Received: 4 June 2022 | Revised: 30 August 2022 | Accepted: 5 September 2022

DOI: 10.1002/pro6.1172

ORIGINAL ARTICLE

WILEY

Assessment of dose-volume histogram statistics using three-dimensional conformal techniques in breast cancer adjuvant radiotherapy treatment

Aula Fadhil Alwan[1] | Manwar Abdulelah Al-Naqqash[2] | Hasan Saad Abbood Al-Nuami[3] | Nawres Ali Mousa[4] | Sura Yousif Ezzulddin[4] | Ahmed Salih Al-shewered[5] | Dalya Al-Nuami[1]

[1]Radiation Oncology Department, Baghdad Center for Radiotherapy and Nuclear Medicine, Medical City Complex, Ministry of Health and Environment, Baghdad, Iraq

[2]Department of Surgery, College of Medicine, Baghdad University, Baghdad, Iraq

[3]Oncology Department, Næstved Hospital, Denmark

[4]Medical Physics Department, Baghdad Center for Radiotherapy and Nuclear Medicine, Medical City Complex, Ministry of Health and Environment, Baghdad, Iraq

[5]Department of Radiotherapy, Misan Radiation Oncology Center, Misan Health Directorate, Ministry of Health and Environment, Misan, Iraq

Correspondence
Aula Fadhil Alwan and Dalya Al-Nuami, Radiation Oncology Department, Baghdad Center for Radiotherapy and Nuclear Medicine, Medical City Complex, Ministry of Health and Environment, Baghdad, Iraq.
Email: Aulaalwan91@gmail.com; daliasaad_115@yahoo.com

Ahmed Alshewered, Department of Radiotherapy, Misan Radiation Oncology Center, Misan Health Directorate, Ministry of Health and Environment, Misan, Iraq.
Email: Ahmedsalihdr2008@yahoo.com

Abstract

Objective: Breast cancer (BC) is first of the top 10 malignancies in Iraq. Dose-volume histograms (DVHs) are most commonly used as a plan evaluation tool. This study aimed to assess DVH statistics using three-dimensional conformal radiotherapies in BC in an adjuvant setting.

Methods: A retrospective study of 70 histologically confirmed women diagnosed with BC was reviewed. The study was conducted between November 2020 and May 2021, planning for treatment with adjuvant three-dimensional conformal radiotherapies. The treatment plan used for each woman was based on an analysis of the volumetric dose, including DVH analysis.

Results: The planning target volume and clinical target volume coverage for tumors at V85% was better than V90% and V95%, with highly significant differences ($p < 0.0001$). The planning target volume and clinical target volume coverage for lymph nodes at V85% was higher than V90% and V95%, with no significant differences.

Conclusions: This is the only study that has been carried out in Iraq that we are aware of that addresses the evaluation of DVH statistics in BC. V85% produced the best chest wall coverage, and V95% made the worst. With little significance, higher lymph nodes coverage was attained at V85%, whereas the lowest coverage was at V95%.

KEYWORDS
breast cancer, dose volume histogram, organs at risk, three-dimensional conformal radiotherapy

1 | INTRODUCTION

Breast cancer (BC) is the most common cancer among women, representing approximately 24.5% of new cases of female cancers worldwide. GLOBOCAN reported 2,261,419 new cases of BC (rank #1), with 684,996 deaths from BC (rank #4) in 2020.[1] In Iraq, there were 3845 cases estimated in 2011.[2] This number rose to 4542 in 2014 according to a World Health Organization report.[3] In contrast, the new cases

of BC in 2020 were 7515.[1] It has been demonstrated that adjuvant radiation administered after BC surgery reduces mortality by 5%, and the risk of locoregional recurrence from 30% to 10% after 20 years. Current trials assess the role of radiation therapy (RT), a conventional treatment for ductal carcinoma *in situ*, in low-risk individuals compared with surgery alone.[4–6]

The normal tissue dose distributions are calculated using dose-volume histograms (DVHs). DVHs are frequently used to evaluate plans to compare dosages from various plans or structures. Different amounts of damage are caused by the dose heterogeneity in the exposed volume, but the organ's structure and function ultimately determine the pathophysiological outcome.[7,8] The large amount of dosimetric data that must be analyzed when a three-dimensional conformal radiotherapies (3DCRT) plan is evaluated has prompted the development of methods of condensing and presenting the data in more easily understandable formats.[9,10] Two types of DVHs, differential and cumulative, are available in 3DCRT planning. The latter is widely used in plan evaluation for assessing planning target volume (PTV) coverage and dose to organs at risk (OARs).[11,12]

The present study aimed to assess DVH statistics using 3DCRT in an adjuvant setting, analyze DVH for all OARs per-patient basis, and evaluate comparative dose distributions for gross target volume (GTV), clinical target volume (CTV), PTV, and OAR on DVH using adjuvant 3DCRT for BC treatment.

2 | PATIENTS AND METHODS

2.1 | Study design and setting

A total of 70 histologically confirmed female patients with BC were treated in the Baghdad Radiation Oncology Center, located in Baghdad Medical City, Iraq. Between November 2020 and May 2021, the survey was carried out in preparation for adjuvant 3DCRT therapy.

2.2 | Data collection

Reviewing medical records allowed for the retrospective collection of data. Age; tumor, node, and metastasis (TNM) staging;, histology; tumor side; patient address; dose; and the number of RT fractions were the variables examined. Imaging tests (conventional radiography, computed tomography, or magnetic resonance imaging) were used to determine the clinical stage of BC, and a tissue sample was used to corroborate the results.

2.3 | DVH

A treatment strategy was developed for each patient based on a volumetric dose study, which included DVH analysis of the PTV and important normal tissues. Beam weights were manually adjusted to maintain a hot spot of 107% while covering the PTV by the isodose line at 95%. The protocol was developed with dose-volume restrictions, including dose restrictions to the ipsilateral and contralateral lung, contralateral breast, heart, liver, and spinal cord (Figure 1).

2.4 | Target volumes and OARs data

The target volumes and vital organs, including the heart, left and right lungs, and the spinal cord, were separately defined. The entire breast was demarcated for patients undergoing breast conservation surgery (BCS), and for those undergoing mastectomy, the chest wall was drawn as a CTV. The CTV was given an additional 10-mm isotropic margin to produce a PTV. For each woman enrolled in this study, PTV and CTV were measured and recorded as following (note: t for tumor; n for lymph nodes; Figure 1):

a) PTV t volume % covered by 85% dose
b) PTV t volume % covered by 90% dose
c) PTV t volume % covered by 95% dose
d) PTV n volume % covered by 85% dose
e) PTV n volume % covered by 90% dose
f) PTV n volume % covered by 95% dose
g) CTV t volume % covered by 85% dose
h) CTV t volume % covered by 90% dose
i) CTV t volume % covered by 95% dose
j) CTV n volume % covered by85% dose
k) CTV n volume % covered by 90% dose
l) CTV n volume % covered by 95% dose

For each patient who underwent RT, each OAR mean and maximum doses of volume percentage of RT received were estimated and documented as following:

a) For the lung (each for right and left)

1. Mean dose
2. Volume percentage received 2000 cGy
3. Volume percentage received 1000 cGy
4. Volume percentage received 500 cGy

b) For the heart

1. Volume percentage received 2500 cGy
2. Mean dose

c) For the liver

1. Mean dose
2. Volume percentage received 3000 cGy

d) Spinal cord (mean dose)
e) Contralateral breast (mean dose)

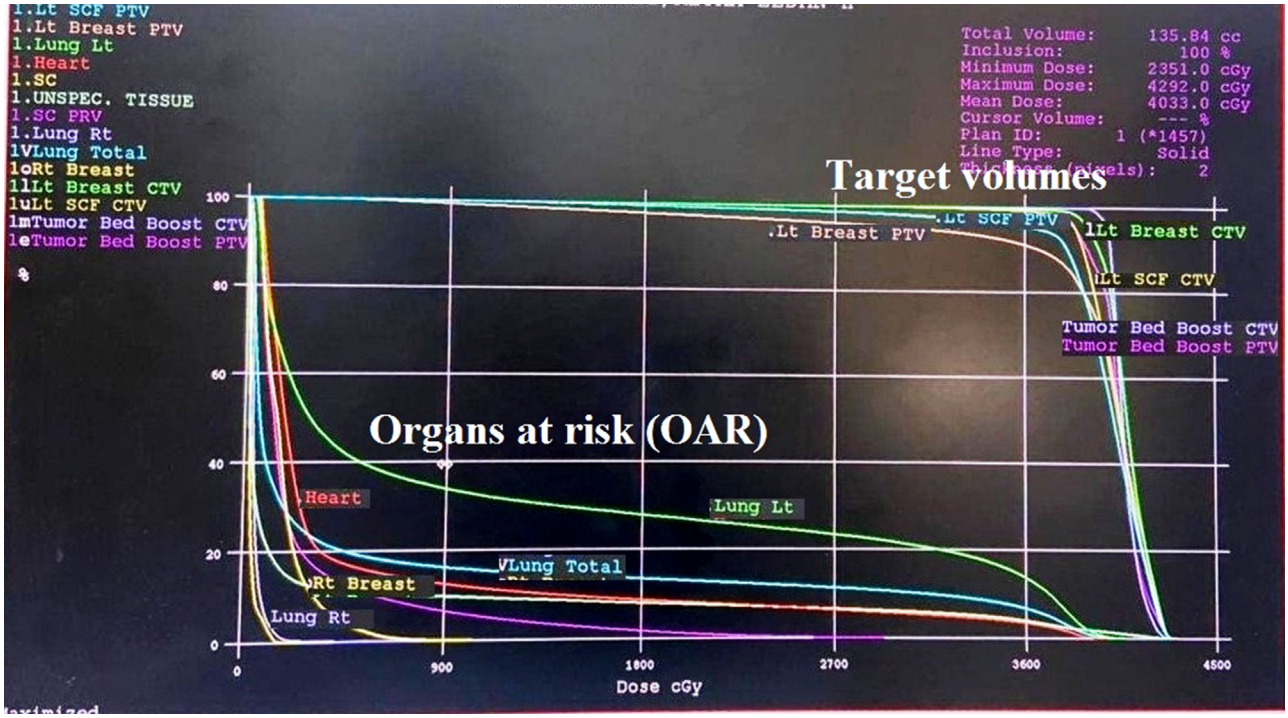

FIGURE 1 The dose-volume histogram statistics for left breast cancer (BC) contain both target volumes and organs at risk, from XiO Elekta system version 5 in Baghdad Radiation Oncology and Nuclear Medicine Center, Medical City Complex

2.5 | Equipment

These included computed tomography pore scanner (85 cm; Philips 16 series), Linear Accelerator (Infinity and Synergy); 2013 (core beam computed tomography), Monaco Elekta HP version 5, and XiO Elekta system version 5.

2.6 | Radiotherapy doses

a) 4005 cGy in 15 fractions over 3 weeks was adopted as standard practice in radiotherapy dosing for women undergo mastectomy.
b) 4005 cGy/15 fractions/3 weeks performed for patients with BCS plus 1000 cGy/5 fractions/1 week as booster dosing.

2.7 | Statistical analysis

All analyses were conducted using SPSS 15.0 (SPSS Inc., Chicago, Illinois, USA). A two-sided p-value of ≤ 0.05 was considered statistically significant for Fisher's exact, Pearson's χ^2-test, Monte Carlo two-sided, and Spearman's correlation. Numbers and percentages of replies in each category made up the descriptive statistics. The one-way ANOVA test for independent measurements was intended to simultaneously compare the means of six separate portal images. The post-hoc Tukey's honestly significant difference (beta) approach made comparing two ANOVA datasets more accessible, and distinguished between the six portal image means.

3 | RESULTS

The mean age of studied women was 50.97 ± 11.34 years, with 50 years as the median, and most women were aged 40–49 years (n = 23; 32.90%), followed by 50–59 years (n = 21; 30.00%). In addition, the 30–39 years and 60–69 years age group reported 10 (14.30%) patients. Age more than 70 years was recorded in five women.

Table 1 shows that BC on the left side was documented more than the right side (52.90 vs. 47.10%). The T2 stage was predominant in 45 (64.30%) patients, followed by T1 in 11 (15.71%) patients. The N1 and N2 stages were mostly found in 30 (42.85%) and 25 (35.70%) patients, respectively. Approximately 58 of 70 (82.90%) patients underwent modified radical mastectomy surgery, whereas 12 of 70 (17.10%) patients were surgically treated by BCS. Most patients , 51 of 70 (72.85%), received a RT dose of 40.05 Gy/15fx. Other doses described were 42.56 Gy/16fx and 50 Gy/25fx in 15.7% and 11.4%, respectively. Only six women received a booster dose of 10 Gy/5fx.

The dosimetry of this study is shown in Table 2 and Figure 2. The PTV coverage for tumor at V85% (92.08 ± 3.55, $p < 0.0001$) was better than V90% (89.60 ± 4.12, $p < 0.0001$) and V95% (82.83 ± 5.90, $p = 0.006$), with a high significant difference regarding the post-hoc Tukey's test (16.56, 12.15, and 4.41), respectively, and ANOVA analysis (73.55, $p < 0.0001$). The PTV coverage for lymph nodes at V85%

TABLE 1 Tumor baseline results of this study ($n = 70$)

Variables		*n*	%
Side	Right	33	47.10
	Left	37	52.90
T staging	T1	11	15.71
	T2	45	64.30
	T3	5	7.14
	T4	9	12.85
N staging	N0	9	12.85
	N1	30	42.85
	N2	25	35.70
	N3	6	8.60
Surgery types	MRM	58	82.90
	BCS	12	17.10
RT dose (cGy/fx)	4005/15fx	51	72.85
	4256/16fx	11	15.71
	5000/25fx	8	11.43
	Only six patients received booster dose of 1000 cGy/5fx		

Abbreviations: BCS, breast conservative surgery; cGy, centi-gray; fx, fraction; MRM, modified radical mastectomy; N, lymph node; RT, radiotherapy; T, tumor.

(97.20 ± 2.25, $p = 0.97$) was higher than that at V90% (95.40 ± 3.23, $p = 0.98$) and V95% (87.14 ± 6.70, $p = 0.10$), with no significant differences ($p = 0.968$). CTV coverage for tumor at V85% (98.10 ± 1.90, $p < 0.0001$) was higher than that at V90% (96.93 ± 2.55, $p < 0.0001$) and V95% (93.14 ± 4.16, $p = 0.058$), with high significant differences regarding the post-hoc Tukey's test (13.73, 10.48, 3.25), respectively, and ANOVA analysis (51.50, $p < 0.0001$). The CTV coverage for lymph nodes at V85% (99.54 ± 0.82, $p = 0.99$) was more than that at V90% (99.10 ± 1.33, $p = 0.99$) and V95% (94.60 ± 4.57, $p = 0.99$), with no significant association ($p = 0.99$).

The dosimetry of OAR in this investigation is shown in Table 3. The right (ipsilateral) lung received an overall mean (median) dose of 750 (125) cGy. In addition, the lung received 2000 cGy in 15.80% of patients, 1000 cGy in 19.29%, and 500 cGy in 24.68% of patients. The left (ipsilateral) lung received an overall mean (median) dose of 786.9 (905) cGy. In addition, in 17.22% of patients, the lung received 2000 cGy; in 20.90%, it received 1000 cGy; in 26.8%, it took 500 cGy. The overall mean (median) dose received by the heart was 338.1 (324) cGy, with a maximum dose reaching 889 cGy, whereas in 12.43% of patients, the heart received 2500 cGy during the course. The overall mean dose received by the liver was 398.31 cGy, with the maximum dose reaching 1021 cGy, whereas 5.80% received 3000 cGy during the course. Accordingly, the overall mean dose received by the spinal cord was 1590 cGy, and the overall maximum dose reached 3534 cGy. Finally, the overall mean dose received by the contralateral breast during RT was 31.14 cGy, and the overall maximum dose received 181 cGy. The results presented here suggested that the RT dose of 4005 cGy had been better for covering target volumes (PTV and CTV) and the lowest doses received by different OARs than doses of 5000 cGy and 4256 cGy, respectively, as shown in Figure 3, which is acceptable for efficacy and safety.

4 | DISCUSSION

By administering various adjuvant RT doses to 70 Iraqi patients with BC, the present study demonstrates our continuous clinical expertise in 3DCRT therapy of BC in Iraq. Although there are no apparent uncertainties in the OAR dose determination during RT, this is acceptable.

TABLE 2 Dosimetric characteristics of planning target volume and clinical target volume ($n = 70$)

Parameters	V%	Coverage (%)	Maximum coverage (%)	Minimum coverage (%)	Post-hoc Tukey HSD (*p*-value)	ANOVA (*p*-value)
PTVt volume % covered	**85%**	92.08 ± 3.55	99.98	82.31	16.56 (<0.0001)	73.55 (<0.0001)
	90%	89.60 ± 4.12	96.15	77.55	12.15 (<0.0001)	
	95%	82.83 ± 5.90	91.90	65.12	4.41 (0.006)	
PTVn volume % covered	**85%**	97.20 ± 2.25	99.97	90.56	0.33 (0.97)	0.03 (0.968)
	90%	95.40 ± 3.23	99.79	85.88	0.27 (0.98)	
	95%	87.14 ± 6.70	98.02	70.99	0.06 (0.1)	
CTVt volume % covered	**85%**	98.10 ± 1.90	100	90.97	13.73 (<0.0001)	51.50 (<0.0001)
	90%	96.93 ± 2.55	100	87.87	10.48 (<0.0001)	
	95%	93.14 ± 4.16	99.38	81.37	3.25 (0.058)	
CTVn volume % covered	**85%**	99.54 ± 0.82	100	96.83	0.17 (0.99)	0.008 (0.99)
	90%	99.10 ± 1.33	100	94.84	0.15 (0.99)	
	95%	94.60 ± 4.57	99.93	82.41	0.02 (0.99)	

Abbreviations: CTV, clinical target volume; n, lymph node; PTV, planning target volume; SD, standard deviation; t, tumor; V, volume.

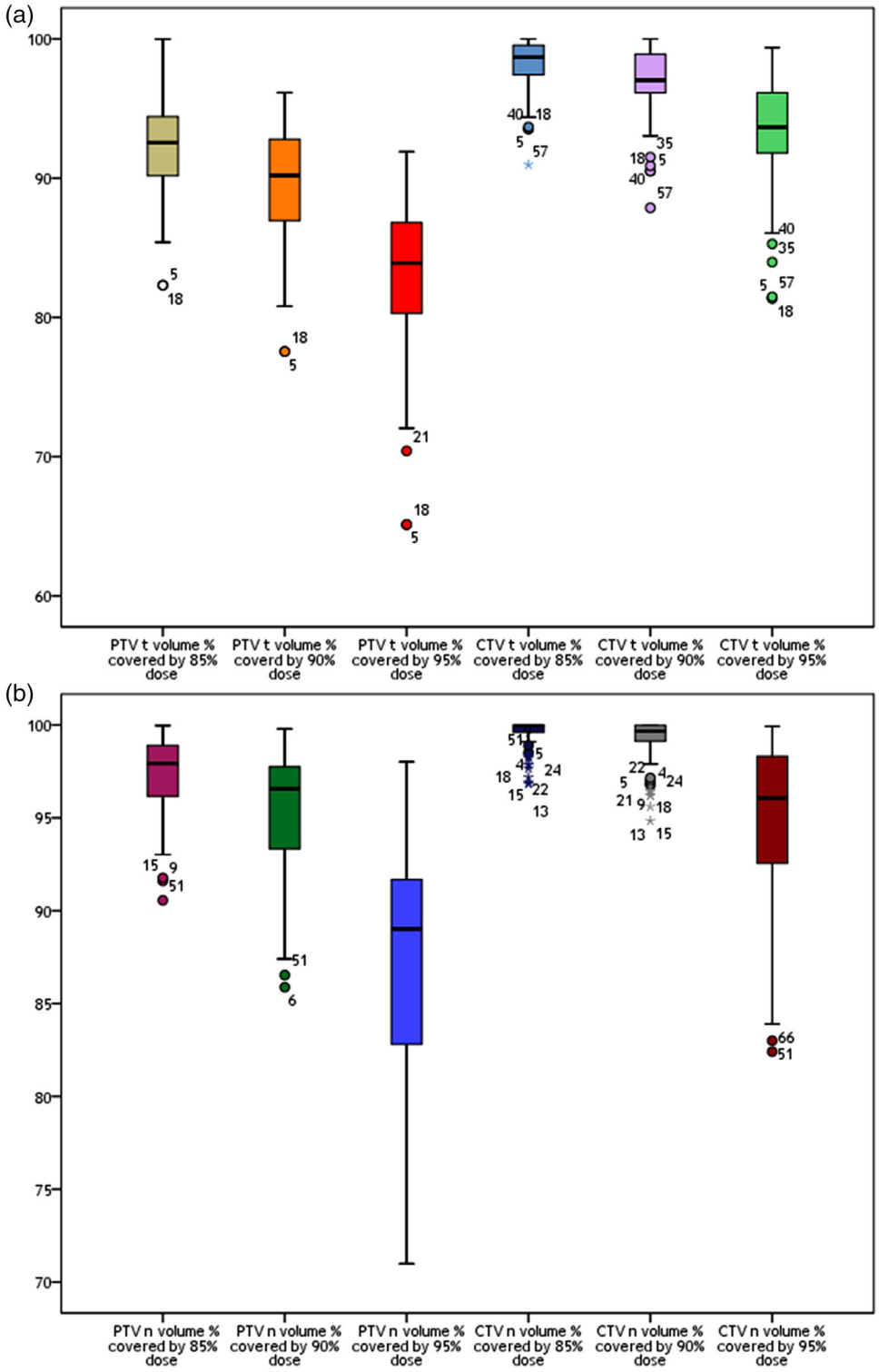

FIGURE 2 (a) Box plot of dosimetry for planning target volume (PTV) and clinical target volume (CTV) of tumor. (b) Box plot of dosimetry for PTV and CTV of lymph nodes

These findings also assist the ongoing research on 3DCRT delivery in our region. The findings confirm several other studies conducted in Iraq.[13–17] Age is an essential factor in the occurrence and management of BC.[18] In the research comparing women from Iraq and Britain, the mean age was higher by over 15 years than what the present results showed. BC was also more prevalent than we had previously estimated among USA women in their sixth decade of life. According to our study, women aged under 50 years were more likely to be diagnosed with BC in most Arabian nations than women aged over 50 in the USA.[18]

TABLE 3 Dosimetric characteristics of organs at risk

OARs	Parameters	Volume %/mean dose (cGy) (median)	Maximum dose received	Minimum dose received
Rt lung (ipsilateral) (V30% ≤17%)	**Mean dose (cGy)**	750 (125)	1861	27
	2000 cGy	15.80%	38.90%	0
	1000 cGy	19.29%	46.14%	0
	500 cGy	24.68%	64.80%	0
Lt lung (ipsilateral) (V30% ≤17%)	**Mean dose (cGy)**	786.90 (905)	1851	0
	2000 cGy	17.22%	39.77%	0
	1000 cGy	20.90%	49.50%	0
	500 cGy	26.80%	79.03%	0
Heart (V25% ≤5%) (V5% ≤30%)	**Mean dose**	338.10 (324)	889	0
	2500 cGy	12.43%	13.99%	0
Liver (V70% < 20G)	**Mean dose**	398.31 (343)	1021	0
	3000 cGy	5.80%	19.80%	0
Spinal cord (Dmax <45 G)	**Mean dose (cGy)**	1590 (1496.5)	3534	58
Contralateral breast	**Mean dose (cGy)**	31.14 (23.5)	181	9

Abbreviations: cGy, centi-gray; Dmax, maximum dose; Lt, left; OARs, organs at risk; Rt, right; V, volume.

The tumor characteristics in the present study revealed that left BC was documented more than the right. The T2 stage was predominant, and N1 and N2 stages were mostly found. Most patients underwent modified radical mastectomy surgery, whereas the rest were surgically treated with BCS. Similarly, data mentioned by Al-Naqqash et al.,[13] Al-Alwan et al.,[15] and Al-Rawaq,[16] differ from the results recorded by Goldhirsch et al.[19] and Al-Khafaji.[20] These are crucial in BC, as the existence and quantity of affected axillary lymph nodes highly correlate with the likelihood of distant metastasis, disease-free survival, and overall survival, all of which are strongly predicted by the tumor size. It serves as a separate prognostic factor. The strongest indicator of systemic micrometastases and the most significant prognostic factor, the lymph node status, is directly associated with survival.[21–24]

In the present study, the protocols utilized to treat those women apply according to international guidelines and trials.[4–7,25–29] Most patients received a RT dose of 40.05 Gy/15fx. Other doses described were 42.56 Gy/16fx and 50 Gy/25fx. Only six women (8.6%) received a booster dose of 10 Gy/5fx. Long-term follow-up shows that early BC patients can receive hypofractionated radiation safely and effectively dosed.[28] When 2236 women were enrolled in START-A in 2013, it was discovered that moderate or marked breast induration, telangiectasia, and breast edema were significantly less common in the 39 Gy group than in the 50 Gy group. The median follow-up was 9.3 years (IQR 8.0–10.0), during which 139 local or regional relapses occurred.[29] In 2013, the START-B found that breast shrinkage, telangiectasia, and breast edema were significantly less common normal tissue effects in the 40 Gy group than in the 50 Gy group. All these were obtained from 2215 enrolled women with a median follow-up of 9.9 years (IQR 7.5–10.1), after which 95 local-regional relapses had occurred.[29] Also, there is increasing interest in adjuvant breast RT with fewer and larger fractions.[26,27] The FAST trial randomized 915 women (age >50 years) with node-negative BC to either 50 Gy in 25 fractions or 28.5 Gy or 30 Gy in five once-weekly fractions of 5.7 Gy or 6.0 Gy. At 3 years of follow-up, the 28.5 Gy arm was comparable with 50 Gy in 25 fractions, but the 30 Gy fractionation was adversely affected. The FAST-Forward trial has completed the recruitment of 4000 women. This randomized trial of women compared a scheme of 40 Gy in 15 fractions with two other schedules, 27 Gy in five fractions over 1 week or 26 Gy in five fractions over 1 week.[29] The proportional gain from RT will be more significant for women irradiated today, because radiotherapy planning has changed, and women with BC today receive better coverage of target areas.[26,27,29] Furthermore, doses to normal tissues are lower today, so the risks of radiotherapy are also likely to be lower. The techniques have been improved over the past few decades, so radiotherapy's proportional benefits are likely to be larger.[30]

The dosimetry of the present study revealed that the PTV coverage for the breast tumor bed at V85% was better than that at V90% and V95%. The CTV coverage for the tumor bed at V85% was higher than that at V90% and V95%, whereas CTV coverage for lymph nodes at V85% was more than that at V90% and V95%, with no significant association according to ANOVA analysis. Due to the lack of such studies in Iraq, the comparison with several studies from other countries is unenviable.

Ohashi et al.[31] documented breast and axillary dosimetric parameters. They found no significant differences in the variability of the V90% and V95% values. The mean volumes of V90% and V95% rose significantly with 3DCRT, which disagreed with our findings. When RT is intended to treat the BC bed and axillary areas, an appropriate

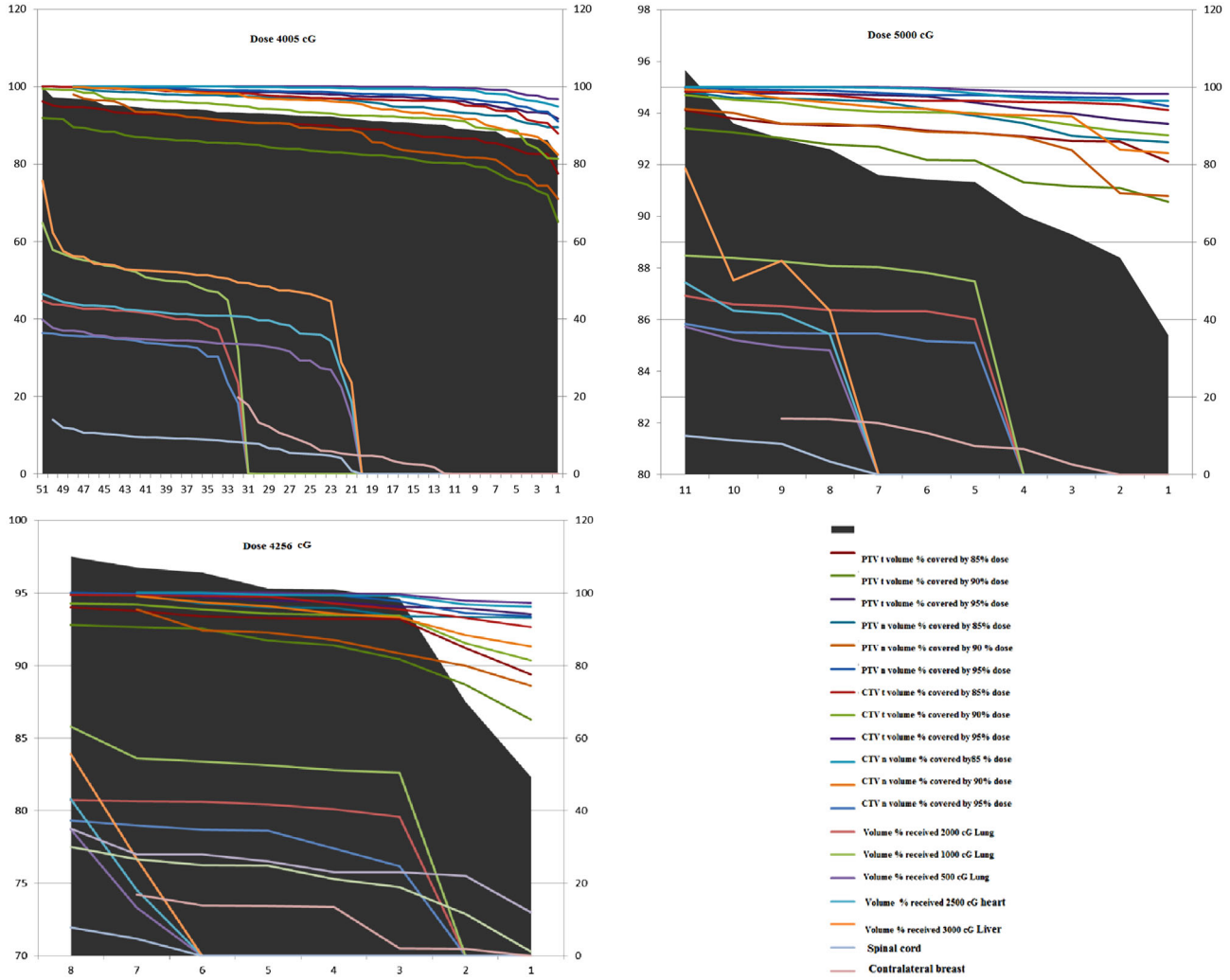

FIGURE 3 Overall dose-volume histogram diagram of three radiotherapy doses. CTV, clinical target volume; PTV, planning target volume

technique is applied to reduce locoregional recurrence rates.[32,33] Their findings concluded that PTV and normal tissue are unaffected by the number of beams. To lessen the scattered radiation, medical physicists must therefore carry out the optimal strategy without using more beams than necessary.[34]

In a study conducted in Egypt, researchers discovered that the target was better covered, and the mean of V95% was more significant, although not considerably, after adding more beams ($p = 0.9152$). Additionally, even though the intensity-modulated RT was more advanced, they only used two tangential fields in the 3DCRT approach compared with five to seven fields in the intensity-modulated RT technique, making the V95% difference inconsequential ($p = 1.000$).[35]

The availability of DVH allows radiophysicists and radiation oncologists to virtually explore different tentative plans, and perform successive modifications of a starting plan for each RT. However, the choice of treatment plans is mainly made by side-to-side comparison of DVHs and isodose curves for each tentative schedule. As differences between them are minor, any selection made by inspection, as is generally the case, may not be easy to justify on clinical terms.[36]

DVH data are generally analyzed within a treatment planning system (TPS) per-patient basis, with an evaluation of single-plan or comparative dose distributions. Meticulous structure-by-structure review is performed on this data during initial and iterative plan evaluation and quality assessment (per physician prescription and treatment goals), applying structure-specific dose constraints. However, the correlation of dosimetric data with clinical information outside of the TPS (e.g., treatment response or follow-up toxicity) remains a significant hurdle for many clinical and research-related inquiries. Moreover, TPS software is generally unable to perform comparative dosimetry simultaneously among a cohort of patients.[37]

The overall mean dose received by the right lung was 750 cGy, whereas 15.80%, 19.29%, and 24.68% received 2000, 1000, and 500 cGy, respectively. In the left lung, the mean dose was 786.9 cGy, and 17.22% received 2000 cGy, 20.90% received 1000 cGy, and 26.80% received 500 cGy. Generally speaking, 12.43% of the heart received 2500 cGy during the RT course, and 5.80% of the liver received 3000 cGy. Accordingly, the overall mean dose received by the spinal cord was 1590 cGy. Finally, the overall mean dose received by the

contralateral breast during RT was 31.14 cGy, which is seemly slightly above the findings of Benson et al.,[37] who recorded that the ipsilateral lung V30% should be kept at ≤17%, and V25% of the heart kept at ≤5% and V5% of the heart kept at ≤30%.

Ohashi et al.[31] investigated the dosimetric parameters for the heart, lungs, and other organs. Whole OARs showed dropped doses with the 3DCRT plan. Heart dose minimizing is a concern for BC on the left side. If the heart receives <30 Gy, the cardiac complications are likely to be lower,[37,38] which supports the present study's results.

Pneumonitis rates in BC treated with standard tangential fields are low and are thus clinically acceptable.[39] Radiation to the axillary area increases the lung volume irradiated,[32] which may increase the probability of pneumonitis.[40] Marks et al.[41] showed that V20% and DVHs of the lung for all patients were acceptable.

The statistical analyses of the heart and lung doses were carried out for only 11 left-sided patients in a study in Egypt. The complication of normal tissue in group b of the heart was lower than in group a, meaning there was no significant association.[34] The main issue with average tissue dose raise of this magnitude is an elevated late secondary malignancy risk.[31,41,42]

Also, Hall and Gao et al.[42,43] discussed this subject again and found to be as it was the most significant issue with a low risk for systemic relapse. There was a report that adjuvant RT may increase the chances of lung cancer and angiosarcoma.[42,44,45] The study of Chitapanarux et al. agrees with the present findings regarding the mean value of the lung (16.4 ± 2.8), which is close to the current research (18.11 ± 1.722) and slightly beyond the value of more fields.[46]

5 | CONCLUSIONS

To our knowledge, this is the first study carried out in Iraq that discusses the examination of DVH statistics when 3DCRT adjuvant is used to treat BC. It also evaluated comparative dose distributions and carried out a per-patient analysis of DVH for all OARs. Planning BC RT can be made more accessible, effective, informative, and accurate by using DVH. The RT dose of 40.05 Gy/15fx gave more outstanding coverage of the target volumes (PTV and CTV) compared with 50 Gy/25fx and 42.56 Gy/16fx, and the lowest doses received by diverse normal tissues. V85% provides the best chest wall coverage, whereas V95% provides the least. With no significance, better coverage of lymph nodes is obtained at V85%, and the lowest coverage at V95%. Significant RT doses result in high tumor bed and lymphatic coverage, but they may also be more hazardous to normal tissues.

6 | LIMITATION

A limitation of the present study are the small number of patients, and the study not clarify the details of the treatment plans, this could be helpful for carrying out a future study on this topic in Iraq.

CONFLICT OF INTEREST

The authors declare that they have read the article and there are no competing interests.

ETHICS STATEMENT

The Medical Ethical Committee of College of Medicine/Baghdad University approved this study (code; 935 in 01/12/2020).

ORCID

Manwar Abdulelah Al-Naqqash https://orcid.org/0000-0002-5009-5146

Ahmed Salih Al-shewered https://orcid.org/0000-0002-0170-1744

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249.
2. Iraqi Cancer Registry. Ministry Of Health, Iraqi Cancer Board, Baghdad. https://moh.gov.iq/upload/upfile/ar/273.pdf.2011
3. WHO. World Cancer Report. p. Chapter 5.2. ISBN 9283204298. [internet] Available at: https://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-2014
4. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Darby S, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;378(9804):1707-1716.
5. 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 DBCGY 82 b&c randomized trials. *Radiother Oncol*. 2007;82(3):247-253.
6. EBCTCGY (Early Breast Cancer Trialists' Collaborative Group), McGyale P, Taylor 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(9935):2127-2135.
7. Goyal S, Buchholz TA, Haffty BG. Breast cancer: early stage. In: Halperin EC et al. eds. *Perez and Brady's Principles and Practice of Radiation Oncology*. 6th ed. Lippincott Williams & Wilkins, a Wolters Kluwer business; 2015:1044-1139.
8. van Herk M, Remeijer P, Rasch C, Lebesque JV. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. *Int J Radiat Oncol Biol Phys*. 2000;47(4):1121-1135.
9. Niemierko A, Goitein M. Modeling of normal tissue response to radiation: the critical volume model. *Int J Radiat Oncol Biol Phys*. 1993;25(1):135-145.
10. Drzymala RE, Mohan R, Brewster L, et al. Dose-volume histograms. *Int J Radiat Oncol Biol Phys*. 1991;21(1):71-78.
11. Purdy JA. In: Halperin EC, Perez CA, Brady LW, et al. eds. *Principles and practice of radiation oncology: Conformal Radiation Therapy Physics, Treatment Planning, and Clinical Aspects: Dose–Volume Histograms*. 6th ed. Lippincott Williams & Wilkins. 2015:214-215.
12. Hasson, Brian F. Dose Volume Histogram (DVH). Encyclopedia of Radiation Oncology. p. 166. ISBN 978-3-540-85513-2. (https://doi.org/10.1007/978-3-540-85516-3_659) 2013.
13. Al-Naqqash MA, Al-Bdaer EK, Saleh WA, et al. Progression free survival in Iraqi breast cancer patients treated with adjuvant 3D conformal radiotherapy: a cross-sectional study. *F1000Research*. 2019;8:71.

14. Al-Naqqash MA, Radhi SM, Tara Farooq Kareem TF, et al. Young age Iraqi Women with Breast Cancer: an overview of the correlation among their clinical and pathological profile. *Med Sci*. 2019; 23(95): 6-11.
15. Al-Alwan NAS, Tawfeeq FN, Mallah NAG. Demographic and clinical profiles of female patients diagnosed with breast cancer in Iraq. *J Contemp Med Sci*. 2019;5(1):14-19.
16. Al-Alwan, Kerr D, Dhafir Al-Okati D, et al. Comparative study on the clinicopathological profiles of breast cancer among Iraqi and British patients. *Open Public Health J*. 2018;11:177-191
17. Al-Rawaq KJ, Al-Naqqash MA, Jassim MK. Molecular classification of Iraqi breast cancer patients and its correlation with patients' profile. *J Fac Med Bagdad [Internet]*. 2016;58(3):197-201.
18. Oussama MNK, Modjtabai A. Guidelines for the early detection and screening of breast cancer: EMRO Technical Publications Series 30 WHO. 2006:11-20.
19. Goldhirsch A, Winer EP, Coates AS, et al. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. *Ann Oncol*. 2013;24(9):2206-2223.
20. Al-Khafaji AH. *Immunohistochemical Expression of Estrogen, Progesterone Receptors, P53 and Ki67 in Iraqi and Syrian Breast Cancer Patients: A Clinicopathological Study*. Thesis. Baghdad-Iraq. Baghdad-Iraq. University of Baghdad College of Medicine. 2010.
21. Al-Naqqash MA. *The Role of c-myc Oncogene as a Prognostic Marker in Breast Cancer Patients Evaluated by Immunno-Histochemistry and In Situ Hypridization (Prospective Study)*. Thesis. Baghdad-Iraq. University of Baghdad College of Medicine. 2009.
22. SEER. Surveillance, Epidemiology, and End Results. Stat Fact Sheets: Breast Cancer. Archived from the original on 3 July 2014. Retrieved 18 June 2014. https://seer.cancer.gov.2014
23. Alwan NAS, Tawfeeq FT, Sattar SA, et al. Assessing the period between diagnosis of breast cancer and surgical treatment among mastectomized female patients in Iraq. *Int J Med Res Health Sci*. 2019;8(1):43-50.
24. Alwan NAS, Tawfeeq FT, Muallah MH, et al. The stage of breast cancer at the time of diagnosis: correlation with the clinicopathological findings among Iraqi patients. *J Neoplasm*. 2017;2(3):11, 1–9.
25. Whelan TJ, Olivotto I, Ackerman I, et al. NCIC-CTG MA.20: an intergroup trial of regional nodal irradiation in early breast cancer. *J Clin Oncol*. 2011;29(18):LBA1003.
26. START Trialists' Group, Bentzen SM, Agrawal RK, et al. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. *Lancet*. 2008;371(9618):1098-1107.
27. START Trialists' Group, Bentzen SM, Agrawal RK, et al. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. *Lancet Oncol*. 2008;9(4):331-341.
28. Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncol*. 2013;14(11):1086-1094.
29. FAST Trialists group, Agrawal RK, Alhasso A, et al. First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015). *Radiother Oncol*. 2011;100(1):93-100.
30. Dancey JE, Dodd LE, Ford R, et al. Recommendations for the assessment of progression in randomised cancer treatment trials. *Eur J Cancer*. 2009;45(2):281-289.
31. Ohashi T, Takeda A, Shigematsu N, et al. Dose distribution analysis of axillary lymph nodes for three-dimensional conformal radiotherapy with a field-in-field technique for breast cancer. *Int J Radiat Oncol Biol Phys*. 2009;73(1):80-87.
32. Takeda A, Shigematsu N, Ikeda T, et al. Evaluation of novel modified tangential irradiation technique for breast cancer patients using dose-volume histograms. *Int J Radiat Oncol Biol Phys*. 2004;58(4):1280-1288.
33. Reznik J, Cicchetti MG, Degaspe B, Fitzgerald TJ. Analysis of axillary coverage during tangential radiation therapy to the breast. *Int J Radiat Oncol Biol Phys*. 2005;61(1):163-168.
34. Bazeed Z, Attalla E, Awad I, Abdel Hamid M, Sarhan A. The effect of the number of fields on radiotherapy plans of breast cancer patients in three-dimensionally conformal radiotherapy plans: dosimetric studies. *Middle East J Cancer*. 2021;12(4):516-526
35. Mansour Z, Ehab MA, Sarhan A, Awad IA, Abdel Hamid MI. Study the Influence of the number of beams on radiotherapy plans for the treatment of breast cancer using biological model. *J Adv Phys*. 2019;16(1):377-390.
36. Alfonso JC, Herrero MA, Núñez L. A dose-volume histogram based decision-support system for dosimetric comparison of radiotherapy treatment plans. *Radiat Oncol*. 2015;10:263.
37. Benson R, Mallick S, Rath GK. Case carcinoma breast. In: Mallick S, Rath GK, Benson R, eds. *Practical Radiation Oncology*. 1st ed. Springer Nature Singapore Pte Ltd. 2020:201-209.
38. Thompson RF. RadOnc: an R package for analysis of dose-volume histogram and three-dimensional structural data. *J Radiat Oncol Info*. 2017;6(1):98-110.
39. Hortobagyi GN. Trastuzumab in the treatment of breast cancer. *N Engl J Med*. 2005;353:1734-1736.
40. Al-Naqqash M, Jasim Al-Serarati W, Farooq Kareem T. Trastuzumab beyond progression in HER2-positive metastatic breast cancer. *Breast J*. 2021;27(3):297-299.
41. Marks LB, Fan M, Clough R, et al. Radiation-induced pulmonary injury: symptomatic versus subclinical endpoints. *Int J Radiat Biol*. 2000;76:469-475.
42. Hall EJ, Wuu CS. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. *Int J Radiat Oncol Biol Phys*. 2003;56(1):83-88.
43. Gao X, Fisher SG, Emami B. Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. *Int J Radiat Oncol Biol Phys*. 2003;56(4):1038-1045.
44. Kirova YM, Gambotti L, De Rycke Y, et al. Risk of second malignancies after adjuvant radiotherapy for breast cancer: a large-scale, single-institution review. *Int J Radiat Oncol Biol Phys*. 2007;68(2):359-363.
45. Mansouri S, Naim A, Glaria L, Marsiglia H. Dosimetric evaluation of 3-D conformal and intensity-modulated radiotherapy for breast cancer after conservative surgery. *Asian Pac J Cancer Prev*. 2014;15(11):4727-4732.
46. Chitapanarux I, Nobnop W, Tippanya D, et al. Clinical outcomes and dosimetric study of hypofractionated Helical TomoTherapy in breast cancer patients. *PLoS One*. 2019;14(1):e0211578.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Alwan AF, Al-Naqqash MA, Al-Nuami HSA, et al. Assessment of dose-volume histogram statistics using three-dimensional conformal techniques in breast cancer adjuvant radiotherapy treatment. *Prec Radiat Oncol*. 2022;6:225–233. https://doi.org/10.1002/pro6.1172