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Dosimetric Comparison between 3D-Conformal Radiotherapy and Volumetric Modulated Arc Therapy for the Heart in Left-Sided Breast Irradiation

Elwan A[1], Hafez AM[2], Elhaggar AF[3], Mostafa E[4], El-Sayed NG[1]

[1] Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[2] Clinical oncology, Alahrar Oncology Center, Zagazig, Egypt
[3] Medical Physics, Kasr Al-Ainy Center of Radiation Oncology and Nuclear Medicine (NEMROCK), Cairo, Egypt
[4] Medical Radiation Physics, International Medical Center, Zagazig University, Cairo, Egypt

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Abstract:

Background: After breast-conserving surgery, irradiation to whole breast lowers the rate of recurrence. Deep inspiration breath-hold technique is the most effective way to lower radiation doses to the heart and if it is not accessible, alternative options like intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT) or three-dimensional conformal radiation therapy(3D-CRT) must be chosen. We aimed for comparing the dosimetric measurements affecting the target and organs-at-risk (OAR) in VMAT+SIB and 3D-CRT+SIB.

Methods: A comprehensive sample of 54 were included in the study. Patients were allocated into 2 Arms, arm A received 3D-CRT+SIB, arm B received VMAT+SIB, each arm received WBI 40 Gy/15 fractions with SIB 8 Gy/15 fractions. Comparison of both arms, treatment plans evaluation, Dose Volume Histograms especially dose constrains to heart and coronary artery, target dose coverage, conformity index, monitor units' number and homogeneity index were analyzed.

Results: A significant difference between two groups was seen regarding to target coverage dosimetry. VMAT demonstrated higher mean CTV than 3D-CRT. Also, a significant difference was noted regarding OAR dosimetry, as the VMAT was associated with higher doses to the heart, right lung, and right breast. In contrast, the 3D-CRT delivered a higher minimum, maximum and mean left anterior descending coronary artery (LAD) doses. The VMAT demonstrated significantly higher CI and MU but HI among both groups did not differ significantly.

Conclusion: multi-fields and arcs arrangements (VMAT) considerably decreased the doses to the LAD and improved doses to the target, although approaches with tangential fields arrangement (3DCRT) provided better OARs dosimetry.

Key words: Left breast cancer, irradiation, 3D-CRT, VMAT, dosimetry.

Authors Information:

Amira Elwan Mohamed
Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
email:essawy1951@gmail.com

Asmaa Magdy Hafez
Clinical oncology, Alahrar Oncology Center, Zagazig, Egypt
email:asmaamagdyy1@gmail.com

Ahmed Farag Elhaggar
Medical Physics, Kasr Al-Ainy Center of Radiation Oncology and Nuclear Medicine (NEMROCK), Cairo, Egypt
email:Ahmedfaragelhaggar91@gmail.com

Emad Mostafa
Medical Radiation Physics, International Medical Center, Zagazig University, Cairo, Egypt
email:emadrabo@yahoo.com

Nehal Gamal El-Sayed
Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
email:nehalg816@gmail.com

Corresponding Author:
Amira Elwan Mohamed
Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
email:essawy1951@gmail.com

Introduction:

After undergoing breast-conserving surgery (BCS), irradiation to whole breast significantly lowers the rate of recurrence and relatively lowers the risk of breast cancer death [1]. However, there is a greater likelihood of radiation-induced coronary artery disease (RICAD) when doses of radiation are administered to the heart and/or cardiac segments. To reduce radiation doses to these structures, radiation oncologists have to decide on the best irradiation method. The deep inspiration breath-hold (DIBH) technique is the most effective way to lower the doses of radiation to the heart. By, physically, removing the heart away from the chest wall, DIBH successfully lowers the radiation doses delivered to the heart [2, 3]. According to EORTC-

Radiation Oncology Group, 19% of institutions (1–30% of patients) could employ breath-hold techniques [4]. If the DIBH technique is not accessible at an institution, a radiation oncologist must choose alternative options like intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), or conventional three-dimensional conformal radiation therapy (3D-CRT). Regarding the identified link between radiation dose to the LAD and long-term cardiac morbidity, VMAT's considerably lower mean dose to the LAD than 3DCRT is clinically important. VMAT's role as an optimal treatment strategy is further supported by the substantial correlation between the reduction of LAD dosage and the lower risk of RICAD and other late cardiac problems [5]. In patients with left-sided breast cancer, we aimed for comparing the dosimetric measurements affecting the target and critical organs-at-risk (OARs) in VMAT+ simultaneous integrated boost (SIB) and 3D-CRT+SIB.

Patients and Methods:

Design, approval & patient eligibility

This dosimetric planning comparative study included 54 patients. Assuming that mean + SD of dosimetric parameter of the heart by VMAT versus 3D-CRT was 2.9+1.7 versus 1.9+ 0.7, so sample size will be 54 patients (27 in each group) using open EPI, CI95%. Patients were allocated into 2 Arms each compromising 27cases, arm A received 3D-CRT-SIB, arm B received VMAT-SIB, each arm received whole breast irradiation (WBI) 40 Gy/ 15 fractions with simultaneous integrated boost 8 Gy/15 fractions. Patient assignment was based on the order of presentation without any influence from investigators. We confirmed the similarity of baseline demographics and clinical features between groups in all characteristics including separation, breast volume, bra size and tumor’s location as shown in table (1), indicating minimal risk of allocation bias. All plans were created using the same contouring protocols, dose-prescription, and organ-at-risk constraints to ensure consistency between groups. Thus, the results reflect the real-world dosimetric performance of both techniques as implemented in clinical practice. Inclusion criteria were cases of left sided cancer breast who underwent BCS while exclusion criteria were cases with incomplete data in medical records, cases underwent modified radical mastectomy, women who were pregnant, possibly pregnant, or breast-feeding and women who wished to become pregnant during the treatment course. Every case that attended the department during the study period and fulfilled the criteria for eligibility was incorporated into the study. Written informed consent was given by each participant. The study was carried out in compliance with the World Medical Association's Code of Ethics (Declaration of Helsinki) for researches involving humans. The Faculty of Medicine International Review Board (IRB) and the Zagazig University Ethical Committee approved this study (Ethics code: ZU- IRB # 151/25-Feb-2024).

Target Coverage, planning and plan evaluation:

All patients underwent most comfortable treatment positioning, simulation and fixation in the supine position on breast board and underwent computed tomography (CT), CT images were taken as 3-5 mm axial slices then were electronically transferred through CD applications or directly to the treatment planning system (TPS) Elekta precise Plan Release 2.12,151204 in 3DCRT and Elekta versa hd Monaco plan version 5.51.10 in VMAT. A radiation oncologists contoured the patients using reference atlas outlines to ensure precise delineation and minimize interobserver variations. Comparison of both arms, treatment plans evaluation and Dose Volume Histogram DVHs especially dose constrains to heart and coronary artery were analyzed.

Clinical Target Volume (CTV): the whole breast includes the lumpectomy site. Cranial: Clinical reference + insertion of the second rib. Caudal: Loss of visible breast tissue on CT + clinical reference. Anterior: Skin. Posterior: Omit the ribs, chest wall muscles and pectoralis muscles. Medial: Junction between sternum and ribs. Lateral: Mid-axillary line + clinical reference, excluding latissimus dorsi muscle. Lumpectomy site: Seroma and surgical clips (placed in the lumpectomy cavity during surgery) with the help of pre-radiotherapy sonar or mammography guide Fig (3). Target volume and OAR delineation was done according to RTOG and reference atlas contours in order to reduce interobserver variation and achieve accurate delineation.

When we subtracted 5mm from the body contour and added a 6 mm margin to the CTV, the planning target volume (PTV) was produced. The following OARs were delineated: heart, both lungs {ipsilateral lung (IL) and contralateral lung (CL)}, contralateral breast (CB) and a left anterior descending coronary artery (LAD). To delineate LAD, a 4 mm brush tool was used. The main anatomical landmarks for the LAD artery are the anterior interventricular groove. During radiotherapy planning, the LAD is identified on planning CT scans by its location running from the base of the heart down to the apex, situated anterior to the interventricular septum [6].

The planning metrics’ objectives included: PTV coverage by the 95% isodose (PTV95%) ≥95%, keep mean heart dose (MHD) < 6 Gy, IL V20 (V20IL) <25%, mean CL dose <4 Gy, mean CB dose <3 Gy and mean LAD dose < 22Gy [7, 8 and 9]. The dose reaching OAR was minimized by shielding them using MLC without interference with the target coverage. The 3D-CRT technique included two tangential open and wedged beams of 6 or 15 MV. Field in field (FIF) plan was created, when be needed, utilizing multi-leaf collimators (MLCs) to eliminate any hot spots while maintaining the same gantry and collimator angles as the 3DCRT technique. VMAT technique used two partial arcs (2pVMAT) of 6MV and agility 120 MLC with 5mm leaf width. A Monte Carlo technique was used to calculate the VMAT plans.

In 3DCRT, patient positioning is typically verified using portal imaging to confirm field alignment with bony landmarks. In VMAT, setup verification often relies on cone-beam CT (CBCT), which provides 3D soft-tissue visualization, allowing for more precise assessment of target coverage and OAR positioning. Both approaches aim to reduce setup errors, improve reproducibility, and enhance treatment accuracy across fractions.

Plan quality indices included the target dose coverage, conformity index (CI), the monitor units' number (MU) and homogeneity index (HI). The dose homogeneity is better when the HI is smaller (nearer to 1) [7]. HI=D2%-D95% / D50%, where D2% defines the dose to 2% volume of the PTV, D95% denotes the dose to 95% volume of the PTV, and D50% indicate the dose to 50% volume of the PTV. CI indicates how closely the recommended isodose volume conforms the target's parameters. CI has a range of 0 to 1, with 1 being the optimal value. CI was calculated as follows: V100% prescribed dose for PTV/ volume of PTV where, PTV-V100% is the volume of the target that 100% of the dose covers.

Statistical analysis:

IBM Corp. Released in 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp was was used to collect, tabulate, and statistically analyze all of the data. The Shapiro-Wilk test was used to test for normality in quantitative data. For qualitative variables which were presented by number and percentage, Chi-square test was used to assess the statistical difference between qualitative variables. For quantitative continuous variables which were presented by mean + SD, T-test and Mann-Whitney test were used to assess the statistical significance of the difference between two population means. Every test had two sides. A p-value of ≤ 0.05 was considered statistically significant, and a p-value of > 0.05 was considered statistically insignificant.

Results:

Fifty four patients diagnosed with breast cancer on the left side were included in this study, equally allocated to the 3D conformal radiotherapy (3D CRT) group (n=27) and the volumetric modulated arc therapy (VMAT) group (n=27). The participants in the 3D CRT group had mean age of 44.2 ± 7.42 years, while in the VMAT group; the mean age was 44.3 ± 7.29 years. Demographic data and tumor characteristics, including histology, grade, stage, and receptor status were equally distributed over the groups (all P>0.05) .Also, therapeutic regimens (chemotherapy, radiation target volume, hormonal therapy) were similarly balanced (all P>0.05) between the groups (Table 1).

A significant difference between the two groups was seen in regards to target coverage dosimetry (Gy). The VMAT group demonstrated statistical significant higher maximum (45.95 ± 0.75 vs. 45.3 ± 0.91 Gy, P=0.006) and mean Clinical target volume (CTV) doses than 3DCRT (40.92 ± 0.37 vs. 39.23 ± 0.34 Gy, P<0.001). Additionally, VMAT was associated with elevated mean boost doses (47.82 ± 0.45 vs. 47.13 ± 1 Gy, P=0.002), maximum (43.12 ± 0.47 vs. 42.73 ± 0.46 Gy, P=0.004) and mean left SC doses (40.64 ± 0.86 vs. 39.98 ± 0.99 Gy, P=0.01) (Table2).

Also, a significant difference was noted regarding OAR dosimetry (Gy), as the VMAT group was associated with a significantly higher doses to critical organs, including the heart, right lung, and right breast, as the VMAT group demonstrated higher mean left lung (8 ± 2.3 vs. 6.01 ± 2.48 Gy, P=0.004), minimum (1.19 ± 0.14 vs. 0.99 ± 0.28 Gy, P=0.002) and mean heart doses (4.6 ± 0.18 vs. 4.39 ± 0.28 Gy, P=0.003). Inspite there is a statistical significance difference in MHD but it is clinically negligible. Also, the VMAT delivered a higher minimum (0.81 ± 0.19 vs. 0.69 ± 0.12 Gy, P=0.01), maximum (4.46 ± 0.95 vs. 3.78 ± 0.58 Gy, P=0.003) and mean right lung doses (0.99 ± 0.17 vs. 0.88 ± 0.08 Gy, P=0.008). Furthermore, the VMAT delivered a higher maximum (8.51 ± 1.64 vs. 4.88 ± 0.37 Gy, P<0.001) and mean right breast doses (1.39 ± 0.38 vs. 1.16 ± 0.26 Gy, P=0.01). In contrast, the 3D CRT delivered a higher minimum (2.82 ± 0.99 vs. 2.1 ± 1.01 Gy, P=0.01), maximum (32.16 ± 4.56 vs. 28.07 ± 4.29 Gy, P=0.001) and mean LAD doses (14.65 ± 5.42 vs. 11.12 ± 4.08 Gy, P=0.009) (Table 3).

In terms of technical metrics, the VMAT group demonstrated significantly higher CI (0.95 ± 0.06 vs. 0.89 ± 0.09, P=0.006) and MU (502.4 ± 125.5 vs. 365.2 ± 88.9, P<0.001). However, HI among both groups did not differ significantly (P > 0.05) (Table 4). The interval plots demonstrated a statistically significant difference, with the VMAT group demonstrating higher mean heart doses (460 ± 18.72 cGy) compared to the 3D CRT group (439 ± 28.8 cGy) (P=0.003). While the 3D CRT group delivered significantly higher mean LAD doses (1465 ± 542.8 cGy) compared to the VMAT group (1112 ± 408.6 cGy) (P=0.009) (Figures 1&2).

Table 1: Tumor characteristics and therapeutic data among the studied groups:

Variables		3D CRT (n=27)	VMAT (n=27)	P Value
Age *(years)*	*Mean ± SD*	44.2 ± 7.42	44.3 ± 7.29	
	Range	(33 – 55)	(33 – 54)	0.96[1]
Menopausal status*(n. %)*	Premenopausal	16 (59.25%)	18 (66.66%)	
	Postmenopausal	11 (40.74%)	9 (33.33%)	0.57[2]
Residence *(n. %)*	Rural	14 (51.85%)	11 (40.74%)	
	Urban	13 (48.14%)	16 (59.25%)	0.41[2]
Type of BCS	Lumpectomy	22 (81.48%)	20 (74.07%)	
	Quadrantectomy	5 (18.51%)	7 (25.92%)	0.51[3]
Tumor location	LOQ	6 (22.22%)	4 (14.85%)	
	UIQ	7 (25.92%)	7 (25.92%)	
	UOQ	14 (51.85%)	16 (59.25%)	0.82[2]
Tumor grade	Grade I	9 (33.33%)	7 (25.92%)	
	Grade II	12 (44.44%)	12 (44.44%)	
	Grade III	6 (22.22%)	8 (29.62%)	0.77[2]
Lymphovascular invasion	Absent	19 (70.37%)	17 (63%)	
	Present	8 (29.62%)	10 (37%)	0.56[2]
Perineural invasion	Absent	19 (70.37%)	17 (63%)	
	Present	8 (29.62%)	10 (37%)	0.56[2]
Histology	IDC	23 (85.18%)	27 (100%)	
	ILC	4 (14.81%)	0 (0%)	0.11[3]
AJCC T stage	T1	8 (29.62%)	7 (25.92%)	
	T2	16 (59.25%)	18 (66.66%)	
	T3	3 (11.11%)	2 (7.4%)	0.85[3]
AJCC N stage	N0	4 (14.81%)	5 (18.51%)	
	N1	17 (63%)	14 (51.85%)	
	N2	2 (7.4%)	4 (14.81%)	
	N3	4 (14.81%)	4 (14.81%)	0.82[3]
Estrogen receptor (ER)	Negative	6 (22.22%)	4 (14.81%)	
	Positive	21 (77.77%)	23 (85.18%)	0.73[3]
Progesterone receptor (PR)	Negative	13 (48.14%)	11 (40.74%)	
	Positive	14 (51.85%)	16 (59.25%)	0.58[2]
HER2 Neu	Negative	22 (81.48%)	24 (88.88%)	
	Positive	5 (18.51%)	3 (11.11%)	0.71[3]
Ki-67	Low	20 (74.07%)	19 (70.37%)	
	High	7 (25.92%)	8 (29.62%)	0.76[2]
Chemotherapy	None	8 (29.62%)	7 (25.92%)	
	AC	7 (25.92%)	8 (29.62%)	
	AC/Taxol	12 (44.44%)	12 (44.44%)	0.94[2]
Radiation target volume	Whole breast	3 (11.11%)	6 (22.22%)	
	Whole breast, SC	24 (88.88%)	21 (77.77%)	0.47[3]
Breast volume (cm^3)	*Mean ± SD*	1790.8±236.6	1786.2±194.8	0.9[1]
Bra size	*Mean ± SD*	48.5±3.41	50±3.65	0.12[1]
Separation	*Mean ± SD*	22.01±3.03	23.13±3.41	0.18[1]
Hormonal	None	3(11.11%)	4 (14.81%)	
	Anstrazol	5 (18.51%)	5 (18.51%)	
	Letrozole, Zoladex	11 (40.74%)	9 (33.33%)	
	Tamoxifen, Zoladex	8 (29.62%)	9 (33.33%)	0.96[3]
Trastuzumab	No	21 (77.77%)	23 (85.18%)	
	Yes	6 (22.22%)	4 (14.81%)	0.73[3]
Pertuzumab	No	23 (85.18%)	25 (92.59%)	
	Yes	4 (14.81%)	2 (7.4%)	0.67[3]

[1]Independant sample t-test,[2]Chi-square test, [3]Fisher exact test, Non-significant: $P > 0.05$, Significant: $P \leq 0.05$

Table 2: Target coverage Dosimetry (Gy) among the studied groups:

Variables		3D CRT (n=27)	VMAT (n=27)	P Value
Min CTV	*Mean ± SD*	25.22 ± 5.86	26.02 ± 4.47	
	Range	(18.50 – 33.50)	(19.73 – 30.92)	0.58
Max CTV	*Mean ± SD*	45.30 ± 0.91	45.95 ± 0.75	
	Range	(44.22 – 47.22)	(43.66 – 48.45)	0.006
Mean CTV	*Mean ± SD*	39.23 ± 0.34	40.92 ± 0.37	
	Range	(37.48 – 39.91)	(40.13 – 41.40)	<0.001
Min boost	*Mean ± SD*	34.91 ± 2.40	35.87 ± 2.83	
	Range	(32 – 38.83)	(34– 43.76)	0.19
Max boost	*Mean ± SD*	50.34 ± 0.71	50.74 ± 1.30	
	Range	(42.42 – 55.46)	(49.91 – 51.46)	0.17
Mean boost	*Mean ± SD*	47.13 ± 1	47.82 ± 0.45	
	Range	(45.49 – 49.58)	(46.76 – 48.36)	0.002
Min left SC (Supra	*Mean ± SD*	33.87 ± 1.19	34.31 ± 1.24	0.19
clavicular LN)	*Range*	(28.90 – 36.99)	(31.99 – 38.77)	
Max left SC	*Mean ± SD*	42.73 ± 0.46	43.12 ± 0.47	0.004
	Range	(41.09 – 43.84)	(42.39 – 44.81)	
Mean left SC	*Mean ± SD*	39.98± 0.99	40.64 ± 0.86	
	Range	(37.49 – 41.19)	(38.78 – 42.03)	0.01

**Independent sample t-test, Non-significant: P >0.05, Significant: P ≤0.05*

Table 3: Organs at risk dosimetry (Gy) among the studied groups:

Variables		3D CRT (n=27)	VMAT (n=27)	P Value
Min left lung	*Mean ± SD*	2.36 ± 0.95	2.94 ± 1.14	
(ipsilateral) IL	*Range*	(1.12 – 4)	(1.13 – 4.21)	0.06
Max left lung	*Mean ± SD*	42.97 ± 3.40	43.56 ± 3.63	
(ipsilateral) IL	*Range*	(39 – 49.48)	(38.37 – 49.09)	0.54
Mean left lung	*Mean ± SD*	6.01 ± 2.48	8± 2.3	
(ipsilateral) IL	*Range*	(3.13 – 9.33)	(4.69 – 11.5)	0.004
Min heart	*Mean ± SD*	0.99 ± 0.28	1.19 ± 0.14	
	Range	(0.5 – 1.5)	(0.98– 1.44)	0.002
Max heart	*Mean ± SD*	5.82 ± 0.65	6.13 ±0. 89	
	Range	(4.33 – 6.7)	(4.84 – 7.92)	0.15
Mean heart	*Mean ± SD*	4.39 ±0.28	4.6 ± 0.18	
	Range	(3.7 – 4.9)	(4.1 – 4.98)	0.003
Min right lung	*Mean ± SD*	0.69 ± 0.12	0.81 ± 0.19	
(contralateral) CL	*Range*	(0.42 – 1.05)	(0.59 – 0.98)	0.01
Max right lung	*Mean ± SD*	3.78 ± 0.58	4.46 ± 0.95	
(contralateral) CL	*Range*	(3 – 4.95)	(3.5–5.61)	0.003
Mean right lung	*Mean ± SD*	0.88 ± 0.08	0.99 ± 0.17	
(contralateral) CL	*Range*	(0.71 – 1)	(0.65 – 1.26)	0.008
Min right breast	*Mean ± SD*	0.49 ± 0.08	0.53 ± 0.09	0.51
(contralateral) CB	*Range*	(0.34 – 0.61)	(0.28– 0.82)	
Max right breast	*Mean ± SD*	4.88 ± 0.37	8.51 ± 1.64	
(contralateral) CB	*Range*	(3.01 – 5.56)	(6.54 – 10.32)	<0.001
Mean right breast	*Mean ± SD*	1.16 ± 0.26	1.39 ± 0.38	
(contralateral) CB	*Range*	(0.86 – 1.53)	(0.84 – 1.99)	0.01
Min LAD	*Mean ± SD*	2.82 ± 0.99	2.1 ± 1.01	
	Range	(1.61 – 4.11)	(0.94 – 3.98)	0.01
Max LAD	*Mean ± SD*	32.16 ± 4.56	28.07 ± 4.29	
	Range	(18.5 – 39.8)	(21.89 – 34.32)	0.001
Mean LAD	*Mean ± SD*	14.65 ± 5.42	11.12 ± 4.08	
	Range	(8.15 – 21.09)	(7.91 – 18.4)	0.009

**Independent sample t-test, Non-significant: P >0.05, Significant: P ≤0.05*

Table 4: Technical metrics among the studied groups:

Variables		3D CRT (n=27)	VMAT (n=27)	P Value
CI (conformity index)	*Mean ± SD*	0.89 ± 0.09	0.95 ± 0.06	
	Range	(0.61 – 0.98)	(0.85 – 0.99)	0.006
HI(Homogeneity index)	*Mean ± SD*	1.08 ± 0.02	1.1 ± 0.05	
	Range	(1.04 – 1.16)	(0.99 – 1.27)	0.06
MU (Monitor units	*Mean ± SD*	365.2 ± 88.9	502.4 ± 125.5	
	Range	(197.5 – 478.4)	(367.2 – 751.1)	<0.001

**Independent sample t-test, Non-significant: P >0.05, Significant: P ≤0.05.*

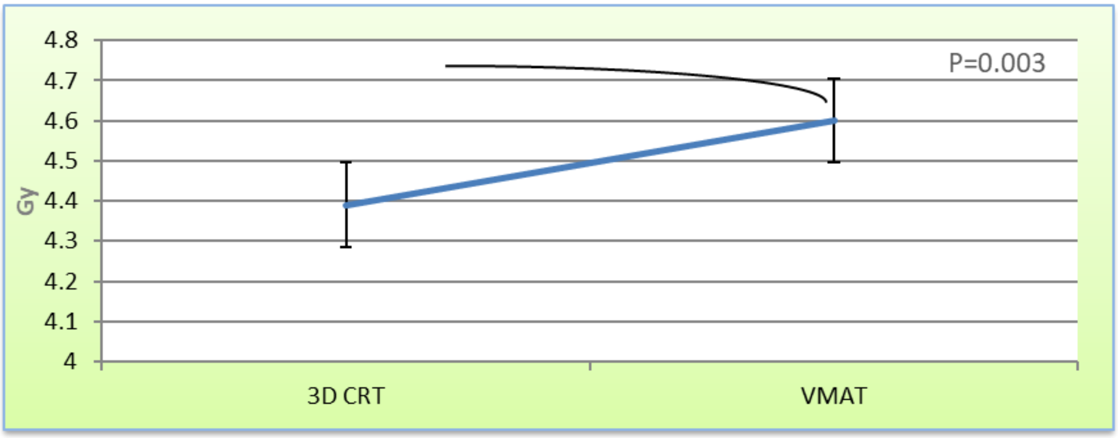

Figure1: Interval plot of the mean heart dose versus radiotherapy techniques

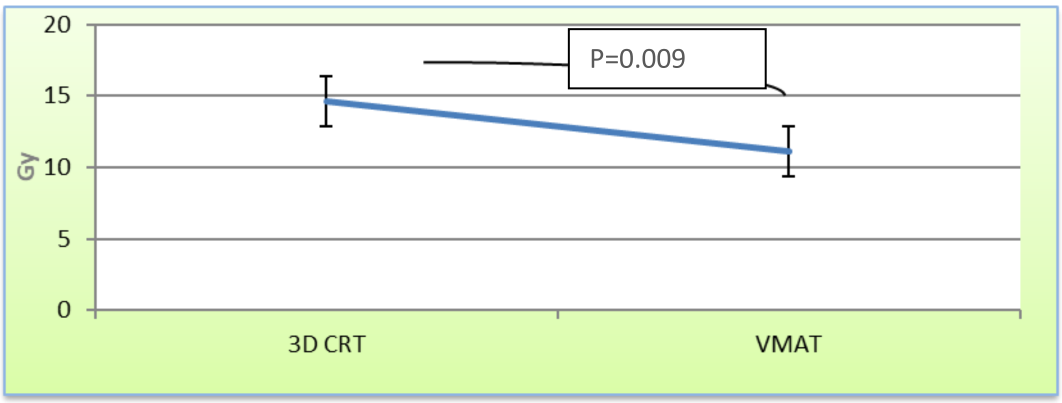

Figure 2: Interval plot of the mean LAD dose versus radiotherapy techniques

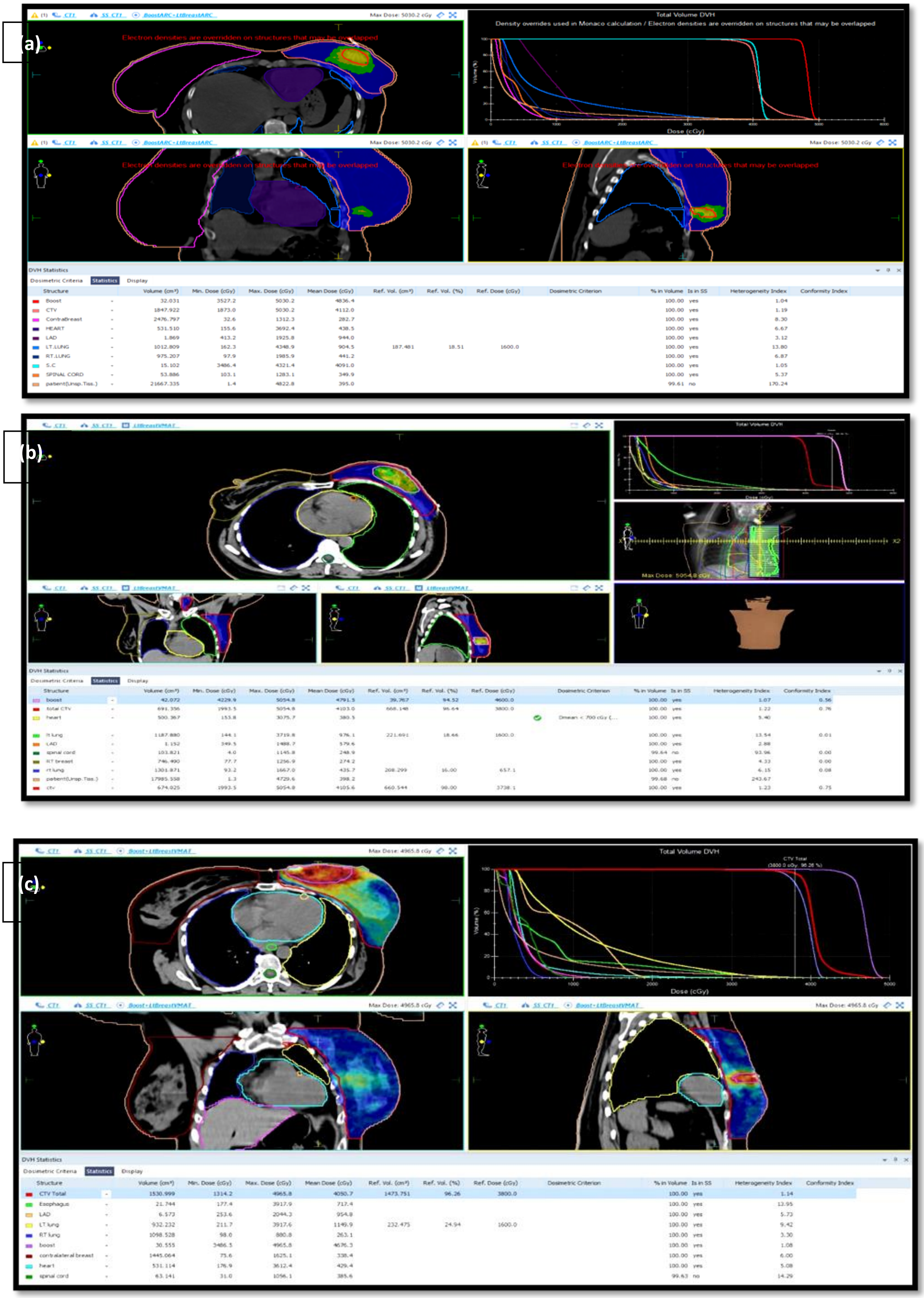

Figure 3 (a, b and c): VMAT plan and DVH.

Discussion:

The current study analyzed the dosimetric measurements of the target and OARs between 3D-CRT-SIB and VMAT-SIB plans for left sided cancer breast patients. The 3D-CRT represents our standard institutional practice, whereas VMAT plans were prepared only for the purpose of this study. We prepared the plans according to our institutional standards, and the results might only be relevant to this particular set of planning objectives.

In line with our findings, Murakami et al., reported that the 3D-CRT + electron boost (EB) plans notably decreased the heart's D mean (1.9 Gy vs 2.9 Gy; P < 0.001, and in our study 4.39Gy vs 4.60 Gy; P=0.003 in 3DCRT vs VMAT respectively). All dosimetric measurements for IL, CL and CB were significantly (P < 0.001) reduced in the plans of 3D-CRT + EB. The SIB-VMAT plans showed a decrease in LAD's dosimetric parameters (P<0.01, and in our study, P was 0.009 for LAD mean dose). In order to lower the risk of RICAD, protection of the heart and cardiac components from radiation doses is almost essential. SIB-VMAT reduced the doses to the LAD while substantially improved the dose to the target. The 3D-CRT + EB plans' MUs were considerably lesser than those of the SIB-VMAT plans (583.0 vs 700.4; P < 0.001, and in our study, 365.2 vs 502.4; P was <0.001). SIB has the potential to decrease the number of treatment visits when compared to a standard sequential boost approach, which typically necessitates an extra 4 to 6 fractions following hypofractionated WBI. In addition, radiation oncologists need to thoroughly evaluate the irradiation technique, considering factors like the patient's age, respiratory function and tumor prognosis [10].

Results of Czeremszynska et al.'s study were in accordance with our dosimetric outcomes which revealed that the VMAT showed superior PTV coverage but higher dose to OAR. They documented that VMAT reduced D max LAD significantly, compared with 3D-CRT (28.9 versus 35.7 Gy, respectively, P = 0.005, and in our study, 28.07Gy vs 32.16 Gy; P was 0.001) although statistically significant, was numerically and clinically unsatisfactory. VMAT produced significantly higher PTV95% and better HI than 3D-CRT. Compared to 3D-CRT, CI was superior in VMAT. The MU's number was the lowest in 3D-CRT plans. Comprehensive analysis of lung doses from radiation therapy for breast cancer showed that IMRT and/or VMAT use increased mean ipsilateral lung dose (MILD), even without RNI (6.7Gy vs 8.5Gy, and in our study, 6.01Gy vs 8Gy for 3DCRT vs VMAT respectively). However, different studies showed contradictory results for MILD – some studies show significant reduction of MILD with inverse-planned IMRT, and in others, MILD was significantly increased with the use of inverse-planned IMRT compared with 3D-CRT. The increased low-dose volumes, however, are almost universally recorded in dynamic techniques like VMAT or IMRT, a higher volume of normal tissue had a "low-dose bath" than with 3D-CRT, raising concerns about the secondary cancers' risk [7]. Therefore, to improve survival with tolerable toxicity, it is crucial to select the best radiotherapy approach to guarantee the highest accessible target volume coverage and dose conformity while concurrently minimizing OAR radiotherapy dose exposure.

Keeping with our study, Chen et al. noted that VMAT had significantly highest IL D mean, CB D max. Also CL D mean is significantly higher in VMAT than 3DCRT (0.47Gy vs 0.04 Gy, and in our study, 0.99Gy vs 0.88Gy). These outcomes were anticipated as there were more beams involved in VMAT, which led to more beams entering and leaving through CL, and this is the reason for the dose impact [11]. Consistent to the findings of the Chen et al. study, additional studies have also documented that the administration of VMAT led to a large low-dose volume to CB, raising the possibility of secondary CB cancers, particularly in patients who are younger [12]. Tangential beam techniques, are comparable in their ability to improve lung preserving and CB dosimetry, hence lowering the risk of radiation pneumonitis and subsequent lung and CB cancer following radiation therapy. The benefit of better OARs sparing and lower cardiac doses using tangential beams approaches over the usage of multi-fields or arcs approaches is highlighted by Chen et al.'s study [11]. With a median follow-up period of 5.1 years after RT completion, the proportion of second cancer diagnoses post 3D-CRT and irradiation looked comparable in real-world data taken from the National Cancer Database [13]. A recent study investigated the long-term secondary malignancies' risk in childhood cancer received RT with IMRT, indicated that numerous secondary malignancies arise in the high-dose areas following IMRT treatments with over 10 years of follow-up [14, 15].

The analysis conducted by Ko et al. revealed that although the mean dosage difference between VMAT and 3D-CRT was about 1 Gy, VMAT caused a higher radiation exposure to the contralateral breast than 3D-CRT. [16]. Additionally, Ranger et al. conducted another dosimetric study and found that the mean dose to the CB from VMAT and 3D-CRT was 1.7 Gy and 1.2 Gy, respectively, with no statistically significant difference, while in our study: D mean of CB was 1.39 Gy vs 1.16 Gy for VMAT and 3D-CRT with significant P-value (0.01) [17].

Unlike our results and the findings published by Zhao et al. [18] and Lin et al. [19], Chen et al., stated the poorest performance for PTV V95% and CI was displayed by VMAT [11]. This disparity can be explained by the different arc arrangements employed in the present study contrasted to those in the studies that were previously stated.

Yeh et al. examined the dosimetric properties of pure VMAT technique under the conditions of free breath (FB) and DIBH versus the 3D-CRT hybrid

VMAT approach to left sided breast cancer patients after BCS. In order to decrease the area of low-dose dissemination in the normal tissue and lungs, the hybrid technique plan for left sided early breast cancer was created through combining two tangential IMRT beams as the base plan and two partial coplanar conformal arcs. Additionally, they studied the 3D-CRT hybrid VMAT's dosimetric properties with DIBH and FB circumstances. They documented that the 3D-CRT hybrid VMAT provided the best results on the conformity index (CI) and homogeneity index (HI) utilizing the DIBH approach. When the 3D-CRT hybrid VMAT technique was used with FB versus DIBH techniques, the MHD reduced from 5.38 Gy to 1.65 Gy ($p = 0.001$) and the LAD's 0.03cc dose lowered from 27.87 Gy to 9.41 Gy ($p = 0.001$). The ipsilateral lung's D mean, V5 and V20, and as well as D mean of the contralateral lung were considerably decreased by the 3D-CRT hybrid VMAT utilizing the DIBH approach. When compared to VMAT utilizing the DIBH approach, the 3D-CRT hybrid VMAT considerably decreased the contralateral breast's D5. Therefore, using DIBH in conjunction with the 3D-CRT hybrid VMAT approach offers the optimum radiation dose-protection benefits for the heart and OAR without impacting target volume homogeneity and conformity in the treatment planning. [20].

The drawbacks of our study include the limited cohort of patients and that we didn't incorporate neither DIBH nor respiratory gating to reduce the heart or LAD doses. The strength of our study that the patients received WBI with regional nodal irradiation (RNI).We demonstrated a limited benefit from the use of VMAT techniques in the reduction of doses to LAD in the left-sided FB-WBI. To further assess the findings and reach better conclusions, we advise the further studies to include a larger sample size and incorporate more cases requiring breast and nodal irradiation, and every attempt, by DIBH or respiratory gating, should be made to achieve maximal cardiac protection because even minimal cardiac exposure reductions may have long-term, clinically real advantages in reducing cardiac morbidity.

Conclusion:

In conclusion, multi-fields and arcs arrangements (VMAT) considerably decreased the doses to the LAD and improved the doses to the target, even though approaches with tangential fields arrangement (3DCRT) provided overall better OARs dosimetry.

Authors' contributions:

N.G.E and A.E: Study design; data acquisition; data analysis and interpretation; drafting and critical reviewing of the manuscript. All authors read and approved the final manuscript version and agreed with all parts of the work in ensuring that any queries about the accuracy or integrity of any component of the work are appropriately investigated and handled.

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List of abbreviations:

BCS	Breast-conserving surgery
CB	Contralateral breast
CBCT	Cone-beam CT
CI	Conformity index
CL	Contralateral lung
CT	Computed tomography
CTV	Clinical Target Volume
3D-CRT	Three-dimensional conformal radiation therapy
DIBH	Deep inspiration breath-hold
EB	Electron boost
ER	Estrogen receptors
FB	Free Breathing
FIF	Field in field
HI	Homogeneity index
IL	Ipsilateral lung
IMRT	Intensity-modulated radiation therapy
IRB	International Review Board
LAD	Left anterior descending coronary artery
MHD	Mean heart dose
MILD	Mean ipsilateral lung dose
MLCs	Multi-leaf collimator
MU	Monitor units' number
OARs	Organs-at-risk
PR	Progesterone receptors
PTV	Planning target volume
2pVMAT	2 partial arcs VMAT
RICAD	Radiation-induced coronary artery disease
RNI	Radiological nodal irradiation
SC	Supraclavicular LN
SIB	Simultaneous integrated boost
TPS	Treatment planning system
VMAT	Volumetric modulated arc therapy
WBI	Whole breast irradiation

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