RESEARCH ARTICLE

# Adjuvant Radiotherapy after Breast Conserving Treatment for Breast Cancer: A Dosimetric Comparison between Volumetric Modulated Arc Therapy and Intensity Modulated Radiotherapy

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## Abstract

**Background: Radiotherapy is an important treatment of choice for breast cancer patients after breast-conserving surgery, and we compare the feasibility of using dual arc volumetric modulated arc therapy (VMAT2), single arc volumetric modulated arc therapy (VMAT1) and Multi-beam Intensity Modulated Radiotherapy (M-IMRT) on patients after breast-conserving surgery. Materials and Methods: Thirty patients with breast cancer (half right-sided and half left-sided) treated by conservative lumpectomy and requiring whole breast radiotherapy with tumor bed boost were planned with three different radiotherapy techniques: 1) VMAT1; 2) VMAT2; 3) M-IMRT. The distributions for the planning target volume (PTV) and organs at risk (OARs) were compared. Dosimetries for all the techniques were compared. Results: All three techniques satisfied the dose constraint well. VMAT2 showed no obvious difference in the homogeneity index (HI) and conformity index (CI) of the PTV with respect to M-IMRT and VMAT1. VMAT2 clearly improved the treatment efficiency and can also decrease the mean dose and V5Gy of the contralateral lung. The mean dose and maximum dose of the spinal cord and contralateral breast were lower for VMAT2 than the other two techniques. The very low dose distribution (V1Gy) of the contralateral breast also showed great reduction in VMAT2 compared with the other two techniques. For the ipsilateral lung of right-sided breast cancer, the mean dose was decreased significantly in VMAT2 compared with VMAT1 and M-IMRT. The V20Gy and V30Gy of the ipsilateral lung of the left-sided breast cancer for VMAT2 showed obvious reduction compared with the other two techniques. The heart statistics of VMAT2 also decreased considerably compared to VMAT1 and M-IMRT. Conclusions: Compared to the other two techniques, the dual arc volumetric modulated arc therapy technique reduced radiation dose exposure to the organs at risk and maintained a reasonable target dose distribution.**

**Keywords:** Breast cancer - VMAT - IMRT - dosimetry - DVH

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## Introduction

During the past several years, the incidence of breast cancer in Asia has increased at an unbelievable rate (McCormack et al., 2011). Although chemotherapy and molecular targeted therapy have advanced rapidly, radiotherapy remains an important treatment of choice for breast cancer for both surgical and non-surgical patients (Cao et al., 2013; Eccles et al., 2013). The comparison of dose distribution for different radiotherapy techniques for breast cancer has been reported frequently (Saibishkumar et al., 2008; Askoxylakis et al., 2011; Rudat et al., 2011; Badakhshi et al., 2013). Both VMAT and IMRT can achieve excellent dose escalation and facilitate the sparing of normal tissue, which may reduce toxicity and improve local control (Kim et al., 2013).

Traditionally, the prescribed dose for the breast radiotherapy is 50 Gy in 25 fractions, with up to an additional 10 Gy in 5 fractions to the boost field (Liljegren et al., 2014). The boost dose is usually delivered after the radiation treatment, but the introduction of the simultaneous integrated boost (SIB) by some studies showed that the boost dose can be delivered at the same time as the whole breast dose. The investigation of SIB has been used to improve dose conformity to the boost volume as well as to decrease doses to the heart, lungs, and many other organs at risk when incorporated with either VMAT or IMRT, compared with a sequential boost (Hurkmans et al., 2006; Singla et al., 2006; van der Laan et al., 2007). It also has the advantage of reducing the overall number of control points for the patient.

The purpose of this study was to investigate a possible

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dosimetric advantage of VMAT2 compared with IMRT and VMAT1 and to assess the dose distribution of different techniques in the same treatment planning system. It has been reported that the Elekta multileaf collimator with 1 cm leaf width (MLCi, Elekta, UK) was employed for previous treatment planning. Compared with the MLCi, the AXESSE™ linac (Elekta AB, Stockholm, Sweden) is equipped with the improved Integrity™ treatment control system and the newly designed Agility™ head. Whether dual arc VMAT can achieve better no compromise CTV coverage and OAR sparing compared with single arc VMAT and Multi beam-IMRT will be addressed in this paper.

## Materials and Methods

*Patient selection and simulation*

This study has been approved by the Ethics Committee of the first affiliated hospital of Nanjing Medical University. Thirty patients who had been treated with

breast-conserving surgery (both left-sided and right-sided) were retrospectively selected for this study. The patients received whole breast radiation and an SIB to the tumor bed after breast conserving surgery. All of the patients selected for this study were evaluated by one radiation oncologist before undergoing surgery.

The dose constraints of the breast cancer are listed in Table 1. All the patients underwent conventional CT and were treated using Elekta AXESSE™ linac-based VMAT and IMRT. Patients were positioned supine with both arms above the head on a breastboard.

The surgical scars were delineated with radio-opaque wires made of lead. The markers were also placed along the mid sternum and midaxillary line, as well as 2 cm below the healthy breast limits. Images were acquired from the top of the head to the mid-abdomen, using a 5-mm slice thickness. A SIMENS SOMATOM Sensation OPEN CT scanner was used to obtain the CT scans. The image sets were transferred to the Focal system for contouring and to the Monaco3.5 TPS for planning .

*Target and normal tissue delineation*

The target volume was defined for the purpose of this study.

Target delineation: The CTV-breast included all the visible breast parenchyma and was defined as the tissue delineated by the lead marker that we mentioned before. On each slice, the breast volume extended from the pectoralis major muscle to the skin, excluding the pectoralis muscle, the ribs and the first 5 mm of skin. The PTV-breast was expanded by 5 mm in all directions around the CTV-breast except for the skin surface, including the set-up margin and patient movement.

The volume of the tumor bed was defined using the planning CT and the preoperative and operative reports. In practice, it included the surgical clips, as well as any hematoma, seroma, or other surgery-induced changes considered to be a part of the lumpectomy cavity (Hijal et al., 2010). CTV contouring was completed by a radiation oncologist, and to minimize interobserver variability in this planning study, all other contouring and treatment planning was completed by one person, a medical dosimetrist. The target volume delineation is presented in Figure 1.

The PRV contours of all the involved organs at risk, including the entire heart, ipsilateral lung, contralateral lung, contralateral breast and spinal cord, were outlined by the treating physician. All targets and OARs were outlined slice by slice in the CT image in the treatment planning system, and the three dimensional contour was reconstructed automatically.

Delineation of OARs: The heart was contoured from the level of the pulmonary trunk to the apex, and included the pericardium but not the major vessels. Both lungs, the contralateral breast, the sternum and the spinal cord were also manually delineated (Hijal et al., 2010).

In our study, the tumor locations of the patients we selected for this study were in the outer quadrants, as inner quadrant tumors usually receive internal mammary chain irradiation in our department, and the dose acquisition of the heart will increase as well. The statistics of the volume (cc) of the PTV in our study are shown in Table 1.

*Treatment planning*

Both M-IMRT and VMATs (VMAT1 and VMAT2) were performed using the Monaco3.5 TPS of the AXESSE linac: the AXESSE linear accelerator with a 160-multileaf collimator (Agility™) with a projected width of 5 mm at the isocenter, and designed to replace the tongue-and-groove system and allow complete interdigitation and non-continuous field shape (Ning et al., 2013). The maximum speed of the dynamic leaf guide (DLG) is 3 cm/s. The MLC maximum speed is 3.5 cm/s and can approach 6.5 cm/s with the aid of the DLG. The gantry maximum rotation velocity is 6%. The minimum segment width was set at 5 mm with the minimum Monitor Units (MUs) of control points (CPs) at 1 MU. The final dose calculation and segment optimization used the X-ray Voxel Monte Carlo (XVMC) algorithm with a calculation grid of 3 mm and 3% standard deviation (Jabbari et al., 2011).

A total dose of 50 Gy with a single fraction dose of 2 Gy for the whole breast was prescribed. A total SIB dose of 60 Gy with 2.4 Gy per fraction was prescribed to the tumor bed. To evaluate treatment plan tolerance doses for the organs at risk, the values described by the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) review were used.

*Planning technique*

Multi-beam IMRT (M-IMRT): A 7-beam or 9-beam plan was reported to be more appropriate for M-IMRT, and the 7-beam plan, which avoided direct exposure to the contralateral breast, was selected in this study (Thilmann et al., 2003). For the right-sided breast cancer, the seven coplanar beam angles were 0°, 30°, 50°, 70°, 215°, 240°, 270°. For the left-sided breast cancer, the beam angles were set as follows: 0°, 110°, 125°, 140°, 295°, 310°, 330°.

*Single arc VMAT (VMAT1) and dual arc VMAT (VMAT2)*

VMAT in which the arc direction is such that the beam enters the breast before exiting through the lung may

increase the dose volume of the lungs and contralateral breast. In this paper, the VMAT plan used the arc field for which the starting angle and ending angle were the same as the tangential beam angle, and a sub-field interval of 4° was used. The single arc angle we designed for right-sided breast cancer was 220°~60°, and it was 300°~145° for left-sided breast cancer. The distributions of the dual arcs were 220°~ 265° and 0°~60° for right-sided breast cancer and 300°~ 360° and 90°~140°, respectively, for left-sided breast cancer.

The maximum CPs for VMAT1 was 100, for VMAT2 it was 80, and the maximum CPs for M-IMRT was 30, which has been shown to be adequate for both efficiency and plan quality in our department.

*Data comparisons*

All the data are based on DVHs calculated using the Monaco 3.5 TPS (Elekta AB, Stockholm Sweden). The dosimetric comparison criteria were as follows.

Dose information was collected to evaluate PTV coverage and doses to OARs. Mean dose (Dmean), dose homogeneity index (HI), dose conformation index (CI) and V95% (47.5 Gy) were reported for PTV-breast coverage comparisons. *i)* Homogeneity Index (HI): used to evaluate the PTV-breast coverage by the prescription isodose. HI was calculated using the formula recommended in ICRU Report #83, with a result closer to zero indicating greater homogeneity. Formula: HI= (D2% -D98%)/D50%. D2%, D50% and D98% mean doses of 2%, 50% and 98% volume of the PTV. *ii)* Conformity Index (CI): used to evaluate the dose homogeneity within the PTV, with both the irradiation of the target volume and the irradiation of healthy tissue considered. Formula: CI = (VTPV^2)/(VPTV×VTV). (VTV is the treatment volume of the body receiving 95% of the prescribed dose, VPTV is the volume of the PTV, and VTPV is the volume of VPTV within the VTV).This value ranges from zero to 1, where 1 is the ideal value, and a higher CI value indicates higher dose conformity to the target. A CI value close to zero indicates either total absence of conformity or a very large volume of healthy tissue being irradiated compared with the target volume. Dmean, Dmax, and volumes receiving specific doses were calculated for the OARs (Feuvret et al., 2006). *iii)* Delivery efficiency and dose verification: MUs and control points per fraction and plan calculation time for all plans were recorded. Treatment time only includes beam-on time, but not time for patient set-up. Dosimetric validation was performed for all plans before being transferred to the Axesse™ linac. The delivered dose was measured by a 2D ionization chamber array (TW30013 S/N005054). The calculated doses and the measured doses were compared using the Delta4 (ScandiDos, Sweden), which employs gamma evaluation criteria of 3% and 3 mm. *iv)* Organs at risk: The normal tissue doses of the VMAT2, VMAT1 and M-IMRT plans were calculated. In particular, the Dmax (maximum point dose) and Dmean (mean dose) to serial organs were determined, as well as the Dmean (mean dose) or V5Gy to parallel organs.

*Data and statistical analysis*

IMRT and VMAT plan parameters derived from the same patient were tested for statistically significant differences using analysis of variance (ANOVA) for repeated measurements.

Data from the VMAT2, VMAT1 and M-IMRT plans were then transferred to the SPSS (Statistical Product and Service Solutions) version 19.0 statistical software (IBM SPSS Statistics) for dose-volume histogram (DVH) generation and analysis. The extracted dosimetric criteria were then compared using a two-tailed Wilcoxon matched-pairs signed-ranks test. All the results are reported as average±standard deviation. Differences were considered significant for $p$ value <0.05.

## Results

*Patient characteristics*

A total of 15 right-sided breast cancer patients and 15 left-sided breast cancer patients who had undergone breast-conserving surgery were selected in our study. Among them,16 of the 30 patients had tumors located in the outer quadrants, and the others had tumors in the inner quadrants.

*Dose coverage for target volume*

*i)* Right-sided breast cancer: The dose constraint of the target volume, which is V47.5>95%, can be met well. The mean volumes receiving at least 95% of the tumor bed boost dose (V95%) were 99.44±0.63%, 99.95±0.05% and 99.40±0.98% for VMAT2, VMAT1, and M-IMRT, respectively; they were 99.32±0.62%, 99.66±0.20%, and 99.32±0.60% for the PTV-breast. The tumor bed volumes receiving more than 105% of the prescribed boost dose were 16.46±9.17%, 6.73±1.03% and 16.05±8.41% for the VMAT2, VMAT1, and M-IMRT plans, respectively. VMAT1 is obviously smaller than VMAT2 and M-IMRT, but VMAT2 has no significant difference from M-IMRT. The mean dose of the PTV-breast is shown in Table 2, with no obvious difference among the three techniques. When comparing the mean dose for the tumor bed of the three techniques, the result remains the same. The result of the HI comparison of PTV-breast among the three techniques shows no significant difference. The CIs for the PTV-boost also show no significant difference among the three techniques. Typical dose distributions of VMAT1, VMAT2, M-IMRT planned for the right-sided breast cancer patients are shown in Figure 2. *ii)* The left-sided breast cancer: The dose distribution in both the VMATs (VMAT1 and VMAT2) and M-IMRT plans for all 15 left-

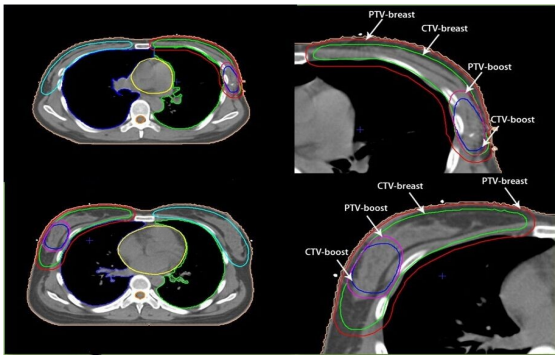


**Figure 1. The Target Volume Delineation**

sided breast cancer patients satisfied clinical requirements. Typical dose distributions of VMAT1, VMAT2, and M-IMRT planned for the left-sided breast cancer patients are shown in Figure 3. All the treatment plans met the target constraint that 95% of the PTV-boost and PTV-breast must receive at least 95% of the prescription dose. The statistics of the PTV-breast and PTV-boost are shown in Table 3. Tumor bed coverage was adequate in all patients for VMAT1, VMAT2 and M-IMRT. The mean volumes receiving at least 95% of the tumor bed boost dose (V95%) were 99.91±0.14%, 99.84±0.24%, and 99.86±0.25%, for VMAT2, VMAT1, and M-IMRT, respectively. For the PTV-breast, the numbers were 99.80±0.28%, 99.77±0.37%, and 99.80±0.24%, respectively. Tumor bed volumes receiving more than 105% of the prescribed boost dose were minimal for VMAT2 techniques, yet significantly larger with M-IMRT and VMAT1; the mean V105% values were 10.42±7.47%,, 15.14±13.25%, and 11.65±9.81% for the VMAT2, VMAT1, and M-IMRT plans, respectively. The mean PTV-breast dose was 5408.58± 96.33, 5421.25± 89.56, and 5403.80±96.23 cGy for VMAT2, VMAT1 and M-IMRT, respectively. The mean dose for the tumor bed was 6202.15±29.13, 6208.50±36.82, 6196.38± 31.94 cGy for VMAT2, VMAT1 and M-IMRT, respectively. The HI for both PTV-breast and PTV-boost shows no significantly difference among the three techniques. The CI for the PTV-boost was significantly better in the VMAT1 and VMAT2 plans than the IMRT plans (V2&M-IMRT=0.01, V1&M-IMRT<0.001), and VMAT1 is better than VMAT2 ($p$=0.008)

*Organs at risk*

The dose statistics for the OARs for all patients are listed in Table 2 and Table 3.

*i)* Right-sided breast cancer: The three plan groups all satisfied the requirements of the OARs dose constraint well for all patients in this study. The mean dose showed no significant difference among the three techniques for the ipsilateral lung. The V20Gy and V30Gy of VMAT2

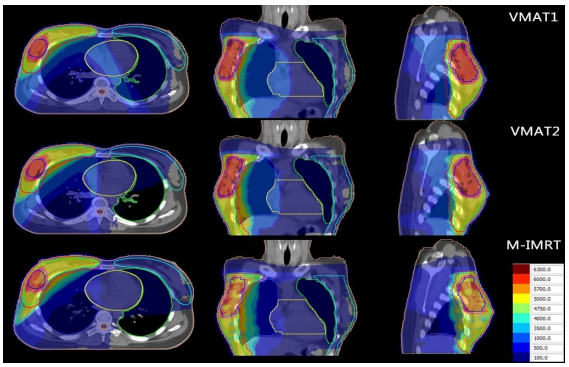


**Figure 2. The dose Distribution for the Right-Sided Breast Cancer**

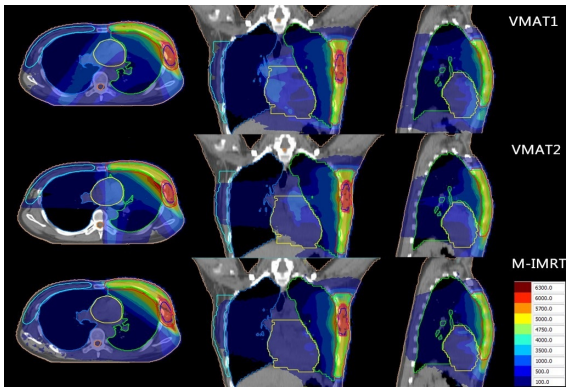


**Figure 3. The dose Distribution for the Left-Sided Breast Cancer**

**Table 1. The Optimization Objective Used for the Planning and the Volume of the PTV**

| | | |
|---|---|---|
| The aim of planning | PTV-breast | V47.5Gy ≥ 95% |
| | PTV-boost | V95% ≥ 95% |
| | PRV-contralateral breast | Dmax < 3Gy,Dmean<2.5Gy |
| | PRV-ipsilateral lung | V10Gy ≤ 40%; V20Gy ≤ 20%; V40Gy ≤ 10%, |
| | PRV-contralateral lung | V5Gy ≤ 5% |
| | PRV-heart | Dmean<4Gy,V10Gy ≤ 20%; V20Gy ≤ 15%; V40Gy ≤ 20% |
| | Spinal cord | Dmax ≤ 45Gy,Dmean<3Gy |
| The right-sided breast cancer | The maximum volume of PTV-breast (cc) | 865.60 |
| | The minimum volume of PTV-breast(cc) | 396.15 |
| | The mean volume of PTV-breast(cc) | 654.87±167.26 |
| | The maximum volume of PTV-boost (cc) | 31.16 |
| | The minimum volume of PTV-boost(cc) | 2.58 |
| | The mean volume of PTV-boost(cc) | 8.69±8.18 |
| The left-sided breast cancer | The maximum volume of PTV-breast (cc) | 658.01 |
| | The minimum volume of PTV-breast(cc) | 303.12 |
| | The mean volume of PTV-breast(cc) | 452.49±96.20 |
| | The maximum volume of PTV-boost (cc) | 77.17 |
| | The minimum volume of PTV-boost(cc) | 24.14 |
| | The mean volume of PTV-boost(cc) | 39.28±13.10 |

**Table 2. Dose Comparison and Delivery Efficiency Right - Sided Breast Cancer**

| Parameter | VMAT2 | VMAT1 | dMLC-IMRT | V2&V1 | V2&M-IMRT | V1&M-IMRT |
|---|---|---|---|---|---|---|
| | | | | pValue | pValue | pValue |
| PTV-Breast | | | | | | |
| Mean dose (Gy) | 5372.96 ±57.80 | 5379.30 ±77.91 | 5369.81 ±88.66 | 0.558 | 0.844 | 0.567 |
| V95% | 99.32 ±0.62 | 99.66 ±0.20 | 99.32 ±0.60 | 0.033 | 0.996 | 0.046 |
| HI | 0.25 ±0.02 | 0.24 ±0.02 | 0.25 ±0.01 | 0.274 | 0.483 | 0.827 |
| PTV-Boost | | | | | | |
| Mean dose (Gy) | 6195.40 ±31.00 | 6197.23 ±25.54 | 6201.39 ±16.00 | 0.458 | 0.464 | 0.128 |
| V95% | 99.44 ±0.63 | 99.95 ±0.05 | 99.40 ±0.98 | 0.007 | 0.899 | 0.050 |
| V105% | 16.46 ±9.17 | 6.73 ±1.03 | 16.05 ±8.41 | 0.001 | 0.918 | <0.001 |
| HI | 0.08 ±0.02 | 0.06 ±0.01 | 0.07 ±0.02 | 0.002 | 0.101 | 0.199 |
| CI | 0.61 ±0.16 | 0.59 ±0.14 | 0.54 ±0.19 | 0.847 | 0.230 | 0.334 |
| Ipsilateral-lung | | | | | | |
| Mean dose(Gy) | 1291.48 ±68.15 | 1328.77 ±72.54 | 1325.72 ±57.65 | 0.050 | 0.160 | 0.886 |
| V5 Gy (%) | 59.46 ±7.73 | 56.95 ±3.76 | 54.23 ±4.36 | 0.392 | 0.036 | 0.0001 |
| V20 Gy (%) | 21.00 ±1.89 | 21.58 ±1.81 | 23.82 ±1.00 | 0.072 | 0.0003 | <0.001 |
| V30Gy (%) | 14.35 ±2.05 | 15.49 ±1.11 | 16.42 ±1.42 | 0.023 | 0.001 | 0.006 |
| Contralateral-breast | | | | | | |
| Mean dose (Gy) | 136.80 ±21.70 | 168.27 ±20.87 | 150.73 ±14.68 | 0.003 | 0.040 | 0.045 |
| Maximum dose (Gy) | 541.59 ±20.05 | 574.55 ±13.70 | 559.15 ±15.64 | <0.001 | 0.040 | 0.001 |
| V1Gy (%) | 62.72 ±13.53 | 92.67 ±2.65 | 81.81 ±13.81 | <0.001 | 0.005 | <0.001 |
| Spinal-cord | | | | | | |
| Mean dose (Gy) | 111.22 ±23.37 | 242.59 ±75.90 | 232.76 ±102.65 | <0.001 | 0.001 | 0.521 |
| Maximum dose (Gy) | 361.85 ±179.87 | 648.69 ±139.18 | 722.20 ±461.98 | <0.001 | 0.031 | 0.614 |
| Heart | | | | | | |
| Mean dose (Gy) | 261.88 ±56.40 | 370.60 ±12.58 | 378.50 ±24.70 | <0.001 | 0.001 | |
| V5Gy (%) | 11.39 ±6.27 | 20.41 ±6.43 | 18.80 ±15.92 | <0.001 | 0.084 | 0.764 |
| V20Gy (%) | 0.0025 ±0.00775 | 0.0025 ±0.01 | 0.18 ±0.49 | 1.000 | 0.166 | 0.705 |
| V30Gy (%) | 0±0 | 0±0 | 0±0 | 1.000 | 1.000 | 0.166 |
| Delivery efficiency | | | | | | |
| Time of treatment(S) | 132.07 ±6.96 | 86.00 ±13.87 | 361.53 ±159.58 | 0 | <0.001 | <0.001 |
| MUs | 508.38 ±67.55 | 616.19 ±78.66 | 681.79 ±85.42 | 0.004 | <0.001 | <0.001 |
| CPs (control points) | 43.60 ±2.50 | 82.60 ±7.87 | 192.07 ±10.63 | <0.001 | <0.001 | <0.001 |

are obviously smaller than for VMAT1 and M-IMRT. However, the V5Gy of M-IMRT is lower compared with VMAT1 and VMAT2. In comparison with M-IMRT and VMAT1, the Dmean of the contralateral lung and contralateral breast in the VMAT2 plans was reduced. The result is the same for the V1Gy of the contralateral breast. VMAT2 showed a magnificent advantage in the V5Gy of the contralateral lung compared to VMAT1and M-IMRT, and the consequence is the same for the maximum dose to the contralateral breast. The mean dose to the heart in the VMAT2 plans was reduced significantly from the VMAT1 and M-IMRT plans. However, the V5Gy of the heart of VMAT2 showed no obvious difference from M-IMRT, and the mean dose to the spinal cord in the VMAT2 plans

**Table 3. Dose Comparison and Delivery Efficiency Left-Sided Breast Cancer**

| Parameter | VMAT2 | VMAT1 | dMLC-IMRT | V2&V1 | V2&M-IMRT | V1&M-IMRT |
|---|---|---|---|---|---|---|
| | | | | pValue | pValue | pValue |
| PTV-Breast | | | | | | |
| Mean dose (Gy) | 5408.58 ±96.33 | 5421.25 ±89.56 | 5403.80± 96.23 | 0.156 | 0.584 | 0.068 |
| V95% | 99.80 ±0.28 | 99.77 ±0.37 | 99.80 ±0.24 | 0.236 | 0.973 | 0.630 |
| HI | 0.25 ±0.03 | 0.24 ±0.02 | 0.24 ±0.03 | 0.186 | 0.097 | 0.925 |
| PTV-Boost | | | | | | |
| Mean dose (Gy) | 6202.15 ±29.13 | 6208.50 ±36.82 | 6196.38 ±31.94 | 0.374 | 0.417 | 0.226 |
| V95% | 99.91 ±0.14 | 99.84 ±0.24 | 99.86 ±0.25 | 0.225 | 0.504 | 0.812 |
| V105% | 10.42 ±7.47 | 15.14 ±13.25 | 11.65 ±9.81 | 0.050 | 0.619 | 0.155 |
| HI | 0.06 ±0.01 | 0.06 ±0.01 | 0.06 ±0.02 | 0.751 | 0.764 | 0.894 |
| CI | 0.65 ±0.04 | 0.61 ±0.07 | 0.57 ±0.09 | 0.008 | <0.001 | 0.001 |
| Ipsilateral-lung | | | | | | |
| Mean dose (Gy) | 1270.57 ±74.90 | 1263.12 ±69.92 | 1264.38 ±78.43 | 0.618 | 0.790 | 0.956 |
| V5Gy (%) | 47.51 ±5.81 | 46.63 ±3.87 | 46.08 ±5.67 | 0.580 | 0.336 | 0.791 |
| V20 Gy (%) | 21.35 ±2.85 | 24.62 ±2.85 | 23.43 ±3.00 | 0.009 | 0.002 | 0.254 |
| V30 Gy (%) | 14.70 ±2.57 | 17.00 ±1.71 | 17.78 ±3.36 | 0.001 | 0.007 | 0.469 |
| Contralateral lung | | | | | | |
| Mean dose (Gy) | 100.31 ±20.71 | 327.06 ±115.40 | 170.06 ±71.00 | <0.001 | 0.001 | <0.001 |
| V5 Gy (%) | 0.41 ±0.41 | 16.58 ±10.75 | 6.55 ±5.77 | <0.001 | 0.001 | 0.001 |
| Contralateral breast | | | | | | |
| Mean dose (Gy) | 132.33 ±23.40 | 165.40 ±23.10 | 150.40 ±17.33 | 0.002 | 0.040 | 0.010 |
| Maximum dose (Gy) | 538.67 ±20.68 | 567.56 ±19.60 | 552.91 ±20.86 | 0.004 | 0.070 | 0.025 |
| V1 Gy (%) | 59.06 ±5.92 | 88.65 ±8.77 | 77.26 ±15.72 | <0.001 | <0.001 | 0.046 |
| Spinal Cord | | | | | | |
| Mean dose (Gy) | 65.99 ±23.32 | 251.62 ±120.00 | 162.21 ±84.24 | <0.001 | <0.001 | <0.001 |
| Maximum dose (Gy) | 149.40 ±82.59 | 680.81 ±312.23 | 542.06 ±272.73 | <0.001 | <0.001 | 0.058 |
| Heart | | | | | | |
| Mean dose (Gy) | 545.78 ±227.11 | 819.64 ±302.90 | 664.22 ±265.17 | 0.001 | <0.001 | 0.024 |
| V5 Gy (%) | 28.45 ±13.00 | 44.56 ±18.08 | 39.94 ±14.70 | 0.001 | <0.001 | 0.301 |
| V20 Gy (%) | 6.26 ±3.76 | 10.65 ±6.45 | 8.12 ±6.50 | 0.011 | 0.108 | 0.167 |
| V30 Gy (%) | 3.60 ±2.66 | 5.72 ±4.07 | 4.76 ±4.06 | 0.050 | 0.084 | 0.371 |
| Delivery efficiency | | | | | | |
| Time of treatment (s) | 131.80 ±3.90 | 100.07 ±87.00 | 282.60 ±27.17 | 0.179 | <0.001 | <0.001 |
| MUs | 480.69 ±50.93 | 534.46 ±56.31 | 604.53 ±53.59 | <0.001 | <0.001 | <0.001 |
| CPs(control points) | 47.93 ±0.88 | 77.20 ±7.91 | 175.73 ±27.22 | <0.001 | <0.001 | <0.001 |

was much lower than in the VMAT1 and M-IMRT plans. The dose advantage is also present in the maximum dose comparison of the spinal cord. *ii)* Left-sided breast cancer: The three plan groups showed no significant difference

in the doses to the ipsilateral lung except the V20Gy and V30Gy, in which the VMAT2 dose was much smaller than for the other two techniques. In comparison with M-IMRT and VMAT1, the mean dose to the contralateral lung and contralateral breast in the VMAT2 plans was clearly reduced. Similarly, comparing the V5Gy of the contralateral lung and the V1Gy of the contralateral breast also showed a significant reduction in VMAT2 compared to the other two techniques. Although the maximum dose to the contralateral breast in VMAT2 and M-IMRT shows no significant difference, both of them showed magnificent differences from VMAT1.The mean dose to the heart in the VMAT2 plans was reduced significantly from the dose in the VMAT1 and M-IMRT plans. The result is the same as for the right-sided breast cancer patients when comparing the mean and maximum dose of the spinal cord, as the values for VMAT2 are obvious lower than for the other two techniques.

*Acute toxicity*

As our study is purely a planning comparison study of different treatment techniques, the acute toxicity can only be evaluated by the dose acquisition of the OARs.

## Discussion

This study compared Multi beam-IMRT, VMAT1 and VMAT2 for whole-breast radiation therapy with an SIB in patients with breast cancer, all of whom have undergone breast-conserving surgery.

Although there have been numerous studies comparing IMRT and single arc VMAT(Popescu et al., 2010; Badakhshi et al., 2013; Onal et al., 2014), none included VMAT2 and SIB at the same time. The aim was to determine which modality provided the best dose distribution and minimized doses to the OARs at the same time.

Our dosimetric comparison showed a small but statistically significant improvement of the conformity index of VMAT2 compared to M-IMRT and VMAT1 plans in the MonacoTPS 3.5 for tumors located in the breast. In addition, M- IMRT and VMAT1 reduced the high-dose volume at the cost of an increased low-dose volume of the OARs. A striking clinical observation of our study was the generally low acute toxicity of patients treated with VMAT2. It can be speculated that the low acute toxicity observed may be due to the improved conformity index indicating a reduced high dose volume around the tumor and that, in the breast, relatively small changes to the dose distribution may have a significant effect on the acute toxicity.

Our results showed that adequate tumor bed coverage can be achieved with all the three techniques. All the techniques matched the set tumor bed coverage goals. Conformality to the whole breast target volume showed no significant difference between the VMAT plans and the M-IMRT plans. VMAT2 produced a better dosimetric profile in the OARs, especially for the contralateral breast, contralateral lung, heart and the spinal cord. These advantages could be achieved for all 30 patients.

During the past several decades, the radiotherapy of breast cancer has been focused on two main goals: improving disease control while reducing the dose to the OARs. The conformality of treatment has improved due to the introduction of CT planning, which can also tailor the treatment to the patient's anatomy. Thus, unnecessary cardiac and pulmonary irradiation can be avoided (Hijal et al., 2010). The investigation of MLCs has led to two important changes in breast cancer radiotherapy. First, local control can be improved by reducing the treatment length and increasing the dose per fraction received by the tumor bed, through treatment of the tumor bed with SIB (Hijal et al., 2010). Second, advanced techniques such as the dynamic MLC IMRT and VMAT techniques can increase the homogeneity of treatment and translate to a decrease in acute toxicity (Pignol et al., 2008) by decreasing the dose acquired by the OARs.

Currently, the most interesting and lasting result of many studies is the further improvement in homogeneity of the whole breast when using VMAT for SIB. In the single arc VMAT plans, the starting and ending degrees of the arc were set according to tangential field techniques, which may lead to a large amount of breast tissue outside the tumor bed being irradiated in the planes containing the tumor bed.

However, dual arc VMAT can decrease the dose to the OARS to a large extent by changing the starting and ending degrees of the two arcs, and thus the target of lower dose spilling for the OARs can be achieved.

Previously, the traditional tumor boost radiation oncology for breast cancer was to give the boost dose after the whole-breast radiotherapy. Now, the boost dose from the simultaneous integrated boost (SIB) is delivered at the same time as the whole breast dose. A clinical advantage can be revealed due to this difference, as high radiation doses to the breast may increase the rate of fibrosis and a worse cosmetic outcome (Bartelink et al., 2007; Collette et al., 2008; Kraus et al., 2012 ; Kaviani et al., 2013). The introduction of SIB can not only improve the homogeneity of breast treatment but also reduce the acute complication rate (Pignol et al., 2008).

At the same time, Bartelink H, et al (Bartelink et al., 2015) focused their attention on higher doses of boost radiation with the aim of further decreasing the local recurrence rate in high risk women. In this approach, reducing excess irradiation to the breast tissue becomes primary, and less acute toxicity may be achieved. As no previous studies have compared VMAT2,VMAT1 and Multi-beam IMRT for breast cancer after lumpectomy surgery in the context of SIB, it is difficult to compare the current study to previous literature. We compared breast cancer on both sides at the same time. The study by Deng XW (Jin et al., 2013), which compares conventional tangential field, field-in-field, Tangential-IMRT, Multi-beam IMRT and VMAT in whole breast radiation, most closely resembles our dosimetric analysis, although no simultaneous integrated boost was used, and only left-sided breast cancer was examined. The whole breast volume was similarly defined in the two studies, and the mean CTV volumes were comparable. However, the delineation of the PTV is noticeably larger. In their work, the PTV included a 7-mm expansion in all directions

around the CTV except for the skin surface, including the set-up margin and patient movement.

The reason VMAT2 can achieve better homogeneity and reduce the dose to the OARs cannot be explained by the optimization parameters used in the dual arc VMAT, as all of the plans were conducted on the same treatment planning system. Perhaps the starting and ending degrees of the two arcs of VMAT2 can partially explain the differences. As it can protect the OARs either completely or partially, this technique greatly contributes to the reduction of low-dose spill to the heart and lungs, as well as the spinal cord. Most importantly, the low-dose distribution (V1Gy) for the contralateral breast can also be decreased in VMAT2 compared with the other two techniques. This point is of interest, as it is well known that low-dose irradiation to large volumes of tissue may increase the risk of secondary malignancy (Kirova et al., 2005; Kirova et al., 2007; Kirova et al., 2008; Johansen et al., 2009; Brooks et al., 2012).

Considering the delivery efficiency, VMAT2 reduced the monitor units used by 17.5% and 25.4% and reduced the control points by 47.2% and 77.3% compared with VMAT1 and M-IMRT, respectively, for right-sided breast cancer. For left-sided breast cancer, the numbers were 10.1%, 20.5% and 37.9%, 72.9%, respectively. However, VMAT1 shortened the treatment delivery time by 34.9% and 76.2% compared with VMAT2 and M-IMRT for right-sided cancer, 24.1% and 56.1% for left-sided cancer. The drawback of the M-IMRT technique is the extended time needed to deliver one fraction, mostly because of the usage of multiple fields and the high number of MUs. The VMAT technique was superior in terms of irradiation MUs compared to M-IMRT. Additionally, both the VMAT1 and VMAT2 plans had apparent advantages in reducing the high-dose volume, but VMAT1 exhibited drawbacks in increasing the lower-dose volume. The statistics of the delivery efficiency are shown in Table 2 and Table 3.

Breast size

Many studies have shown that breast size is an important determinant of breast dose homogeneity. One study (Huang et al., 2008) reported that the maximum and mean volume of the planning target volume (PTV) of Chinese patients were 589.77 cc and 427.2 cc, which are obviously smaller than in Caucasians, whose maximum and mean volume are 2170 cc and 994 cc, respectively (Beckham et al., 2007). The different results when using various radiotherapy techniques may be for this reason. Most of the existing literature (Lohr et al., 2009; Taylor et al., 2011) has mainly focused on the volumetric dose of the heart, and some investigators (Xu et al., 2006) have conjectured that the cardiac dose might be associated with the breast volume. Popescu CC et al reported with the consequence that the single arc VMAT technique was able to improve treatment efficiency and dose conformality compared to conventional IMRT of radiotherapy for left-sided breast cancer (Popescu et al., 2010).

However, Andrea Michalski et al conducted a study finding that breast size had little effect regardless of the modality used (Michalski et al., 2014). This result may be due to the small sample size used in their study or the inclusion of a boost treatment.

According to the results of our study, dual arc VMAT is an adequate technique for Chinese patients who undergo breast-conserving surgery. The single arc VMAT plan presented advantages in improving the HI of the PTV but may increase the dose irradiation to the OARs, including the contralateral lung, contralateral breast and spinal cord. The dual arc VMAT plan may be better for clinical use.

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