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Dosimetric Effect on Breast Cancer Patients Treated with Volumetric-Modulated Arc Therapy: Single Institutional Experience

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ABSTRACT

Objective: *To examine the dosimetric effect of Breast Cancer (BC) patients Receiving Radiotherapy (RT) with Volumetric-Modulated Arc Therapy (VMAT).* ***Methodology:*** *This retrospective study enrolled 53 BC women, treated with VMAT between Oct 2013 and Nov 2018. The fractionation was within 40 Gray-50 Gray (Gy) in 15-25 fractions. Dosimetric parameters, Homogeneity Index (HI), Conformity Index (CI), Mean Heart Dose (MHD), and doses to the Ipsilateral Lung (IPL) and Mean Contralateral Breast (MCB) were analyzed.* ***Results:*** *Dosimetric results for 50 Gy/25 Fx showed, D98% (mean ± standard deviation) was 47.5± 0.8 Gy, PTV D2% was 53 ± 0.4 Gy, and D50% was 51 ± 0.3 Gy. The maximum point dose (D_{max}), mean ± SD was 110 ± (1.4) and the minimum point dose (D_{min}), was 72 ± (9.1). The HI and CI were 0.11 ± 0.02 and 0.1 ± 0.07. The average MHD was 10.6 ± 3.3 Gy, and the MCB dose 4.5 ± 1.4 Gy, IPL V20Gy 31.5 ± 4.7%. For hypofractionated dose, D98% (mean dose ± SD) was 41 ± 1.6 Gy, PTV D2% was 45 ± 01.9 Gy and, D50 was 43 ± 1.8 Gy. The D_{max}, mean ± SD was 111 ± (5.0) and the D_{min}, mean ± SD was 75 ± (11). The HI and CI were 0.1 ± 0.02, and 0.1 ± 0.34. The average MHD was 10.5 ± 3.55 Gy, MCB 3.7 ± 1.4 G, IPL V20 Gy 31.5 ± 4.7%.* ***Conclusion:*** *VMAT is favorable with complex patient anatomy or when the internal mammary region is included.*

Keywords: Breast cancer, Radiotherapy, VMAT, Dosimetry

INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy worldwide in women [1]. Adjuvant Radiotherapy (RT) is essential in the management of breast cancer. Currently, the general principle of treating breast cancer after surgery is to irradiate the primary site breast or Chest Wall (CW) with or without the Regional Lymph Nodes (RLNs) in patients with a high risk of locoregional recurrence. RT has benefits in terms of reduced locoregional recurrence and distant metastases and increased overall survival [2-8]. However, this comes with the trade-off of radiating the surrounding Organs at Risk (OAR), such as the heart and lungs, and subsequent induced toxicity and morbidity such as radiation pneumonitis, and cardiotoxicity [9-11].

The recent decades have witnessed many advances in radiation treatment. Volumetric-Modulated Arc Therapy (VMAT) is being increasingly used in the management of breast cancer to optimize the dose distribution to the contoured target(s) while reducing the high doses to OAR, especially to the heart and ipsilateral lung, despite its disadvantage of increasing the OAR volumes that receive low dose radiation [12,13].

Several studies have compared the current treatment methods for breast cancer: three-Dimensional Conformal Ra-

diotherapy (3D-CRT), Intensity-Modulated Radiation Therapy (IMRT), and VMAT [14-17]. IMRT and VMAT were found to have superior coverage and uniformity of dose to the target volume than that of 3D-CRT. Both IMRT and VMAT improved dose conformity and sparing of OAR for an optimal therapeutic ratio; however, VMAT reduced the number of Monitor Units (MU) by 30% and the treatment time by 55% [16,18,19].

This study aimed to review the dosimetric data of breast cancer patients treated with adjuvant radiotherapy to the breast/CW and nodal irradiation via VMAT at our institution. The study received ethics approval from the institutional review board.

MATERIALS AND METHODS

Patients and Simulation

All patients with invasive breast cancer (left and right-sided) with the stage (PT1-T4 N1-N3 M0) were treated with surgery followed by adjuvant radiotherapy at King Abdul Aziz university hospital in Saudi Arabia, between October 2013 and November 2018, both inclusive, were selected in this retrospective study. The Research Ethics Committee of King Abdul Aziz university hospital approved this study.

All patients were simulated in the supine position with their arms over their heads using CT soma tom sensation open, version 2014A, with a CT image slice thickness of 3 mm.

Treatment Planning System (TPS)

VMAT plans were generated and optimized using Monaco treatment planning system version 5.11, with treatment energy of 6 MV, and a single isocenter.

Delineation of target and OARs: At our center, the delineation of the Clinical Target Volume (CTV) and, OARs were contoured based on the RTOG guidelines. As per our institutional protocol, the Planning Target Volume (PTV) was generated by expanding 0.5 cm from the CTV in all directions (the superior-inferior/anterior-posterior/left-right directions). The volumes inside the lung were excluded from the PTV, and the PTV was cropped 3 mm from the skin.

The CTV, PTV, and the heart were delineated by a radiation oncologist, whereas the ipsilateral, contralateral lung, spinal canal, and contralateral breast were contoured by a dosimetrist.

Beam Arrangement: 1 or 2 partial arcs were used depending on the patient contour and geometry. The arc increment was either (15 or 20) degrees. For right breast cancer, the arc started approximately at 60 degrees and finished at 180 degrees, whereas, for left breast cancer, it was approximately from 295 degrees to 180 degrees. The arc length at couch 0 degrees ranged from 240 degrees-250 degrees. Where there was an arc at 90 degrees couch value, the arc started at 30 degrees and stopped at 330 degrees with a length of 60 degrees. The number of control points was between 100 degrees and 180 degrees. See Figures 1 and 2 for the arc direction at 0 degrees and 90 degrees couch direction respectively.

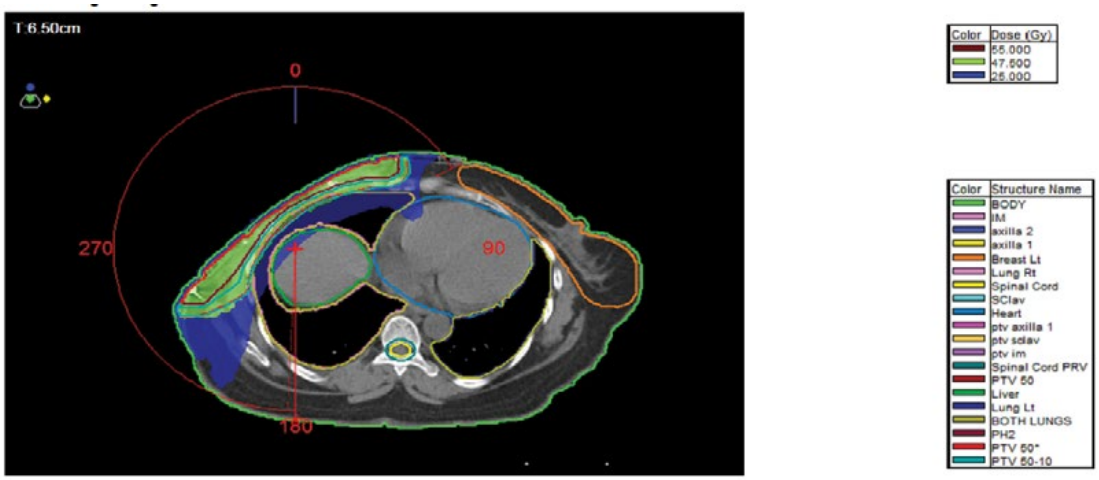

Figure 1 Shows arc orientation and dose distribution in the sagittal slice for couch 0 degrees

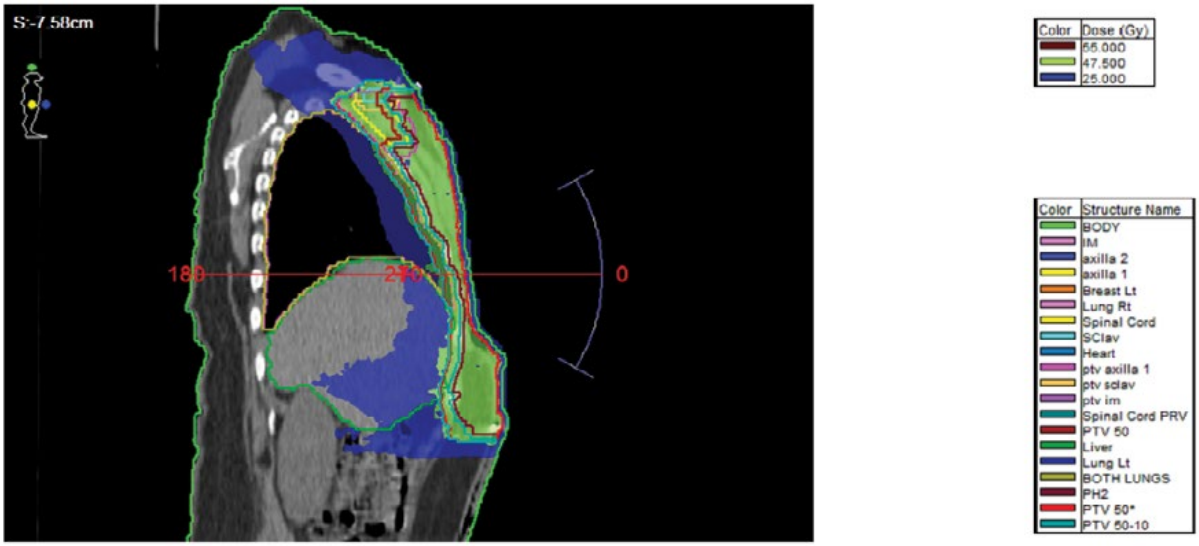

Figure 2 Shows arc orientation and dose distribution in the sagittal slice for couch 90 degrees

Plan analysis

Dose-Volume Histograms (DVHs) of the treatment plans were generated to analyze target coverage and doses administered to the OARs. For plan evaluation, the following parameters were recorded. The maximum point dose (D_{max}) and the minimum point dose (D_{min}), the volumes of the ipsilateral lung receiving 5 Gy and 20 Gy (V5, V20), as well as the mean ipsilateral lung dose (D_{mean}), and were evaluated. For the heart V5, V25, and the mean heart dose were examined. For the contralateral breast, the D_{max} and D_{mean} were reported. Furthermore, the plan qualities were evaluated by the Homogeneity Index (HI) and the Conformity Index (CI). The CI of PTV was defined as BV95%/PTV (BV95%=the volume of the body receiving 95% of the prescribed dose, and the dose Homogeneity Index (HI) of PTV was calculated according to ICRU 83 [20,21]. See Figure 3 for the display of the DVH.

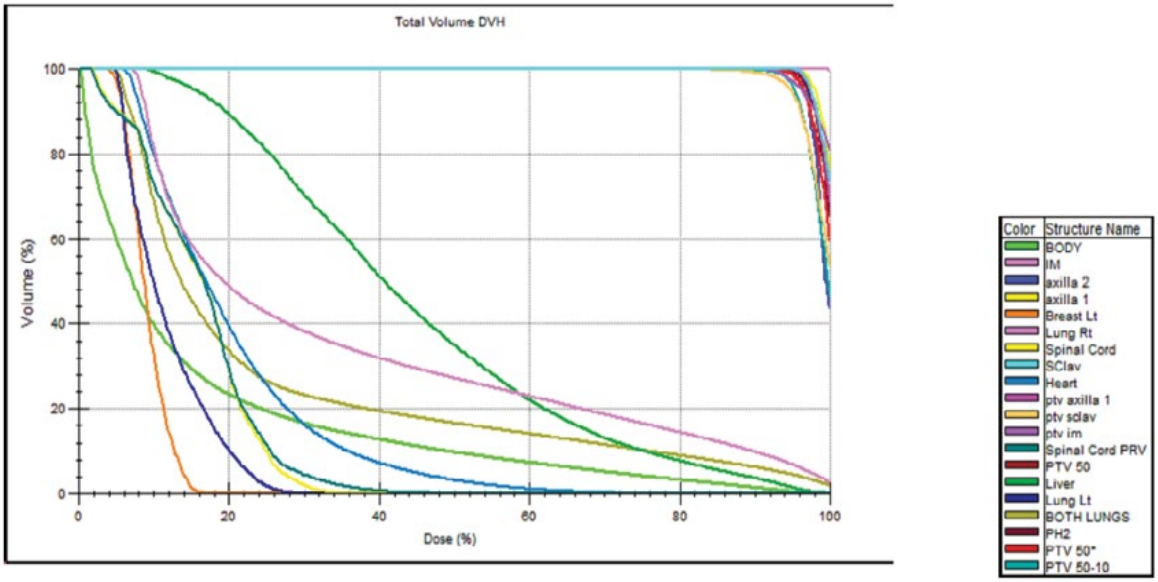

Figure 3 Dose Volume Histograms (DVH) and organ at risk for VMAT

VMAT QA (Plan Verification)

The absolute dose was checked using the calculated dose from the TPS at the center of the chamber and was compared with the measured dose in the 2D array (± 3%).

The fluence dose map was evaluated by a unified tool called Gamma Analysis metrics, and consists of 2 units:

Dose difference delta (D) (%).

Space Domain Distance to Agreement (DTA) (mm).

A group of points was chosen and calculated mathematically. The acceptance criteria D and DTA are usually (3%, 3 mm) or (2%, 2 mm) respectively. Finally, the plan verification depended on the number of passing points (>90%). All VMAT treatment plans passed the QA verification process.

RESULTS

Between October 2013 and November 2018, 53 women with breast cancer who received VMAT Radiotherapy at our institution were enrolled in this study. Twenty-nine patients were right-sided, 23 patients were left-sided, while one patient was treated for bilateral breast cancer. The TNM staging of the patients was pT1-4N1-N3M0. The mean age at treatment was 45 years (range: 30-75 years). All were treated in a supine position. Thirty patients with the hypo-fractionated treatment regimen, 22 patients were treated with standard fractionation and one was treated with 66 Gy/33 fractions.

The prescription dose for the entire treatment volume ranged between 40-50 Gy in 15-25 fractions. Plans were optimized so that a minimum of 95% of the PTV received 100% of the prescribed dose while keeping the volume of the lung receiving 20 Gy (V20) at less than 30%-35% and the V25 of the heart at <10%, and as low mean heart dose as possible. The average treatment duration per fraction was 16 minutes; VMAT plans were optimized for the RapidArc technique in the Monaco treatment planning system. DVHs were analyzed; the dosimetric results are reported as mean value and Standard Deviation (SD) of each parameter for all patients.

Tables 1 and 2 summarize all results presented as mean values and SD for included patients.

Table 1 Summary of dose-volume histogram parameters for target volumes and organs at risk for patients treated with 50 Gray/25 fractions (standard fractionation)

PTV	VMAT
V95 mean% (± SD)	98 ± (1.18)
D2% (Gy) (± SD)	53 ± (0.4)
D98% (Gy) (± SD)	47.5 ± (0.8)
D_{max}, mean (± SD)	110 ± (1.4)
D_{min}, mean (± SD)	72 ± (9.1)
CI	0.1 ± (0.07)
HI	0. 11 ± (0.02)
Ipsilateral lung	
D_{mean} (Gy) (± SD)	16.9 ± (2.1)
V20Gy (%) (± SD)	31.5 ± (4.7)
V5Gy (%) (± SD)	80 ± (11)
Heart	
D_{mean} (Gy) (± SD)	10.6 ± (3.3)
V25Gy (%) (± SD)	6.8 ± (6.7)
V5Gy (%) (± SD)	78.8 ± (18)
Contralateral breast	
D_{mean} (Gy) (± SD)	4.5 ± (1.4)
PTV: Planning Target Volume; D98% and D2%: indicating dose to 98% and 2% (near-maximum dose)	

Table 2 Summary of dose-volume histogram parameters for target volumes and organs at risk for patients treated with 42.4 Gray/16 fractions (hypofractionated dose)

PTV	VMAT Mean + SD
V95 mean% (± SD)	98 ± (0.74)
D2% (Gy) (± SD)	45± (1.9)
D98% (Gy) (± SD)	41 ± (1.68)
D_{max}, mean	111 ± (5.0)
D_{min}, mean	75 ± (11)
CI	0.1 ± (0.03)
HI	0. 1 ± (0.01)
Ipsilateral lung	
D_{mean} (Gy) (± SD)	15.1 ± (1.6)
V20Gy (%) (± SD)	29.4 ± (4.6)
V5Gy (%) (± SD)	74 ± (11)
Heart	
D_{mean} (Gy) (± SD)	10.5 ± (3.55)
V25Gy (%) (± SD)	7.1 ± (6.2)
V5Gy (%) (± SD)	76 ± (21)
Contralateral breast	
D_{mean} (Gy) (± SD)	3.7 ± (1.4)
PTV: Planning Target Volume; D98% and D2%: indicating dose to 98% and 2% (near-maximum dose)	

On the evaluation of the plans that received a total dose of 50 Gy/25 fractions, the D98% mean dose ± (SD) was 47.5 ± 0.8 Gy, PTV D2% was 53 ± 0.4 Gy, and D50 was 51 ± 0.3 Gy. V95 was (98 ± 1.18)%. D_{max}, mean ± SD was 110 ± (1.4) and D_{min}, mean ± SD was 72 ± (9.1). The HI and CI were 0.11 ± 0.02 and 0.1 ± 0.07, respectively. On analyzing OAR sparing, the average mean dose to the heart was 10.6 ± 3.3 Gy, whereas V25 and V5Gy were (6.8 ± 6.7)%, and (78.8 ± 18)%, respectively. The dose to the contralateral breast was 4.5 ± 1.4 Gy. The ipsilateral lung V20Gy and V5Gy were (31.5 ± 4.7)% and (80 ± 11)% respectively.

On analysis of the target coverage for a total dose of 42 Gy/16 fractions, the D98% mean dose ± (SD) was 41 ± 1.6 Gy, PTV D2% was 45 ± 01.9 Gy and D50 was 43 ± 1.8 Gy. V95 was found to be 98.7 ± 0.74%. The D_{max}, mean ± SD was 111 ± (5.0) and the D_{min}, mean ± SD was 75 ± (11). The HI and CI were 0.1 ± 0.02 and 0.1 ± 0.34 respectively. While evaluating OAR, the average mean dose to the heart was 10.5 ± 3.55 Gy, whereas V25 and V5Gy were (7.1 ± 6.2)%, and (76 ± 21)% respectively. The contralateral breast dose was 3.7 ± 1.4 Gy. The ipsilateral lung V20Gy and V5Gy were (31.5 ± 4.7)% and (74 ± 11)% respectively.

DISCUSSION

At our center, like many other centers worldwide, most breast cancer patients are treated with field-based 3D conformal RT. However, because of patient's anatomical variation (where the patient's arm is not raised high enough due to morbidity, when the constraint of the heart is high for 3-D conformal, and in some cases where the dose to the ipsilateral lung is not meeting the dose constraints) or when we choose to treat the internal mammary region, coverage can be challenging to achieve without exceeding normal tissue tolerance. In those situations, we choose to use advanced treatment techniques, including VMAT, to achieve better and conformal coverage, with acceptable OAR doses. This study reviewed our experience and compared it with the results of other major centers that have extensive experience in breast cancer radiotherapy.

A study conducted by Johansen, et al. and N. Supakalin concluded that VMAT has superior homogeneity and conformity in terms of PTV; furthermore, the Rapid Arc plan better spared ipsilateral lung and decreased the mean dose to the contralateral breast [18,22]. Popescu, et al. determined that compared with IMRT, VMAT achieved similar PTV

coverage with shorter delivery time than IMRT, and lesser MUs [12]. According to Oliver, et al. RapidArc is qualified for producing better plans than IMRT with better dose distribution conformity [23]. The study by Nicolini, et al. concluded that VMAT indicated dosimetric improvements concerning IMRT [24]. Tuomas Virén, et al. showed that the dose coverage (V47.5Gy) was significantly superior with VMAT than with FinF and tIMRT [25]. We have also reported similar results in this study as we achieved excellent PTV coverage, with good conformity and homogeneity.

However, our heart dose was initially a concern. Although there is not a specific standard cardiac dose constraint, the aim is to keep it as low as possible [26]. The toxic effect of radiotherapy on the heart has always been a concern. However, it has recently gained more attention after the study by Darby, et al. in 2013 [11]. They found that every gray of mean heart dose increased the estimated risk of ischemic heart disease by 7.4%, starting soon after radiotherapy. Thus, efforts should be directed to minimize the irradiated cardiac volume [27]. The mean heart dose has not been routinely looked at in our plans, until recently, and the main constraint used has been the V25. We believe our mean heart dose was unacceptably high, and the use of deep inspiration breath-hold technique with or without VMAT would achieve better results [28].

The other concerning number was the V20 of the lung. There is an association between V20 and pulmonary toxicity [29]. The usual maximum acceptable dose in our daily practice is 35%. If anything, one would expect better results with IMRT/VMAT. Six of our patients had V20 in the range of 36%-41%, five of whom were treated in 2013-2014. There was no documented toxicity in those patients with V20>35%, or heart V25>10% who maintained follow-up. Our reported data for OAR is higher than the reported data of the previous studies for VMAT; variability in contouring could be a contributing factor. It is likely, however, that this was the first step in the learning curve [30,31]. In fact, in 2017-2018, the OAR constraints were much improved, with only two patients with V20>35%, or heart V25>10%.

There is a deficiency in the literature about the effect of lower doses (V5) on the heart and lung, which is commonly a concern with IMRT/VMAT; Vishruta, et al. revealed a heart V5 of 48% with VMAT [32]. VMAT alone reduced the lung dose by 20%, but the expense was an increase in V5Gy by almost 20% [31]. Cendales, et al. reported lung V5 of 78% using helical tomotherapy [33]. Our data showed that among patients treated with 50 Gy radiation, the V5Gy of the heart was 78.8 ± 18%, and that of the ipsilateral lung was 80 ± 11%. Among patients treated with 42.4 Gy, the V5Gy of the heart was 76 ± 21% and that of the ipsilateral lung was (74 ± 11)%.

Regarding D_{max} and D_{min}, the D_{max} (110% ± 1.4) in this study, for patients treated with 50 Gy, was slightly higher than the study by Supakalin, et al. (106.99% ± 1.16), although the D_{min} (72% ± 9.1), showed a better result than the latter's (80.69% ± 7.06) [18].

Giving the lower average age of our patient population (45 years), and the potential risk of contralateral breast cancer, the dose to the contralateral breast is an important variable. Our mean dose of 4.5 Gy is comparable to what has been documented in the literature [12,13,18].

This study was the first study in the Middle East, it was meant to be a pure dosimetrist assessment, and however, a comparison with 3D plans would have also added some strength, particularly in those patients with high OAR doses. One would assume the 3D planning would have yielded even higher OAR numbers, particularly concerning high dose levels. However, occasionally, 3D planning might offer a better alternative and notably smaller lower isodose volumes.

No toxicities were recorded among the treated patient. Long-term follow-up is needed to assess late toxicity.

CONCLUSION

VMAT is a widely used radiotherapy technology and favoured in patients with complex anatomy or when used in higher volumes to include the internal mammary region. Our results revealed that our learning curve improved, and, in 2018 the result turns out to be consistent with previously reported results from the western world. Furthermore, continuous quality assurance assessments and education are essential to maximizing the safe and optimal use of VMAT.

DECLARATIONS

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None.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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