Original Article

Dosimetric Comparision of Coplanar versus Noncoplanar Volumetric Modulated Arc Therapy for Treatment of Bilateral Breast Cancers

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Abstract

Introduction: The purpose of this study was to compare the dosimetric parameters of volumetric modulated arc therapy (VMAT) treatment plans using coplanar and noncoplanar beams in patients with bilateral breast cancer/s (BBCs) in terms of organ at risk sparing and target volume coverage. The hypothesis was to test whether VMAT with noncoplanar beams can result in lesser dose delivery to critical organs such as heart and lung, which will result in lesser overall toxicity. **Materials and Methods:** Data of nine BBC cases treated at our hospital were retrieved. Computed tomography simulation data of these cases was used to generate noncoplanar VMAT plans and the parameters were compared with standard VMAT coplanar plans. Contouring was done using radiation therapy oncology group guidelines. Forty-five Gray in 25 fractions was planned followed by 10 Gy in five fractions boost in breast conservation cases. **Results:** No significant difference in planning target volume (PTV) coverage was found for the right breast/chestwall ($P = 0.940$), left breast/chestwall ($P = 0.872$), and in the total PTV ($P = 0.929$). Noncoplanar beams resulted in better cardiac sparing in terms of D_{mean} heart. The difference in mean dose was >1 Gy ($8.80 \pm 0.28 - 7.28 \pm 0.33$, $P < 0.001$). The D_{mean}, V_{20} and V_{30} values for total lung slightly favor noncoplanar beams, although there was no statistically significant difference. The average monitor units (MUs) were similar for coplanar plans (1515 MU) and noncoplanar plans (1455 MU), but the overall treatment time was higher in noncoplanar plans due to more complex setup and beam arrangement. For noncoplanar VMAT plans, the mean conformity index was slightly better although the homogeneity indices were similar. **Conclusion:** VMAT plans with noncoplanar beam arrangements had significant dosimetric advantages in terms of sparing of critical organs, that is D_{mean} of heart doses with almost equivalent lung doses and equally good target coverage. Larger studies with clinical implications need to be considered to validate this data.

Keywords: Bilateral breast cancer, noncoplanar, organ at risk, target coverage, volumetric modulated arc therapy

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Introduction

Cancers in both breasts accounts for 1%–3.5% of all breast tumors.[1] The treatment options for bilateral breast cancers (BBCs) are similar to unilateral breast cancers. The options include neoadjuvant chemotherapy followed by breast conservation therapy, adjuvant chemotherapy and irradiation, or modified radical mastectomy (MRM) followed by chemotherapy and radiotherapy (RT) depending on the stage of the tumor.[1]

There are no defined guidelines about the management of BBCs.[2] There are many problems with RT in BBCs, including increased dose at the center of the chest wall, increased overall lung dose, and increased heart dose.[3] It is also troublesome to irradiate bilateral supraclavicular fields with conventional portals, as there is a risk of geographical miss along with the risk of higher cord dose. To avoid all these problems, techniques such as 3-dimensional conformal RT (3-DCRT),[4,5]

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intensity-modulated RT (IMRT),[5-7] volumetric-modulated arc therapy (VMAT),[6,7] and tomotherapy[8] have become popular in irradiating these large volume tumors. Several authors have tried to evaluate these techniques with mixed results. Treating these cancers with newer techniques is a challenge owing to cumulative toxicity and higher total dose delivered to some critical organs by these techniques which is totally avoidable with conventional RT.[9]

VMAT with coplanar beams is a popular method often employed in this scenario. In the past several studies have tried to evaluate the dosimetric differences in the usage of noncoplanar and coplanar plans in treatment of carcinoma breast.[10,11] However, none of the studies have used the technique for the treatment of BBCs. Hence, we designed a study aimed at analyzing the possible dosimetric advantages and disadvantages of using noncoplanar plans in the treatment of BBCs. The literature gives us various examples of noncoplanar RT plans from different sites. Various methods[10] have been followed like (i) VMAT static couch mode at different couch orientation, (ii) a coronal VMAT technique that combines dynamic couch rotation with fixed gantry positions, and (iii) A trajectory VMAT technique that combines dynamic couch rotation with dynamic gantry rotation. The authors have also tried fixed gantry and dynamic couch rotation for accelerated partial breast irradiation (APBI).[11] This technique, however, leads to reduction of ipsilateral lung dose at the cost of increased ipsilateral breast dose in patients with central and inner tumor location as compared to coplanar VMAT plans. Coronal VMAT technique has been found to be useful for prone patient orientation. In order to avoid collision between linear accelerator (LINAC) gantry and patient couch, lateral couch translation was introduced.[12,13] It was observed that this technique leads to reduction of ipsilateral normal breast volume receiving high and intermediate doses and better conformity. This advantage was, however, limited due to the scope of patient setup and alignment for unfavorable target location.

Delivery of noncoplanar treatment plan have certain challenges such as delivery accuracy, delivery efficiency, patient safety and compliance, and inter-fraction patient motion.[14] A VMAT plan includes synchronization of multi-leaf collimator (MLC) motion, gantry rotation, and dose rate, but a noncoplanar VMAT plan has an additional component, i.e., couch rotation. The other factor which concerns a busy RT department is the additional time consumption for the delivery of the treatment of noncoplanar plan. Furthermore, noncoplanar plan has a risk involved due to the potential collision between LINAC gantry and patient or patient immobilization system. Even perception of the collision risk could affect patient compliance. Inter-fraction motion in noncoplanar treatment has two components. One is the uncertainty or the change in patient anatomy during the treatment due to increased treatment duration, and, the other uncertainty is the change in patient anatomy induced due to the treatment motion because of couch movement.

We intend to present a dosimetric comparison of VMAT with coplanar versus noncoplanar arcs in these cohort of patients, trying to analyze the doses delivered to the organs at risk (OARs) and the target volume coverage. The hypothesis was to test whether VMAT with noncoplanar beams can result in delivery lesser dose to critical organs like heart and lung, and hence result in lesser overall toxicity.

Materials and Methods

Between 2013 and 2019, data of 1400 breast cancer patients treated with irradiation for breast malignancies were retrieved. Of these, nine cases were BBCs which were managed with bilateral breast and/or chest wall irradiation with regional nodal irradiation. Out of these, six cases underwent bilateral MRM and three patients underwent breast conservation surgery. All the cases underwent adequate bilateral axillary dissection. The patient characteristics are explained in detail in Table 1.

Treatment planning

All the patients underwent contrast-enhanced computed tomography simulation (CT simulation) with breast board in the supine position with both arms elevated. Five mm thick slices were obtained in free breathing pattern with CT simulator (Siemens Somatom Sensation Open, Siemens Healthineers, Forcheim, Germany).

Table 1: Patient demographics

Age	BCS/MRM	Left breast stage	Right breast stage	RT dose	Hormonal stage
41	Bilateral BCS	pT1N0	pT1N0	45Gy/25#+10Gy/5#	ER/PR+
45	Bilateral MRM	pT3N2a	pT3N0	45Gy/25#	ER/PR+
51	Bilateral MRM	ypT2N3	ypT1N1	45Gy/25#	TNBC
48	Bilateral MRM	ypT3N1	ypT2N0	45Gy/25#	ER+/PR−
43	Bilateral BCS	pT2N0	pT2N0	45Gy/25#+10Gy/5#	TNBC
55	Bilateral MRM	pT2N0	pT2N1	45Gy/25#	ER+/PR−
54	Bilateral MRM	pT2N0	ypT3N1	45Gy/25#	TNBC
58	Bilateral BCS	pT1N0	pT1N0	45Gy/25#+10Gy/5#	ER/PR+
49	Bilateral MRM	pT2N2	pT1N1	45Gy/25#	ER/PR+

BCS: Breast-conserving surgery, MRM: Modified radical mastectomy, TNBC: Triple-negative breast cancer, RT: Radiotherapy, ER: Estrogen receptor, PR: Progesterone receptor

The data were then transferred to Monaco™ treatment planning software via DICOM. Target volumes were contoured using radiation therapy oncology group (RTOG) contouring guidelines.[15,16] The clinical target volumes (CTVs)-CTV Breast, CTV Chestwall and CTV Nodal volumes were contoured as per the RTOG contouring guidelines. The CTV breast was defined as the volume that envelopes the whole breast and the tumor bed. The CTV chestwall included clinical chestwall at the time of CT, including the mastectomy scar. Regional nodal volumes were contoured as per clinical indication. Axillary and SCF nodal volumes were treated as per the clinical case. The planning target volumes (PTVs) were obtained by expansion of 7 mm in all directions from the CTVs and were also restricted to have the skin gap (trim) of 5 mm from the surface and to exclude the ribs[15,17] [Figure 1a-d]. The target volume delineation and the OAR dose constraints of this study were drawn with reference to the RTOG target volume contouring atlas. As there is no distinct treatment protocol for BBC, the OAR dose constraints guideline was set up using several unilateral breast study group[18,19] and a previous BBC research paper by Nicolini *et al*.[6] To establish the dose constraints. Besides, clinically relevant organs when treating patients were established in addition.

All the patients were planned in the Monaco planning system (version 5.11.02). The patients were planned for 45 Gy to be delivered in 25 fractions in case of breast conserving surgery (BCS) and MRM cases and an additional boost of 10 Gy in 5 fractions in BCS cases requiring boost to lumpectomy cavity. Two plans were generated: One with coplanar arcs and another with noncoplanar beams.

Two treatment plans, a coplanar and a noncoplanar plan were generated for each patient [Figure 2]. The coplanar plan comprised of two full arcs. One of the arcs was clockwise and the other was anticlockwise. The plans were generated with following parameters, number of control points-250, grid spacing-0.3 cm, statistical uncertainty per control points-1% and couch angle of 0°.

A noncoplanar plan consists of beams in different geometric planes with respect to patient. Non-coplanar beams are often used in APBI to spare the ipsilateral breast outside the target volume. Use of noncoplanar partial beams also achieves better dose fall-off in brain and, head and neck sites and so helps in reduction of neurocognitive side effects. Noncoplanar plans comprised of 4 arcs. Of these, two were full arcs, one clockwise and the other one was anti-clockwise. The other two arcs were delivered with 90° couch rotation. These 2 non-coplanar arcs were of 30°–45° in clockwise and anti-clockwise direction based upon patient geometry in order to avoid any collision with gantry head or anti-collision device. These two arcs were rotating along cranio-caudal direction of patient. All the dose calculation were done using Monte–Carlo algorithm available with the Monaco™ treatment planning system (TPS). Treatment plans were optimized with the same dose constraints for OARs.

The patients were treated by VMAT using coplanar beams. The exercise pertaining to comparision of coplanar versus noncoplanar beams was undertaken only for dosimetric purposes to ascertain any benefit in dose reduction to OARs. The treatment was delivered using Elekta Infinity LINAC (Crawley, UK). All plans were created and evaluated by one physician and one physicist to maintain coherence of planning and evaluation.

Statistical analysis was performed with statistical package for social sciences (SPSS) software package for Mac (version 23.0; IBM, Armonk, NY, USA). The independent samples *t*-test was utilized for analysing the data. The results were considered significant if $P < 0.05$.

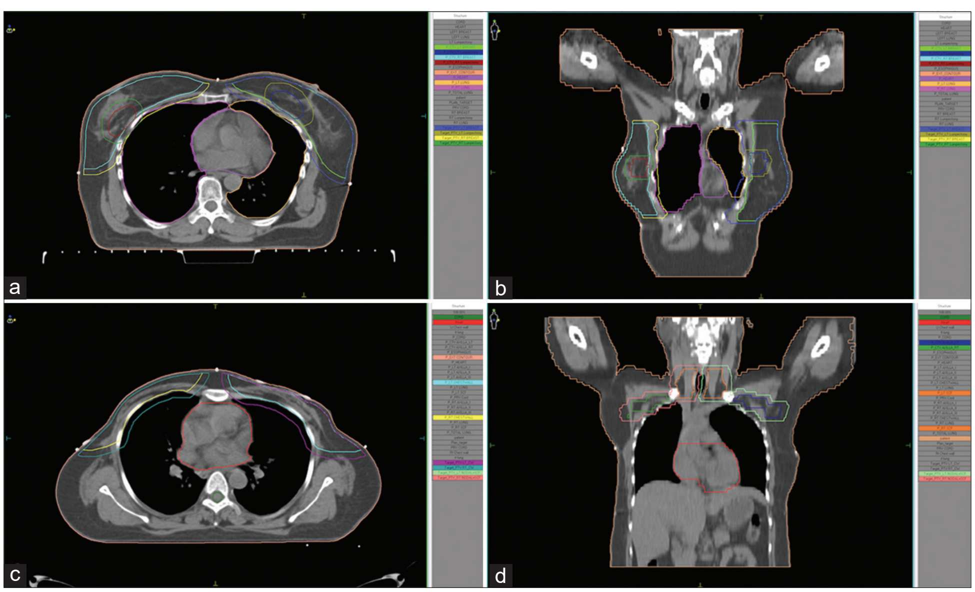

Figure 1: Contouring images – (a and b) Depict contouring of breast conservation cases in axial and coronal slices, (c and d) Depict contouring of modified radical mastectomy cases in axial and coronal slices showing both chestwall and nodal contouring

Results

The demographic details of the cases, postoperative histopathological details and RT details has been mentioned in the Table 1. All the patients completed the prescribed dose schedules.

Planning target volume coverage

All plans were normalized to 95% volume of PTV Total with prescription dose of 45 Gy. The dosimetric parameters for PTV Total, PTV Right Breast and PTV Left Breast are mentioned in Table 2. No significant difference in PTV coverage was found for the right breast/chestwall ($P = 0.940$), left breast/chestwall ($P = 0.872$) and in the total PTV ($P = 0.929$) volumes. The differences in terms of different parameters for coplanar and noncoplanar VMAT plans have been mentioned in Table 2 and Figure 3.

Heart

Noncoplanar beams resulted in better cardiac sparing in terms of mean heart doses. The difference in mean dose was >1 Gy (8.80 ± 0.28–7.28 ± 0.33, $P < 0.001$). This translates into a 12% reduction in mean dose delivered to heart. There was also significant difference in V_{20} (5.48 ± 1.79 vs. 2.49 ± 0.65, $P = 0.008$), with noncoplanar beams delivering almost half the doses compared to coplanar beams. There was no difference in low dose volumes, i.e. V_5. Although there was marked difference in the V_{30} values, but it was not significant.

Lungs

It can be seen in Table 2 that the mean values of V_5, V_{20} and V_{30} vary significantly for both right and left lung in coplanar or non-coplanar beams. The D_{mean} values of right and left lung slightly favor non coplanar beams, albeit without any statistical significance. Similarly, the D_{mean}, V_{20} and V_{30} values for total lung (including both right and left lung) although slightly favor noncoplanar beams, there was no statistically significant difference.

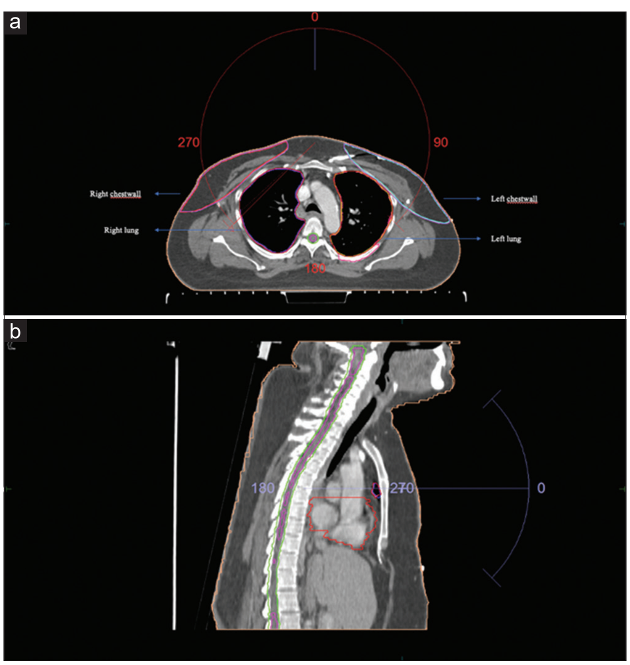

Figure 2: Images showing planning arcs: (a) Transverse arcs and (b) Sagittal arcs used

Other organ at risks

The other OARs like Oesophagus or Spinal cord also did not receive significantly different mean doses for coplanar or noncoplanar beams. The mean values of D_{mean} Oesophagus and D_{max} spinal cord were almost similar.

Monitor unit and treatment time

The average monitor units (MU's) were similar for coplanar (1515 MU) and noncoplanar plans (1455 MU). But the overall treatment time is expected to be higher in non colplanar plans due to more complex setup and beam arrangement. For noncoplanar VMAT plans the mean conformity index increases from 0.71 ± 0.07 to 0.75 ± 0.08. The homogeneity index for both coplanar and noncoplanar plans were similar.

Table 2: Comparision of dosimetric parameters of co-planar and non-coplanar techniques

	Coplanar	Noncoplanar	*P*
PTV			
Total (%)	97.31±1.21	97.24±1.18	0.929
Right breast/CW (%)	97.83±2.16	97.94±1.97	0.940
Left breast/CW (%)	97.38±3.26	97.07±2.47	0.872
Heart			
D_{mean} (Gy)	8.80±0.28	7.28±0.33	<0.001
V5 (%)	81.56±8.88	78.92±13.44	0.724
V20 (%)	5.48±1.79	2.49±0.65	0.008
V30 (%)	1.99±1.28	0.70±0.31	0.06
Right lung			
D_{mean} (Gy)	14.48±2.31	13.79±1.92	0.620
V5 (%)	76.94±12.12	83.33±9.33	0.405
V20 (%)	25.87±7.83	22.52±6.10	0.472
V30 (%)	15.91±6.19	12.62±5.11	0.385
Left lung			
D_{mean} (Gy)	14.64±3.05	13.87±1.94	0.646
V5 (%)	68.60±13.61	78.54±8.43	0.202
V20 (%)	27.26±7.45	23.41±5.30	0.374
V30 (%)	17.77±6.09	13.48±5.09	0.261
Total lung			
D_{mean} (Gy)	14.6±2.49	13.9±1.86	0.627
V20 (%)	26.59±7.11	23.11±5.43	0.410
V30 (%)	16.97±5.90	13.26±4.85	0.309
Spinal cord			
D_{max} (Gy)	26.23±14.55	26.25±7.78	0.998
PRV_spinal cord			
D_{max} (Gy)	27.73±8.91	27.44±14.87	0.970
Esophagus			
D_{mean} (Gy)	12.88±4.60	12.58±4.80	0.924

PTV: Planning target volume, CW: Chest wall, PRV: Planning organ at risk volumes

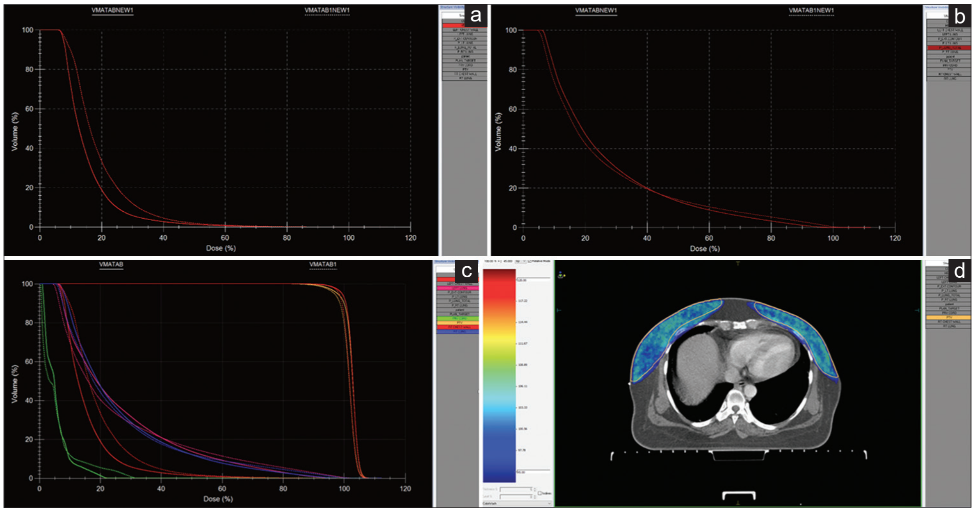

Figure 3: Dose volume histograms (DVH) showing, (a) Organ at risk – Heart DVH, (b) Organ at risk – Total lung DVH, (c) Cumulative DVH showing comparison of both coplanar and non-coplanar plans and (d) planning target volume coverage

Discussion

Attempts have been made in various sites to use noncoplanar beams instead of coplanar beams to achieve improved target coverage and/or spare the OARs better. Noncoplanar beams in VMAT have previously been used in treatment of sinonasal cancers,[20] head and neck cancers,[21] brain tumors like gliomas and craniopharyngiomas,[22,23] and pancreatic cancers.[24] While delivering noncoplanar beam is a challenge, the benefits they provide have compelled researchers to try them in dosimetric studies. Similarly, for unilateral breast cancers, noncoplanar beams have been reported in several studies reporting dosimetric advantages. But noncoplanar plans have rarely been studied in BBCs. We intended to report the outcomes of noncoplanar beams in these cancers.

BBCs have a huge C-shaped target volume, and the shape and volume of the target can vary greatly. In addition, the target is closer to the skin and OARs with large volumes. The radiation therapy plan for BBCs using 3DCRT has several limitations, including inadequate target coverage and inhomogeneous dose distribution. Yusoff *et al.*[5] compared the 3DCRT and IMRT treatment plans for BBC patients. They reported that both treatment plans showed similar results for PTV coverage, whereas IMRT was superior for OAR dose distributions to the lungs and heart. VMAT showed a shorter irradiation time than IMRT. The authors inferred that shorter delivery time can be achieved through continuous movement of gantry and MLC. Therefore, we used arc therapy and compared the conventional coplanar arcs with noncoplanar arcs.

Several researchers have compared coplanar and noncoplanar planar plans in the treatment of unilateral carcinoma of the breast. Fogliata *et al.*[25] compared noncoplanar static fields and coplanar arcs for whole breast RT of patients with concave geometry and found 3 field noncoplanar technique having better dosimetric outcomes. The D_{mean} and V_{20} lung doses were superior compared to other plans. VMAT plans have several advantages.[26] Over conventional breast RT, like better conformity, lesser dose to ipsilateral lung and normal breast tissue and, fewer delivered MUs. Few other studies have also reported better sparing of OARs in VMAT and IMRT.[27,28] With similar target coverage VMAT achieved better dose homogeneity lower cardiac dose and lower lung dose especially for low dose volumes. However, the integral and mean doses were higher for VMAT plans.[27]

Patients of left breast cancers are known to have higher probability of radiation induced ischemic heart diseases. Hence, it becomes very essential to optimize and reduce the heart dose as much as possible for the patients of BBC. Darby *et al*. reported that the rate of major coronary events increased by 7.4% with the dose to heart increasing by 1 Gy.[29] Therefore, it is critical to reduce the dose delivered to heart to as low as possible. In our study, a mean reduction of 1.52 Gy for the mean dose of the heart was achieved with noncoplanar technique compared to coplanar plans. The D_{mean} heart reported in our study with noncoplanar beams was 7.28 Gy, which was 12% lower than that using coplanar beams (8.8 Gy). The dose achieved for D_{mean} heart for noncoplanar plans is superior to D_{mean} heart of helical tomotherapy (HT) plans, as mentioned in reports by Balaji Subramanian *et al*. and Cho *et al*., who reported D_{mean} heart doses of 10.5 Gy[30] and 13.2 Gy,[31] respectively. The comparative doses of lung and heart in similar studies have been reported in Table 3.

Kim *et al*.[7] reported on dosimetric comparisons in BBCs for 3DCRT, IMRT and VMAT (using coplanar beams). They showed for D_{mean} heart, 3DCRT (8.18 ± 3.06 Gy) was the best with the lowest mean dose distribution, followed by IMRT (9.46 ± 16.6 Gy) and VMAT (14.47 ± 2.39 Gy). For V_{40} heart, VMAT (2.18% ±1.47%) was better than 3DCRT (7.77% ±4.70%). Our V_{20} for heart was significantly better for noncoplanar versus coplanar plans (2.49% ±0.65% vs. 5.48% ±1.79%, $P = 0.008$). Wadasadawala *et al*.[32] compared bilateral

Table 3: Review of literature

Studies	Heart D mean (Gy)	Lung total D mean (Gy)
Kim *et al*., 2018 (VMAT)[7]	14.47	15.84 (left), 18.32 (right)
Wadasadawala *et al*., 2015 (HT-IMRT)[32]	4.68	5.99
Balaji Subramanian *et al*., 2016 (VMAT)[30]	10.5, 16.2	12.1, 13.8
Fiorentino *et al*., 2017 (VMAT)[34]	5	9.3
Popescu *et al*., 2010 (VMAT)[27]	13.2	14.4
Wang and Park 2015 (VMAT)[33]	10.3	10.3
Present study	7.28	13.9

VMAT: Volumetric-mediated arc therapy, IMRT: Intensity-modulated radiotherapy, HT: Helical tomotherapy

tangential plans with HT and Tomo-direct (TD) plans. They achieved D_{mean} heart doses of 4.68 Gy, 3.65 Gy and 3.38 Gy for HT, TD-3DCRT and TD-IMRT plans, respectively. The V_{20} heart doses for these plans were 2.77 Gy, 4.1 Gy, and 3.93 Gy, respectively. Our V_{20} heart doses are better than these doses, although D_{mean} heart doses are higher. Wang and Park[33] reported D_{mean} heart doses of 10.3 Gy.

Similarly for lung doses, quantitative analysis of normal tissue effects in the clinic for lung emphasizes the need to limit the $V_{20\ Gy}$ to <30%–35%.[32] This is generally difficult to achieve in BBCs as the integral dose increases due to large volume irradiation. In the current study, we achieved 0.7 Gy mean dose reduction in total lung D_{mean} doses with noncoplanar plans compared to coplanar plans, although the difference was nonsignificant (13.9 ± 1.86 Gy vs. 14.6 ± 2.49 Gy, $P = 0.627$). Kim *et al*.[7] reported Rt Lung D_{mean} doses of 11.84, 11.68 and 18.32 Gy and Lt lung D_{mean} doses of 11.76, 12.02 and 15.84 Gy doses for 3DCRT, IMRT and VMAT plans, respectively. Similarly, V_{20} lung doses were slightly better for 3DCRT and IMRT compared to VMAT plans. Wadasadawala *et al*.[32] reported D_{mean} lung doses of 5.99, 5.3 and 4.76 Gy and V_{20} lung doses of 7.25, 8.57 and 7.56 Gy for HT, TD-3DCRT and TD-IMRT plans, respectively. The mean lung doses achieved were favourable to that achieved in the other studies reporting lung doses with VMAT techniques like Kim *et al*.[7] and Fiorentino *et al*.[34] The D_{mean} oesophagus dose mentioned in Fiorentino *et al*.[34] is 9.3 Gy which is comparable to the dose in the present study. The CT data sets used in planning were obtained in free breathing mode. So it can be said that with reasonable certainty that dose received by OARs and target may be not so accurate or correct as shown by TPS. Gating method would have been a better approach of treatment in carcinoma of breast especially for OAR's affected by respiratory motion. Since the study was a comparison of dosimetry of target volume coverage and OAR sparing with two different techniques, the effect of respiratory motion can be safely assumed to have an equal impact on accuracy of dose calculation.

Several studies have been published on breast RT comparing different treatment modalities like conventional, IMRT, VMAT and tomotherapy plans. There are also published research comparing coplanar and noncoplanar breast RT, but none of them have attempted to do a dosimetric analysis of bilateral breast RT for noncoplanar and coplanar field arrangement. One of the probable reasons for lack of literature or published research on bilateral breast RT may be rarity of occurrence of bilateral carcinoma of breast. In our study, the dosimetric advantage in the treatment of BBCs was investigated and the OAR sparing in the planning techniques was assessed by comparing noncoplanar VMAT and coplanar VMAT in photon therapy. We found that the noncoplanar VMAT plan spares heart better than the coplanar VMAT plan without affecting PTV coverage and without increasing lung or spinal cord doses.

Advantages of the study

The study is the first study of its kind exploring the benefits of noncoplanar beams for VMAT in BBCs. It uses a homogeneous dataset of patients. The contouring, planning, and plan evaluation was performed by same physician and physicist, thereby minimizing inter-observer error.

Limitations of the study

This is a feasibility study performed on data sets of homogenous BBCs (bilateral mastectomy and bilateral breast conservation cases); results of the study need to be validated in a larger study set. This is a dosimetric study, so it needs to be validated with clinical outcomes. Also to be taken into consideration are the effects of inverse planning in breast cases, increased low dose spill to nontarget areas and higher integral dose and longer treatment times.

Conclusion

In conclusion, VMAT plans with noncoplanar beam arrangements showed significant dosimetric advantages in terms of sparing or critical organ that is D_{mean} of heart doses with almost similar lung doses and equally good target coverage which can translate into better clinical outcomes and lesser comorbidities in future. Larger studies with clinical implications need to be considered to validate this data.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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