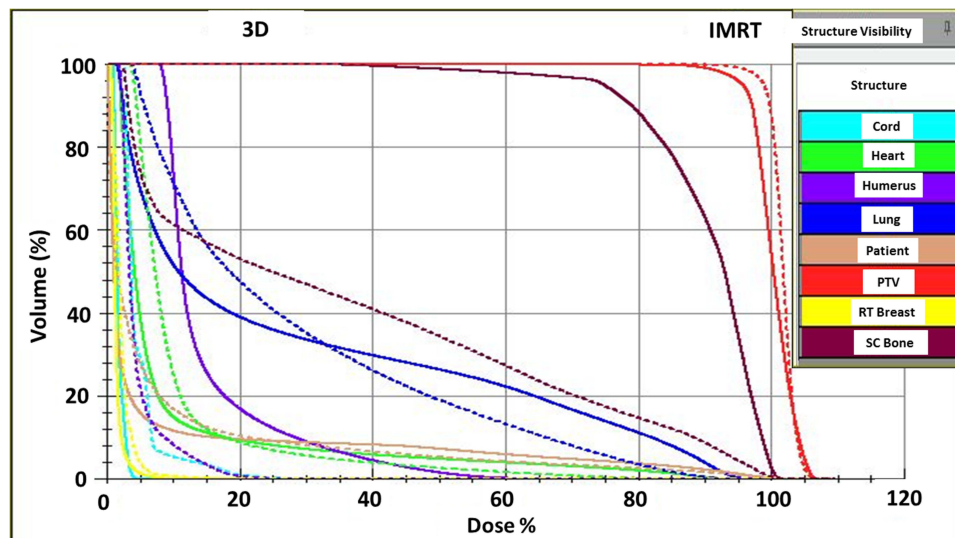


Figure 7 DVH comparison between two techniques in one case.

advanced in recent decades, coupled with remarkable progress in dosimetry software, have enabled the visualization of dosage distribution patterns around target volumes. This has played a pivotal role in attaining the fundamental objectives of radiation therapy.

Consequently, obtaining diverse treatment plans for a single patient became both swift and uncomplicated. The incorporation of additional parameters facilitated informed decision-making, enhancing the likelihood of selecting optimal planning strategies.^{42,43} Key features such as maximum dose (D-max), minimum dose (D-min), and mean

Table 2 Different Values of Doses Delivered to the Ipsilateral Lung & Different Percentage of Volumes of Lt Lung

Parameter	Data Analysis	3D	IMRT	Test of sig.	P	Sig.
Min Dose(cGy)	Mean± SD	110.0 ±156.7	187.2 ± 42.8	z=-2.556	0.011*	S
	Median (IQR, Range)	70.7(14.6, 627.0)	189.7(44.1, 143.1)			
Max Dose(cGy)	Mean± SD	4860.7 ± 249.5	4809.9 ± 197.4	t=0.628	0.540	NS
	Median (IQR, Range)	4949.7(203.0, 793.8)	4754.6(201.1, 744.8)			
Mean Dose(cGy)	Mean± SD	903.3 ± 273.5	1282.2 ± 130.3	t=-6.421	<0.000*	HS
	Median (IQR, Range)	961.4 (379.1, 996.4)	1255.9(211.4, 431.3)			
V20Gy	Mean± SD	16.7 ± 6.1	18.4 ± 4.3	z=-1.079	0.281	NS
	Median (IQR, Range)	18.1(10.5, 19.5)	18.2(8.1, 14.2)			
V80(%)	Mean± SD	5.26 ± 3.1	4.8 ± 5.3	z=-2.215	0.027*	S
	Median (IQR, Range)	5.2(4.2, 11.1)	2.7(5.9, 20.4)			
V95 (%)	Mean± SD	0.4 ± 0.8	0.2 ± 0.4	z=-0.283	0.777	NS
	Median (IQR, Range)	0.34(0.4, 3.5)	0.23(0.2, 1.6)			

Notes: t: Paired t- test in case of normal distribution, Z: Wilcoxon test in case of non-normal distribution, Mean dose: 50% of the volume receives the dose, V20 Gy: volume covered with 20Gy of 50 Gy V80%: volume covered with 80% of 50 Gy, V95%: volume covered with 95% of 50 Gy S: Significant, NS: Not significant, HS: Highly significant, p: p value for comparing between 3D and IMRT and *: Statistically significant at $p \leq 0.05$.

Abbreviations: IQR, Inter quartile range; SD, Standard deviation.

dose (D-mean) applied to each Volume of Interest (VOI) were defined using isodose or cumulative dose-volume histograms (DVHs) and differential curves, allowing for the examination of dose distribution within these plans.⁴⁴⁻⁴⁶

A substantial amount of data may be gathered using these histograms, curves and lines, and this data can then be compared amongst the numerous treatment options used for each treatment case. Radiation dose constraints for the target planning volume, the organs at risk associated with each tumor's location, and any adjacent critical organs that require minimal predetermined doses have been established by the Radiation Therapy Oncology Group (RTOG).⁴⁷⁻⁴⁹

In most cases, the imperative lies in opting for a strategy that ensures both comprehensive coverage of the tumor and optimal protection of surrounding healthy tissues. The present study focused on 15 female breast cancer patients, for whom two treatment plans were devised per patient for the sake of comparison. The initial plan employed a 3D approach, while the alternative plan involved Intensity-Modulated Radiation Therapy (IMRT).

Doses That Were Received for SC Nodes Plus Left Breast (PTV)

Based on the data in the first table, the findings of this study indicated notable disparities between 3-DCRT and IMRT in terms of D-min, D-max, V95%, and globe max values for corresponding Planning Target Volume (PTV) regions. Notably, the D-min received by the left breast with positive nodes was higher with the IMRT approach compared to the 3-DCRT technique. Similarly, the D-max exhibited a slightly higher value in the IMRT plan, although the difference was modest. The two methodologies likewise show no significant difference in the case of the top limit of the required dose, ie, V107%. The mean doses, which equate to 50% of the organ's volume that receives the given dose, are not significant. The hot spot refers to the behavior of the optimization process when a portion of the target region is blocked. It is a significant characteristic that may be used to evaluate the validity of the proposed planning approach and to compare other planning strategies. Whether a patient has a small or large tumor, the 3-D technique is favored because it may be used to shrink hotspots to tolerable levels in 3-D.⁵⁰

Doses That are Received by the Organ at Risk (OARs)

The two techniques in the current Organs at Risk investigation differ greatly from one another. Particularly when treating left breast cancer, the left side of the lung and heart are the only identified organs at risk in most radiation planning procedures. Tables 2–5 illustrate how we broadened this goal in our study to include the spinal cord, humeral head, contralateral breast, the thyroid gland, and clavicular head bone in addition to these two organs.

Table 3 The Different Doses Delivered to the Spinal Cord

Parameter	Data Analysis	3D	IMRT	Test of sig.	P	Sig.
Min Dose (cGy)	Mean± SD	41.7 ± 12.1	80.8 ± 43.1	t=-4.694	<0.000*	HS
	Median (IQR, Range)	39.8	76.0			
Max Dose (cGy)	Mean± SD	646.3 ± 525.6	1118.6 ± 662.9	z=-2.480	0.013*	S
	Median (IQR, Range)	576.1(510, 1972)	809.4 (1274.6, 1991.6)			
Mean Dose (cGy)	Mean± SD	101.9 ± 29.0	298.6 ± 103.0	t=-7.468	<0.000*	HS
	Median (IQR, Range)	97.6(31.3, 124)	308.0 (154.6, 389.5)			

Notes: t: Paired t- test in case of normal distribution, Z: Wilcoxon test in case of non-normal distribution, Mean dose: 50% of the volume receives the dose, S: Significant, HS: Highly significant, p: p value for comparing between 3D and IMRT and *: Statistically significant at p ≤ 0.05.

Abbreviations: IQR, Inter quartile range; SD, Standard deviation.

Table 4 The Different Values of Doses Delivered to the Contralateral Breast

Parameter	Data Analysis	3D	IMRT	Test of sig.	P	Sig.
Min Dose (cGy)	Mean± SD	19.9 ± 11.5	21.0 ± 12.7	t=0.887	0.390	NS
	Median (IQR, Range)	21.1 (14.5, 39.8)	22.9 (18.8, 42.2)			
Max Dose (cGy)	Mean± SD	561.7± 115.0	599.0 ± 288.6	t=-0.868	0.400	NS
	Median (IQR, Range)	550.9 (137, 469.5)	569.3 (336, 1182.2)			
Mean Dose (cGy)	Mean± SD	78.2 ± 16.8	98.5 ± 32.4	t=-2.561	0.023*	S
	Median (IQR, Range)	75.9 (24.0, 61.9)	102.7 (23.4, 144.9)			

Notes: t: Paired t- test in case of normal distribution, Mean dose: 50% of the volume receives the dose, S: Significant, NS: Not significant, p: p value for comparing between 3D and IMRT and *: Statistically significant at p ≤ 0.05.

Abbreviations: IQR, Inter quartile range; SD, Standard deviation.

Table 5 The Different Values of Doses Delivered to the Clavicle Head Bone

Parameter	Data Analysis	3D	IMRT	Test of sig.	P	Sig.
Min Dose (cGy)	Mean± SD	1451.8 ± 85.7	1118.4 ± 93.5	t=1.095	0.016*	S
	Median (IQR, Range)	1204.5 (1100.1, 291.2)	139.9 (101.9, 298.1)			
Max Dose (cGy)	Mean± SD	5095 ±153.9	5104 ± 123.0	t=-1.288	0.049*	S
	Median (IQR, Range)	4940.5 (199.8, 377.5)	4956.8 (165.2, 328.0)			
Mean Dose (cGy)	Mean± SD	4503.1 ± 198.8	1780.7 ± 441.8	t=-1.122	0.034*	S
	Median (IQR, Range)	348.2 (279.6, 759.6)	556.8 (773.5, 1388.1)			

Notes: t: Paired t- test in case of normal distribution, Mean dose: 50% of the volume receives the dose, S: Significant, p: p value for comparing between 3D and IMRT and *Statistically significant at p ≤ 0.05.

Abbreviations: IQR: Inter quartile range, SD: Standard deviation.

The Ipsilateral Lung

Referring to Table 2, the findings of this study showed that, with the exception of V20% and D-max, respectively, the 3-D and IMRT differed significantly in D-min and V80% received by the corresponding volumes of the left lung and a highly significant difference in the D-mean.^{51–57} Volume enclosed by approximately 40% of the approved dose (20Gy) is another parameter that is estimated to allow for more comparisons between the two techniques, but the V80% shows that there is a significant difference between 3D and IMRT, which in the case of 3D is higher than IMRT.

The Heart

Figure 8a–f shows that, with the exception of D-max V80% and V95%, There is an extremely significant difference in both of them in minimum doses and significant differences in D-mean and V20% of the prescribed dose (10Gy) received by the two described procedures. This is because the heart is a key organ that is in danger.^{58–60}

Spinal Cord

There were noticeable disparities between the received radiation doses by the two approaches according to all assessed parameters of the spinal cord, including D-min and D-mean doses. There were highly significant differences in D-max, but in the case of IMRT, the values were higher than the other technique as represented in Table 3.^{61,62}

Head of Humerus

Only significant variations between the two treatment modalities were seen in the radiation doses D-max and D-mean, but no significant variations were seen in D-min, as shown in Figure 9a–c.

Right Breast

Only received, The D-mean revealed considerable variations in the radiation dose treatments, while the remaining parameters revealed no appreciable variations between the two methods as represented in Table 4.⁶³

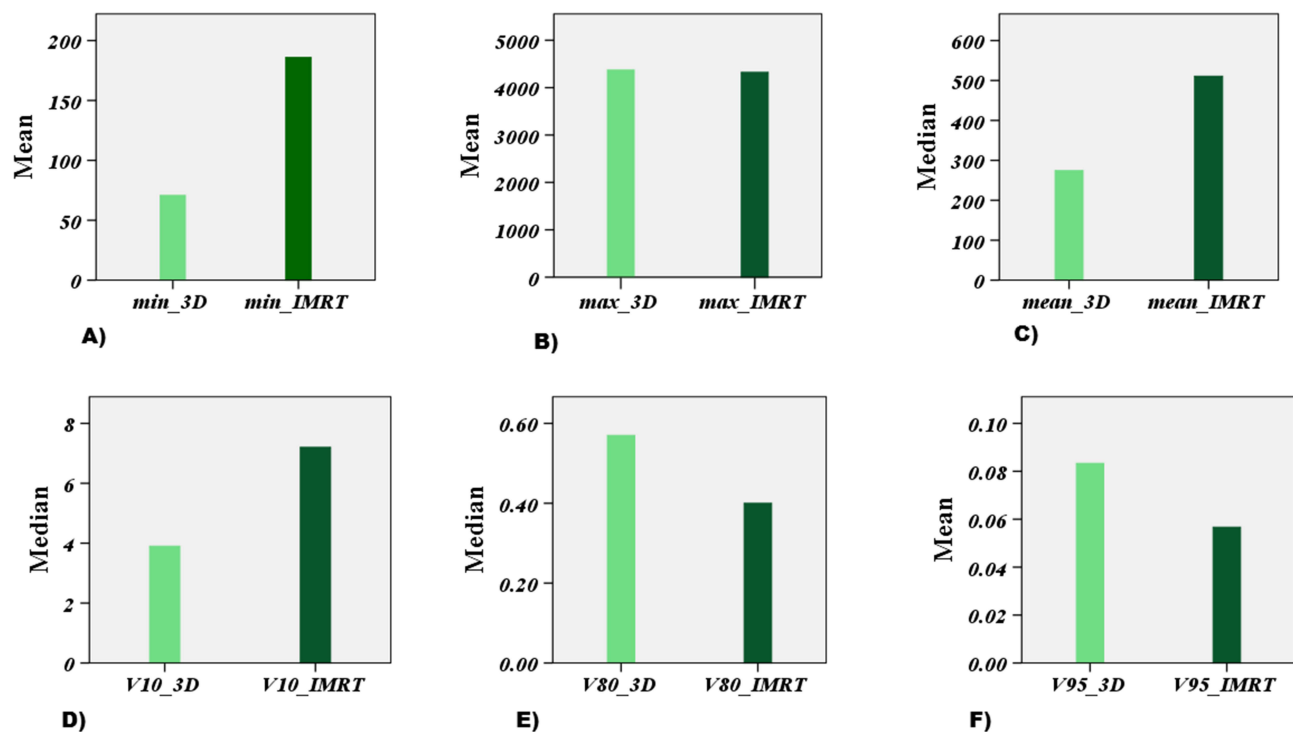


Figure 8 (A–F) Comparison between the different doses and different volumes in the two techniques for the Heart. (A) Minimum dose of Heart. (B) Maximum dose of Heart. (C) Mean dose of Heart. (D) Volume of Heart covered by 10 Gy of prescribed dose. (E) Volume of Heart covered by 80% of prescribed dose. (F) Volume of Heart covered by 95% of prescribed dose.

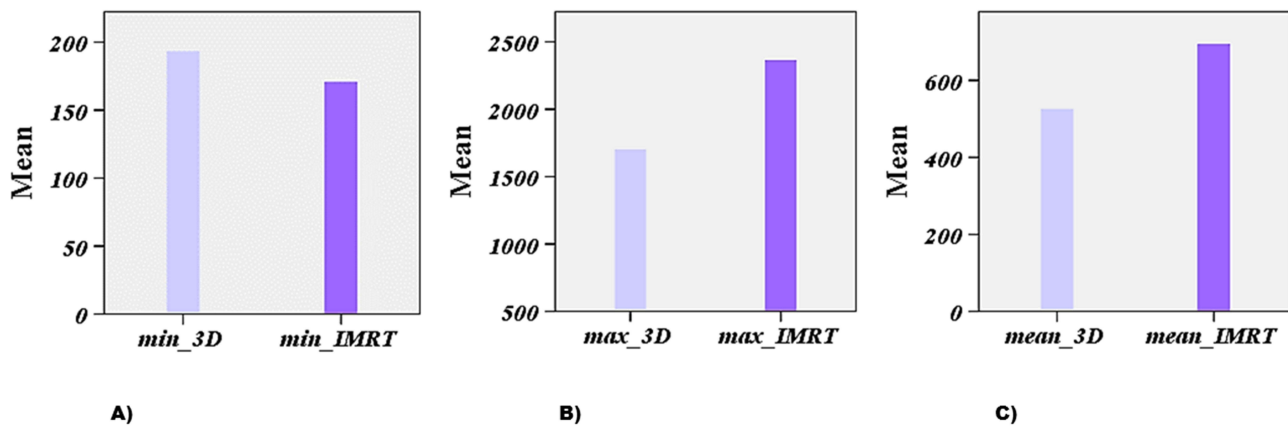


Figure 9 (A–C) Comparison between the Minimum, Maximum and the Mean doses for Head of Humerus bone. (A) Minimum dose of Humerus. (B) Maximum dose of Humerus. (C) Mean dose of Humerus.

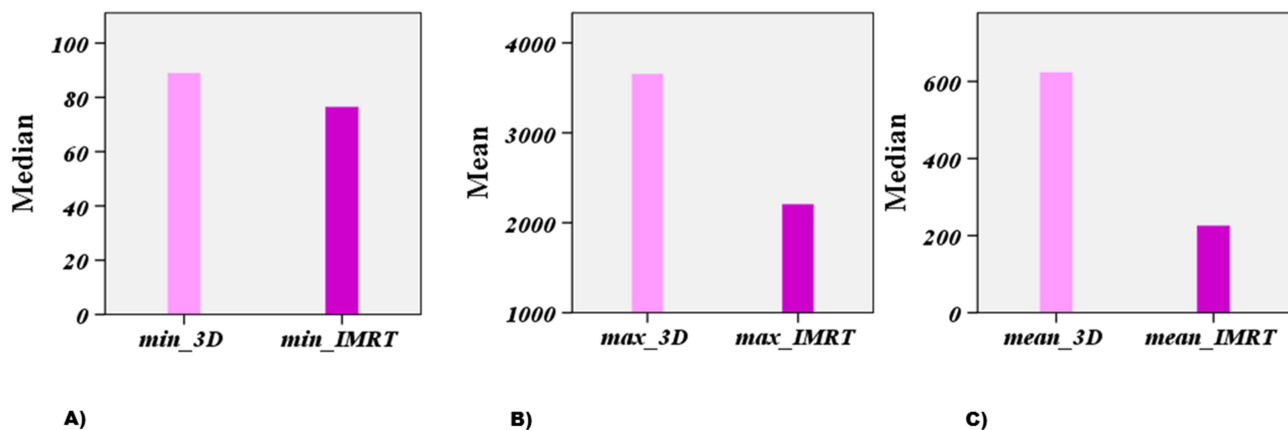


Figure 10 (A–C) Comparison between the Minimum, Maximum and the Mean doses for Thyroid gland. (A) Minimum dose of Thyroid gland. (B) Maximum dose of Thyroid gland. (C) Mean dose of Thyroid gland.

Thyroid Gland

D-max and D-mean were significant, thus radiotherapy for breast cancer provided varied quantities of radiation to the thyroid gland, while D-min was not, and IMRT gave lower values as shown in Figure 10a–c.^{64,65}

Clavicular Head Bone

Although there was a highly significant difference in D-min, and IMRT displayed lower doses than in the case of 3DCRT, the Clavicular head bone received considerably different radiation doses during irradiation for the treatment of breast cancer based on the values of D-max and D-mean as represented in Table 5.^{66–68}

Conclusion

The findings indicated that the IMRT plan’s out-of-field OAR dose increased when compared to 3D-CRT because a larger volume was exposed to lower doses and the total number of MUs in IMRT was higher than in 3D-CRT. This increased probability that a second primary cancer would be induced in out-of-field OAR in IMRT as opposed to 3D-CRT, while the IMRT plan’s infield OAR doses were significantly lower than in 3D-conformal, which decreased the probability of inducing a second primary cancer in out-of-field OAR in IMRT as compared to 3D-CRT.

There is an increasing concern in the potential dangers of second cancer induction for patients receiving curative radiation therapy due to the increasing use of intensity modulated radiation therapy (IMRT) and an associated increase in

whole body exposure to low doses from scattered and leakage radiation. Because many patients with common cancers now have longer life expectancies due to modern procedures like radiotherapy, this issue has gained significance.⁶⁹

To deliver the appropriate radiation dosage in the treatment of breast cancer patients, medical professionals employ two techniques: 3D conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT).^{70,71}

These techniques are facilitated using a medical linear accelerator (LINAC) with a 6 megavolt (MV) power output. The study revealed notable differences in the dosages delivered when utilizing the IMRT technique compared to the 3D technique. The doses delivered during IMRT exposure were significantly higher, reaching around 40% of the dosage administered during the 3D procedure. While certain organs within the irradiated region were protected, the IMRT approach resulted in increased dosages to other areas compared to the 3D technique. The minimal doses received by both the Planning Target Volume (PTV) (left breast with positive nodes) and the left side of the lungs are roughly comparable. However, the dose delivered during IMRT exposure is considerably higher compared to the dose delivered during 3D exposure. Consequently, the recommendation is to avoid utilizing IMRT for cases involving left breasts and, instead, to opt for the 3D approach. In ER+, node-positive breast cancer, the SWOG S8814 trial showed that the predicted cumulative incidence of locoregional recurrences over 8.6 years was 9.7% for patients with a low-risk RS and 16.5% for those with high-risk RS.⁷²

In terms of the number of malignancies induced, the number of probable fatalities, and the number of woman-years of life lost, the estimated risk of radiation-related breast cancer from mammography screening is minimal. The projected benefit of routine mammography screening in terms of lives saved or woman-years of life saved considerably outweighs the risk for women 40 years of age and older in terms of reducing early mortality.⁷³

The authors emphasize that there is currently a lack of evidence supporting the notion that the utilization of inverse IMRT leads to improvements in terms of late toxicity or oncological outcomes for patients with breast cancer. Consequently, the adoption of inverse IMRT remains infrequent. Furthermore, insurance companies often withhold approval for this approach unless there's a specific need related to cardiac avoidance.

Ethical Approval

The study received approval from the Research Ethics Committee of the Medical Research Institute at Alexandria University (Ethics code: IORG0008812), adhering to the guidelines of the 1975 and 1983 Declaration of Helsinki. Written informed consent was obtained from all participating patients.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Youlden DR, Cramb SM, Yip CH, Baade PD. Incidence and mortality of female breast cancer in the Asia-Pacific region. *Cancer Biol Med.* 2014;11. doi:10.7497/j.issn.2095-3941.2014.02.005
2. Shaaban NZ, Ibrahim NK, Saada HN, et al. The Implication of microRNAs as non-invasive biomarkers in 179 Egyptian breast cancer female patients. *Oncol Res.* 2022;30:269–276. doi:10.32604/or.2022.027277

3. Shaban NZ, Ibrahim NK, Saada HN, et al. miR-34a and miR-21 as biomarkers in evaluating the response of chemo-radiotherapy in Egyptian breast cancer patients. *J Radiat Res Appl Sci*. 2022;15:285–292. doi:10.1016/j.jrras.2022.08.001
4. National Cancer Institute. *SEER-Medicare: brief Description of the SEER-Medicare Database*. National Cancer Institute; 2017.
5. Awofeso O, Roberts A, Salako O, et al. Prevalence and pattern of late-stage presentation in women with breast and cervical cancers in Lagos University Teaching Hospital, Nigeria. *Niger Med J*. 2018;59:74. doi:10.4103/nmj.nmj_112_17
6. Moo TA, Sanford R, Dang C, Morrow M. Overview of Breast Cancer Therapy. *PET Clin*. 2018;13:339–354. doi:10.1016/j.cpet.2018.02.006
7. Baskar R, Dai J, Wenlong N, et al. Biological response of cancer cells to radiation treatment. *Front Mol Biosci*. 2014;1. doi:10.3389/fmolb.2014.00024
8. Fortin A, Dagnault A, Blondeau L, et al. The impact of the number of excised axillary nodes and of the percentage of involved nodes on regional nodal failure in patients treated by breast-conserving surgery with or without regional irradiation. *Int J Radiat Oncol Biol Phys*. 2006;65:65. doi:10.1016/j.ijrobp.2005.12.014
9. Yarnold J. Early and Locally Advanced Breast Cancer: diagnosis and Treatment National Institute for Health and Clinical Excellence Guideline 2009. *Clin Oncol*. 2009;21:159–160. doi:10.1016/j.clon.2008.12.008
10. Truong PT, Olivetto IA, Whelan TJ, Levine M. Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional post-mastectomy radiotherapy. *C Can Med Assoc J*. 2004;170:1.
11. Taylor ME, Haffty BG, Rabinovitch R, et al. ACR Appropriateness Criteria® on Postmastectomy Radiotherapy. Expert Panel on Radiation Oncology-Breast. *Int J Radiat Oncol Biol Phys*. 2009;73:997–1002. doi:10.1016/j.ijrobp.2008.10.080
12. Sautter-Bihl ML, Sedlmayer F, Budach W, et al. DEGRO practical guidelines: radiotherapy of breast cancer III - Radiotherapy of the lymphatic pathways. *Strahlentherapie und Onkol*. 2014;190:1.
13. Dragun AE, Huang B, Gupta S, et al. One decade later: trends and disparities in the application of post-mastectomy radiotherapy since the release of the American society of clinical oncology clinical practice guidelines. *Int J Radiat Oncol Biol Phys*. 2012;83:e591–e596. doi:10.1016/j.ijrobp.2012.02.002
14. McGale P, Taylor C, Correa C, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet*. 2014;383. doi:10.1016/S0140-6736(14)60488-8
15. Verhey LJ. Comparison of three-dimensional conformal radiation therapy and intensity-modulated radiation therapy systems. *Semin Radiat Oncol*. 1999;9:78–98. doi:10.1016/S1053-4296(99)80056-3
16. Zakiya ZS, Al Mandhari Z, Ravichandran R, et al. Dosimetric comparison of intensity modulated radiotherapy isocentric field plans and field in field (FIF) forward plans in the treatment of breast cancer. *J Med Phys*. 2013;38. doi:10.4103/0971-6203.106601
17. Radiation Therapy for Breast Cancer: types & Side Effects. Available from: <https://www.cancercenter.com/cancer-types/breast-cancer/treatments/radiation-therapy>. Accessed July 27, 2023.
18. Fisher B, Anderson S, Bryant J, et al. Twenty-Year Follow-up of a Randomized Trial Comparing Total Mastectomy, Lumpectomy, and Lumpectomy plus Irradiation for the Treatment of Invasive Breast Cancer. *N Engl J Med*. 2002;347. doi:10.1056/nejmoa022152
19. Fisher B, Dignam J, Wolmark N, et al. Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-17. *J Clin Oncol*. 1998;16:441–452. doi:10.1200/JCO.1998.16.2.441
20. Hathout L, Hijal T, Théberge V, et al. Hypofractionated radiation therapy for breast ductal carcinoma in situ. *Int J Radiat Oncol Biol Phys*. 2013;87:1058–1063. doi:10.1016/j.ijrobp.2013.08.026
21. Ciervide R, Dhage S, Guth A, et al. Five year outcome of 145 patients with ductal carcinoma in situ (DCIS) after accelerated breast radiotherapy. *Int J Radiat Oncol Biol Phys*. 2012;83:e159–e164. doi:10.1016/j.ijrobp.2011.11.025
22. Yang PS, Chen CM, Liu MC, et al. Radiotherapy Can Decrease Locoregional Recurrence and Increase Survival in Mastectomy Patients With T1 to T2 Breast Cancer and One to Three Positive Nodes With Negative Estrogen Receptor and Positive Lymphovascular Invasion Status. *Int J Radiat Oncol Biol Phys*. 2010;77:516–522. doi:10.1016/j.ijrobp.2009.05.016
23. MacDonald SM, Abi-Raad RF, Alm El-Din MA, et al. Chest Wall Radiotherapy: middle Ground for Treatment of Patients With One to Three Positive Lymph Nodes After Mastectomy. *Int J Radiat Oncol Biol Phys*. 2009;75:1297–1303. doi:10.1016/j.ijrobp.2009.01.007
24. Overgaard M, Nielsen HM, Overgaard J. Is the benefit of postmastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b&c randomized trials. *Radiother Oncol*. 2007;82:247–253. doi:10.1016/j.radonc.2007.02.001
25. Killander F, Anderson H, Rydén S, et al. Radiotherapy and tamoxifen after mastectomy in postmenopausal women - 20 year follow-up of the South Sweden Breast Cancer group randomised trial SSBG II:1. *Eur J Cancer*. 2007;43:2100–2108. doi:10.1016/j.ejca.2007.05.026
26. Bowersox JA. National institutes of health consensus development conference statement: adjuvant therapy for breast cancer, November 1-3, 2000. *J Natl Cancer Inst*. 2001;93. doi:10.1093/jnci/93.13.979
27. Abe O, Abe R, Enomoto K, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;366. doi:10.1016/S0140-6736(05)67887-7
28. Sharma R, Bedrosian I, Lucci A, et al. Present-day locoregional control in patients with T1 or T2 breast cancer with 0 and 1 to 3 positive lymph nodes after mastectomy without radiotherapy. *Ann Surg Oncol*. 2010;17:2899–2908. doi:10.1245/s10434-010-1089-x
29. Taghian AG, Jeong JH, Mamounas EP, et al. Low locoregional recurrence rate among node-negative breast cancer patients with tumors 5 cm or larger treated by mastectomy, with or without adjuvant systemic therapy and without radiotherapy: results from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. *J Clin Oncol*. 2006;24:3927–3932. doi:10.1200/JCO.2006.06.9054
30. Abi-Raad R, Boutrus R, Wang R, et al. Patterns and risk factors of locoregional recurrence in T1-T2 node negative breast cancer patients treated with mastectomy: implications for postmastectomy radiotherapy. *Int J Radiat Oncol Biol Phys*. 2011;81:e151–e157. doi:10.1016/j.ijrobp.2011.01.015
31. Skrzynski W, Ślusarczyk-Kacprzyk W. Measurement of image rotation angle in CT for radiotherapy treatment planning. *J Appl Clin Med Phys*. 2016;17. doi:10.1120/jacmp.v17i4.6203
32. Alkuwari M, Kamal RY, Shelby S, et al. Low-dose CT angiography for evaluation of great vessels and airway in arterial tortuosity syndrome. *Eur Heart J Cardiovasc Imaging*. 2012;13:1054. doi:10.1093/ehjci/jes146
33. Doss V, Healy E, Beyer S, et al. Abstract P3-19-17: radiation of the low axilla in the prone position. *Cancer Res*. 2022;82:17. doi:10.1158/1538-7445.sabcs21-p3-19-17

34. Kim SJ, Kim SK, Kim DH. Comparison of pencil-beam, collapsed-cone and Monte-Carlo algorithms in radiotherapy treatment planning for 6-MV photons. *J Korean Phys Soc.* 2015;67. doi:10.3938/jkps.67.153
35. Knoos T, Ahnesjö A, Nilsson P, Weber L. Limitations of a pencil beam approach to photon dose calculations in lung tissue. *Phys Med Biol.* 1995;40:1411–1420. doi:10.1088/0031-9155/40/9/002
36. Ahnesjö A, Aspradakis MM. Dose calculations for external photon beams in radiotherapy. *Phys Med Biol.* 1999;44:R99–R155. doi:10.1088/0031-9155/44/11/201
37. de Martino F, Clemente S, Graeff C, et al. Dose calculation algorithms for external radiation therapy: an overview for practitioners. *Appl Sci.* 2021;11:6806. doi:10.3390/app11156806
38. Li JS, Pawlicki T, Deng J, et al. Validation of a Monte Carlo dose calculation tool for radiotherapy treatment planning. *Phys Med Biol.* 2000;45:2969–2985. doi:10.1088/0031-9155/45/10/316
39. Wu VV, Teddy KH, Ho CL, Yeung ECY. A comparison between anisotropic analytical and multigrid superposition dose calculation algorithms in radiotherapy treatment planning. *Med Dosim.* 2013;38:209–214. doi:10.1016/j.meddos.2013.02.001
40. Narayanasamy G, Saenz D, Cruz W, et al. Commissioning an Elekta Versa HD linear accelerator. *J Appl Clin Med Phys.* 2016;17:179–191. doi:10.1120/jacmp.v17i1.5799
41. Lee CK. Evolving role of radiation therapy for hematologic malignancies. *Hematol Oncol Clin North Am.* 2006;20:471–503. doi:10.1016/J.HOC.2006.01.020
42. Tseng YD, Ng AK. Hematologic Malignancies. *Hematol Oncol Clin North Am.* 2020;34:127–142. doi:10.1016/J.HOC.2019.08.020
43. Dabaja BS, Ng AK. *Radiation Therapy in Hematologic Malignancies.* Springer International Publishing; 2017. doi:10.1007/978-3-319-42615-0
44. Gibbons JP. *Khan's the Physics of Radiation Therapy.* Lippincott Williams & Wilkins; 2019.
45. Chandarana H, Wang H, Tijssen RHN, Das JJ. Emerging Role of MRI in Radiation Therapy. *J Magn Reson Imaging.* 2018;48:1468. doi:10.1002/JMRI.26271
46. Ghazy SG, Kotb MA, Kodous AS, Al-Sherif DA. Doses delivered to small and large breasts and adjacent organs in left breast cancer patients utilizing 3D and IM radiotherapy. *J Radiat Res Appl Sci.* 2023;16(1):100494. doi:10.1016/j.jrras.2022.100494
47. Coolens C, Gwilliam MN, Alcaide-Leon P, et al. Transformational role of medical imaging in (Radiation) oncology. *Cancers.* 2021;13:2557. doi:10.3390/cancers13112557
48. Dawson LA, Jaffray DA. Advances in image-guided radiation therapy. *J Clin Oncol.* 2007;25:938–946. doi:10.1200/JCO.2006.09.9515
49. Cheng CW, Das JJ. Treatment plan evaluation using dose-volume histogram (DVH) and spatial dose-volume histogram (zDVH). *Int J Radiat Oncol Biol Phys.* 1999;43:1143–1150. doi:10.1016/S0360-3016(98)00492-1
50. Collins SP, Coppa ND, Zhang Y, et al. CyberKnife® radiosurgery in the treatment of complex skull base tumors: analysis of treatment planning parameters. *Radiat Oncol.* 2006;1. doi:10.1186/1748-717X-1-46
51. Yani S. Analisis Kurva Dose Volume Histogram (DVH) pada Teknik 3D Konformal dengan Metode Monte Carlo. *Positron.* 2021;11:19. doi:10.26418/positron.v11i1.44052
52. Pokhrel D, Sood S, Badkul R, et al. Assessment of Monte Carlo algorithm for compliance with RTOG 0915 dosimetric criteria in peripheral lung cancer patients treated with stereotactic body radiotherapy. *J Appl Clin Med Phys.* 2016;17:277–293. doi:10.1120/jacmp.v17i3.6077
53. Hieken TJ, Mutter RW, Jakub JW, et al. A Novel Treatment Schedule for Rapid Completion of Surgery and Radiation in Early-Stage Breast Cancer. *Ann Surg Oncol.* 2016;23:3297–3303. doi:10.1245/S10434-016-5321-1
54. Jannah F, Hariyanto AP, Aisyah, et al. Evaluation of doses distribution in breast cancer mastectomy using SlicerRT. *J Phys Conf Ser.* 2021;1943:012046. doi:10.1088/1742-6596/1943/1/012046
55. Mutter RW, Jethwa KR, Gonuguntla K, et al. 3 fraction pencil-beam scanning proton accelerated partial breast irradiation: early provider and patient reported outcomes of a novel regimen. *Radiat Oncol.* 2019;14. doi:10.1186/S13014-019-1417-7
56. Kataria T, Sharma K, Subramani V, et al. Homogeneity Index: an objective tool for assessment of conformal radiation treatments. *J Med Phys.* 2012;37:207. doi:10.4103/0971-6203.103606
57. Kang Z, Chen S, Shi L, et al. Predictors of heart and lung dose in left-sided breast cancer treated with VMAT relative to 3D-CRT: a retrospective study. *PLoS One.* 2021;16:e0252552. doi:10.1371/JOURNAL.PONE.0252552
58. Finazzi T, Nguyen VT, Zimmermann F, Papachristofilou A. Impact of patient and treatment characteristics on heart and lung dose in adjuvant radiotherapy for left-sided breast cancer. *Radiat Oncol.* 2019;14. doi:10.1186/s13014-019-1364-3
59. Ratoso I, Jenko A, Sljivic Z, et al. Breast Size and Dose to Cardiac Substructures in Adjuvant Three-dimensional Conformal Radiotherapy Compared to Tangential Intensity Modulated Radiotherapy. *Radiol Oncol.* 2020;54:470. doi:10.2478/RAON-2020-0050
60. Tanaka O, Ono K, Taniguchi T, et al. Dosimetric evaluation of the heart and left anterior descending artery dose in radiotherapy for Japanese patients with breast cancer. *J Radiat Res.* 2020;61:134. doi:10.1093/JRR/RRZ087
61. Zheng BM, Dong XX, Wu H, et al. Dosimetry Comparison between Volumetric Modulated Arc Therapy with Rapid Arc and Fixed Field Dynamic IMRT for Local-Regionally Advanced Nasopharyngeal Carcinoma. *Chinese J Cancer Res.* 2011;23:259. doi:10.1007/S11670-011-0259-0
62. Kovach AE. Rubin's Pathology, Clinicopathologic Foundations of Medicine. *Am J Surg Pathol.* 2008;32:1427. doi:10.1097/pas.0b013e31816d7194
63. van der Laan HP, Korevaar EW, Dolsma WV, Maduro JH, Langendijk JA. Minimising contralateral breast dose in post-mastectomy intensity-modulated radiotherapy by incorporating conformal electron irradiation. *Radiother Oncol.* 2010;93:235–240. doi:10.1016/j.radonc.2009.12.015
64. Johansen S, Reinertsen KV, Knutstad K, et al. Dose distribution in the thyroid gland following radiation therapy of breast cancer—a retrospective study. *Radiat Oncol.* 2011;6:1–7. doi:10.1186/1748-717X-6-68/TABLES/2
65. Smith GL, Smith BD, Giordano SH, et al. Risk of hypothyroidism in older breast cancer patients treated with radiation. *Cancer.* 2008;112:1371–1379. doi:10.1002/CNCR.23307
66. Supakalin N, Pese M, Thamronganantasakul K, et al. Comparison of different radiotherapy planning techniques for breast cancer after breast conserving surgery. *Asian Pacific J Cancer Prev.* 2018;19:2929–2934. doi:10.22034/APJCP.2018.19.10.2929
67. Dellapasqua S, Bagnardi V, Balduzzi A, et al. Outcomes of patients with breast cancer who present with ipsilateral supraclavicular or internal mammary lymph node metastases. *Clin Breast Cancer.* 2014;14:53–60. doi:10.1016/J.CLBC.2013.09.008
68. Abo-Madyan Y, Aziz MH, Aly M, et al. Second cancer risk after 3D-CRT, IMRT and VMAT for breast cancer. *Radiother Oncol.* 2014;110. doi:10.1016/j.radonc.2013.12.002

69. Jagsi R, Barlow W, Woodward WA, et al. Radiotherapy use and locoregional recurrence rates on SWOG 1007, a US cooperative group trial enrolling patients with favorable-risk node-positive breast cancer. *Int J Radiat Oncol Biol Phys.* 2022;114(Suppl):43. doi:10.1016/j.ijrobp.2022.07.410
70. Elgendy RA, Attalla EM, Elnaggar MA, Kotb MA. Evaluation of The Second Cancer's Risk In Conformal Therapy And Intensity Modulated Radiotherapy For The Organs Inside The Primary Radiation Fields. *IOSR J Appl Phys.* 2016;8:44–52.
71. Demircan NV, Bese N. New Approaches in Breast Cancer Radiotherapy. *Eur J Breast Health.* 2024;20(1):1–7. doi:10.4274/ejbh.galenos.2023.2023-11-4
72. Marrazzo L, Meattini I, Simontacchi G, Livi L, Pallotta S. Updates on the APBI-IMRT-Florence Trial (NCT02104895) Technique: from the Intensity Modulated Radiation Therapy Trial to the Volumetric Modulated Arc Therapy Clinical Practice. *Pract Radiat Oncol.* 2022;13:28–34. doi:10.1016/j.ppro.2022.05.010
73. Yaffe MJ, Mainprize JG. Risk of Radiation-induced Breast Cancer from Mammographic Screening. *Radiology.* 2011;258:98–105. doi:10.1148/radiol.10100655

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