Modified Volumetric Modulated Arc Therapy in Left Sided Breast Cancer After Radical Mastectomy With Flattening Filter Free Versus Flattened Beams

Youqun Lai, MS, Yanyan Chen, BSc, Sangang Wu, MD, MS, Liwan Shi, BSc, Lirong Fu, BSc, Huiming Ha, BSc, and Qin Lin, MD, PhD

Abstract: Conventional volumetric modulated arc therapy (C-VMAT) for breast cancer after radical mastectomy had its limitation that resulted in larger volumes of normal tissue receiving low doses. We explored whether there was a way to deal with this disadvantage and determined the potential benefit of flattening filter-free (FFF) beams.

Twenty patients with breast cancer after radical mastectomy were subjected to 3D conformal radiotherapy (3DCRT) and VMAT treatment planning. For VMAT plans, 3 different designs were employed with RapidArc form: conventional-VMAT plan (C-VMAT), modified-VMAT plan (M-VMAT), and modified-VMAT plan using FFF beams (M-VMAT-F). Plan quality and efficiency were assessed for all plans.

For each technique in homogeneity, there were no statistically significant differences. VMAT plans showed superiority compared with 3DCRT in conformity. C-VMAT plans were obviously not only superior to 3DCRT in the medium to high-dose regions (about 15–50 Gy) but also resulted in larger volumes in low-dose regions (about 0–10 Gy). M-VMAT plans were similar to M-VMAT-F. Both of them might significantly reduce the regions of low dose compared with C-VMAT (V5lung: ~11.5%; V5heart: ~23.8%, P < 0.05), even less than 3DCRT in heart irradiation (V2.5heart: 9.4%, P < 0.05). For liver, contralateral breast, and lung irradiation, M-VMAT-F plans were slightly superior to M-VMAT with a reduction of ~0.08, 0.2, and 0.24 Gy in the respective mean doses (P < 0.05).

C-VMAT plans showed superiority compared with 3DCRT, while also resulted in larger volumes of normal tissue receiving low doses. M-VMAT and M-VMAT-F plans might not only reduce the region in the medium to high doses but also have lower volumes in low-dose regions. M-VMAT-F plans were slightly superior compared with M-VMAT due to further contralateral organs sparing.

INTRODUCTION

Radical mastectomy remains the most-accepted surgical modality in the last decade in many countries,1 and radiation therapy is a standard and most important treatment for breast cancer after modified radical mastectomy.2,3 Traditionally, 3D conformal radiotherapy (3DCRT) is adopted in a postmastectomy approach with tangential fields for chest wall and separate fields for supraclavicular nodes region. Although tangential beam orientation is optimal for limiting low doses to normal tissues, traditional 3DCRT plans provide inadequate nodal coverage and the conformity of dose distributions is relatively poor.4

In recent years, several investigators have studied the role of intensity-modulated radiation therapy (IMRT) for breast cancer after radical mastectomy, and compared dosimetric characteristics of 3DCRT versus IMRT treatment planning techniques.4–7 IMRT facilitates to achieve a more homogeneous dose distribution and to decrease normal tissue irradiation by providing more degrees of freedom in the planning process. Nevertheless, the influence of target motion on dose homogeneity and conformity degree will be increased with the increase of beam on times (BOT) for static gantry IMRT.8,9 Several authors have investigated the application of volumetric-modulated arc therapy (VMAT) for whole or partial breast treatment.10–14 It is clear that VMAT may improve dosimetry and reduce treatment time compared with multiple-field IMRT. However, both IMRT and VMAT will result in increased low doses to large volumes of normal tissue. The effects of an increase in the low-dose region with IMRT or VMAT techniques have to be taken into consideration, for example, whether this will potentially increase estimated risk of secondary cancers. Radiation-induced pulmonary and cardiac toxicity in breast cancer patients have been widely reported by several investigators.15–17

In this planning study, we designed a new modified-VMAT plan and evaluated the significance of this technique in left-sided breast cancer after radical mastectomy by comparing with conventional VMAT. With more and more widespread and profound application of TrueBeam® linear accelerator (TrueBeam SN1402, Varian Medical Systems, Palo Alto, CA) in radiotherapy, flattening filter-free (FFF) beams have been
investigated for breast treatment.\textsuperscript{10,18} We also employed FFF beams for modified-VMAT and determined the potential benefit in breast cancer after radical mastectomy.

**MATERIALS AND METHODS**

**Patients and Delineation**

The study was approved by the ethics committee of the First Affiliated Hospital of Xiamen University. All patients provided written consent for storage of their medical information in the hospital database and for research use of this information, and the information of patients was anonymized and de-identified before analysis.

Twenty computed tomographic (CT) scans of patients with left-sided breast cancer involving supraclavicular nodes, who underwent radical mastectomy, were selected for this treatment planning study. All patients underwent a planning CT scan with 5 mm slice thickness (General Electric Medical Systems (GE Healthcare, USA), CT Lightspeed 16).

Clinical target volume (CTV) was defined by the entire ipsilateral chest wall along with supraclavicular nodes region. The planning target volume (PTV) was added a 5-mm margin around the CTV. Mean PTV size and standard deviation were $612.6 \pm 138.7 \text{ cm}^3$ (range: $443.9–825.8 \text{ cm}^3$). The PTV\textsubscript{objective} was derived from PTV along with a 5-mm margin on the skin surface around PTV (Figure 1A). Organs at risk (OAR), such as ipsilateral lung, heart, contralateral breast and lung, and liver, were outlined in the axial CT sections. For optimization and analysis purposes, a 1-cm bolus was applied to the skin surface around PTV to prevent the optimizer compensating for lack of dose in the buildup region during optimization. Considering the influence of physiological motion, the PTV\textsubscript{objective} was as the objective structure during optimization to reduce uncertainties in dose delivery. Before the final dose calculation,\textsuperscript{18} the 1-cm bolus was replaced with a 0.5-cm bolus (Figure 1B).

**Treatment Planning**

Treatment plans were generated for a TrueBeam linac, equipped with standard Millennium MLC with 120 leaves (0.5 cm spatial resolution at isocenter in the inner 20 and 1.0 cm spatial resolution for the 2 × 10 cm outer length of the field). Four techniques (3DCRT, C-VMAT, M-VMAT, and M-VMAT-F) for treatment plans were designed for all patients as described below. For VMAT techniques, treatment planning was performed in the Eclipse treatment planning system (Varian Medical Systems, Paolo Alto, CA, PRO 11.0, AAA 11.0) using 6X-FF or 6X-FFF beams. The maximum dose rate of 600 MU/min for 6X-FF beams and 1400 MU/min for 6X-FFF beams was selected. The prescribed dose (PD) was $25 \times 2 \text{ Gy (50 Gy)}$ and plans were normalized so that 95% of PTV received 95% of the PD. The same objectives were used for each RapidArc plan, and to minimize the volume inside the PTV receiving $>107\%$ of the dose. The Normal Tissue Objective automatic tool in Eclipse TPS was used to minimize dose spread outside the PTV. For the OARs, the mean dose for ipsilateral lung was received $<15 \text{ Gy}$ and $V_{20 \text{ Gy}} < 22\%$.

**3D Conformal Technique (3DCRT)**

3DCRT plans were designed with 4 fields, using 6MV photon beams, with 2 wedged tangential fields for chest wall and 2 wedged separate fields for supraclavicular nodes region. Each field included 0 to 2 subsegments shaped by multileaf collimators (MLCs) to ensure the D\textsubscript{max} of PTV not more than 107% of the PD.

**Conventional VMAT Plans With RapidArc form (C-VMAT)**

For C-VMAT plans,\textsuperscript{8} as shown in Figure 2A, double ipsilateral partial arcs with a maximum individual length of 240° starting from the mid-sternum were adopted in this study. In clockwise direction (CW), collimator angles were ranged from 15° to 30°, and 6MV photon beams were used. Similarly, in counter-clockwise (CCW) direction, the collimator settings were kept constant.

**Modified VMAT Plans With Half-field Technique (M-VMAT)**

Figure 2B shows the beam setup of modified VMAT plans. One 240° arc was divided into 2 equal sections covering 120° each. In CW rotation, the collimator angle was set to 15° to 30° and a half-field was opened at X2 of the collimator for the first part of arc, while in second part of arc, the collimator angle was 345° to 330° and a half-field was opened at X1 of the collimator. In CCW rotation, the collimator settings were kept constant. For M-VMAT-F plans, 6X-FFF beams were used and the same beam settings were applied. The maximum dose rate was set to 1400 MU/min.

![FIGURE 1. Delineated planning target volume in breast cancer of radical mastectomy for optimization. (A) A 1-cm bolus was inserted and the PTV\textsubscript{objective} was as the objective structure during optimization. The PTV\textsubscript{objective} was derived from PTV along with a 5-mm margin on the skin surface around PTV. (B) For final dose calculation and analysis, the 1-cm bolus was replaced with a 0.5-cm bolus.](image-url)
Plan Evaluation and Statistical Tools

For the quantitative evaluation of the plans, the standard dose volume histograms (DVHs) were used. The values of D98% and D2% (dose received by 98% and 2% of the PTV) for the PTV were defined as metrics for minimum and maximum doses. The conformity index (CI) was defined as: 
\[ CI = \frac{V_{PTV}}{TV}_{PTV} / \frac{TV}_{PTV} \]. VPTV is the volume of PTV, TVPTV is the portion of the VPTV within the 95% of prescribed isodose line. VTV is the volume of the body that received 95% of the PD. The homogeneity index (HI) was defined as: 
\[ HI = \frac{D_{95}}{D_{95}} / (dose \text{ received by } 5\% \text{ and } 95\% \text{ of the PTV}) \]. For OARs, the mean doses, and a set of appropriate Vx(Gy) and Dy(%) values to ipsilateral lung, heart, contralateral breast and lung, and liver were analyzed. To evaluate the efficiency of each technique, total MUs, BOT, and mean dose rate [monitor unit (MU)/min] were compared.

Statistical analyses were performed in order to compare the different techniques using a paired t-test. P value \(\leq 0.05\) was considered statistically significant.

RESULTS

PTV Coverage and Dose Distribution

Table 1 presented dosimetric parameters of PTV for all 4 groups of treatment plans created with different planning techniques. No substantial differences were observed between the 4 treatment plans in homogeneity, while VMAT plans showed superiority compared with 3DCRT in the conformity. Transversal, coronal, and sagittal dose distributions are displayed in Figure 3 for 1 patient with left-sided breast cancer after radical mastectomy. It was evident that C-VMAT plans would result in larger volumes of normal tissue receiving low doses compared with 3DCRT plans. Dose distributions in M-VMAT plans were much better than C-VMAT, and M-VMAT-F plans were similar to M-VMAT. Both M-VMAT and M-VMAT-F plans might not only reduce the region in the medium to high doses but also have lower volumes in low-dose regions for normal tissue.

Dose to Organs at Risk

Figure 4 shows average dose-volume histogram (DVH) comparison for ipsilateral lung and heart with different planning techniques.
techniques. For ipsilateral lung and heart irradiation, C-VMAT plans were obviously not only superior to 3DCRT in the medium to high-dose regions (about 15–50 Gy) but also resulted in larger volumes in low-dose regions (about 0–10 Gy). M-VMAT plans were similar to M-VMAT-F, and both might significantly reduce the regions of low dose compared with C-VMAT (V5lung: ~11.5%; V5heart: ~23.8%, \(P < 0.05\)), even less than 3DCRT in heart irradiation (V2.5heart, 9.4%, \(P < 0.05\)). That is, for heart irradiation, M-VMAT and M-VMAT-F plans might not only reduce the region in the medium to high doses but also have lower volumes in low-dose regions than 3DCRT.

Table 2 presents the results of DVH numerical analysis for the organs at risk: ipsilateral lung, heart, contralateral breast, contralateral lung, and liver. For the irradiation of liver, contralateral breast and lung, M-VMAT-F plans were slightly
TABLE 2. Results of Dose-Volume Histogram (DVH) Numerical Analysis for the Organs at Risk: Ipsilateral Lung, Heart, Contralateral Breast, Contralateral Lung, and Liver

|                     | 3DCRT       | C-VMAT      | M-VMAT      | M-VMAT-F     | P*  |
|---------------------|-------------|-------------|-------------|--------------|-----|
| Ipsilateral Lung    |             |             |             |              |     |
| (Left) Volume (cm³) | 887.5 ± 142 | 71.0 ± 4.1  | 703.0 ± 5.8 |              |     |
| V5 Gy (%)           | 59.9 ± 4.4  | 83.0 ± 7.0  |             |              |     |
| V20 Gy (%)          | (48.2–64.6) | (70.1–92.8) | (64.2–77.6) |              |     |
| Dmax (Gy)           | 19.9 ± 3.0  | 14.5 ± 0.6  |             |              |     |
| Heart volume (cm³)  | 549.9 ± 39.7| 58.1 ± 5.9  |             |              |     |
| V2.5 Gy (%)         | 67.5 ± 9.3  | 94.4 ± 3.8  |             |              |     |
| V5 Gy (%)           | (47.4–87.9) | (86.7–98.1) |             |              |     |
| V40 Gy (%)          | 13.9 ± 3.9  | 1.3 ± 1.6   |             |              |     |
| D15 Gy (Gy)         | 50.2 ± 1.3  | 40.4 ± 5.4  |             |              |     |
| Dmean (Gy)          | 11.0 ± 2.2  | 9.4 ± 1.5   |             |              |     |
| Contralateral breast|             |             |             |              |     |
| (Right) Volume (cm³)| 570.9 ± 158 | 12.2 ± 2.6  |             |              |     |
| V5 Gy (%)           | 35.9 ± 16.1 | 12.1 ± 1.4  |             |              |     |
| V20 Gy (%)          | (8.2–52.6)  | (9.8–13.7)  |             |              |     |
| Dmax (Gy)           | 18.5 ± 16.0 | 7.8 ± 0.7   |             |              |     |
| D15 Gy (Gy)         | (4.4–46.7)  | (6.5–8.9)   |             |              |     |
| Dmean (Gy)          | 2.3 ± 1.0   | 3.3 ± 0.5   |             |              |     |
| Contralateral lung  |             |             |             |              |     |
| (Right) Volume (cm³)| 1181.9 ± 260.3 | 12.2 ± 2.6 |             |              |     |
| V5 Gy (%)           | 8.9 ± 2.7   | 42.4 ± 9.0  |             |              |     |
| V20 Gy (%)          | (3.7–12.7)  | (25.6–51.7) |             |              |     |
| Dmax (Gy)           | 0.08 ± 0.2  | 0.5 ± 0.6   |             |              |     |
| Dmean (Gy)          | 2.4 ± 0.5   | 5.3 ± 0.7   |             |              |     |
| Liver Volume (cm³)  | 1321 ± 310  | 4.0 ± 1.7   |             |              |     |
| V15 Gy (Gy)         | 3.2 ± 1.4   | 4.5 ± 1.5   |             |              |     |
| Dmax (Gy)           | 0.7 ± 0.2   | 1.2 ± 0.3   |             |              |     |
| Dmean (Gy)          | (0.34–1.1)  | (0.8–2.0)   |             |              |     |

3DCRT = 3D conformal technique, C-VMAT = VMAT plans with RapidArc form in Eclipse treatment planning system, M-VMAT = modified-VMAT plans with RapidArc form, M-VMAT-F = modified-VMAT plans using flattening filter-free (FFF) beams.

P* value corresponds to the paired t-test: a = 3DCRT vs. C-VMAT, b = C-VMAT vs. M-VMAT, c = M-VMAT vs. M-VMAT-F.

DISCUSSION

The present study addressed a comparative appraisal of 4 different techniques using flattened or FFF beams for left-sided breast cancer after radical mastectomy. For radiotherapy of chest wall and supraclavicular nodes region, traditional 3DCRT is still a common treatment technique in many countries. However, due to inadequate nodal coverage and poor conformity of dose distributions (Table 1), the radiation-induced skin injury was likely to be observed in many patients, especially injury of armpit skin. As expected with a rotational technique, C-VMAT plans resulted in larger volumes of normal tissue receiving low doses compared with 3DCRT (Figure 3). This was no difference compared with earlier investigations.8

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.
TABLE 3. The Number of Monitor Units (MU), Beam-on Time (BOT), and Mean dose Rate (MDR) for Treatment Plans Created With Different Planning Techniques

|        | 3DCRT       | C-VMAT       | M-VMAT       | M-VMAT-F     |
|--------|-------------|--------------|--------------|--------------|
| MU     | 822 ± 53    | 626 ± 32     | 671 ± 18     | 839 ± 87     |
| (770–1001) | (579–683)   | (619–695)    | (637–926)    |              |
| BOT (min) | 1.37 ± 0.1  | 1.37 ± 0.03  | 1.38 ± 0.02  | 1.32 ± 0.01  |
| (1.28–1.66) | (1.34–1.44) | (1.35–1.42)  | (1.31–1.36)  |              |
| MDR (MU/min) | 600 ± 15   | 458 ± 22     | 486 ± 10     | 634 ± 70     |

3DCRT = 3D conformal technique, C-VMAT = VMAT plans with RapidArc form in Eclipse treatment planning system, M-VMAT = modified-VMAT plans using flattening filter-free (FFF) beams. M-VMAT-F plans was only 634 MU/min (Table 3), though the maximum dose rate could reach 1400 MU/min. About the beam delivery times, the BOT was similar for each VMAT technique, as the VMAT BOT was limited by the gantry speed. Because of this, the potential for a higher dose rate of FFF beams could not be exploited in conventional radiotherapy (2 Gy/fraction).

CONCLUSIONS

The results demonstrate that with respect to the radiotherapy of chest wall and supraclavicular nodes region for left-sided breast cancer after radical mastectomy, C-VMAT plans not only showed superiority compared with 3DCRT while also resulted in larger volumes of normal tissue receiving low doses. Dose distributions in M-VMAT plans were much better than C-VMAT, and M-VMAT-F plans were similar to M-VMAT. For ipsilateral lung and heart irradiation, both M-VMAT and M-VMAT-F plans might not only reduce the region in the medium to high doses but also have lower volumes in low-dose regions. By use of FFF beams, M-VMAT-F plans were slightly superior compared with M-VMAT due to further contralateral organs sparing.

REFERENCES

1. Yu K-D, Di G-H, Wu J, et al. Development and trends of surgical modalities for breast cancer in China: a review of 16-year data. Ann Surg Oncol. 2007;14:2502–2509.
2. Janni W, Dimpl T, Braun S, et al. Radiotherapy of the chest wall following mastectomy for early-stage breast cancer: Impact on local recurrence and overall survival. Int J Radiat Oncol Biol Phys. 2000;40:967–975.
3. Claassen J, Nitsche S, Wallwiener D, et al. Fibrotic changes after postmastectomy radiotherapy and reconstructive surgery in breast cancer. Strahlenther Onkol. 2010;186:630–636.
4. Sethi RA, No HS, Jozsef G, et al. Comparison of three-dimensional versus intensity-modulated radiotherapy techniques to treat breast and axillary level III and supraclavicular nodes in a prone versus supine position. Radiother Oncol. 2012;102:74–81.
5. Ma JL, Li JY, Xie J, et al. Post mastectomy linac IMRT irradiation of chest wall and regional nodes: dosimetry data and acute toxicities. Radiat Oncol. 2013;8:81.
6. Schubert LK, Gondi V, Sengbusch E, et al. Dosimetric comparison of left-sided whole breast irradiation with 3DCRT, forward-planned IMRT, inverse-planned IMRT, helical tomotherapy, and tomotherapy. Radiother Oncol. 2011;100:241–246.
7. Alnberg SS, Lindmo T, Frengen J. Superficial doses in breast cancer radiotherapy using conventional and IMRT techniques: a film-based phantom study. Radiother Oncol. 2011;100:259–264.
8. Subramaniam S, Thirumalaiswamy S, Srinivas C, et al. Chest wall radiotherapy with volumetric modulated arcs and the potential role of flattening filter free photon beams. Strahlenther Onkol. 2012;188:484–490.

9. George R, Keall PJ, Kini VR, et al. Quantifying the effect of intrafraction motion during breast IMRT planning and dose delivery. Med Phys. 2003;30:552–562.

10. Moeckly SR, Lamba M, Elson HR. Respiratory motion effects on whole breast helical tomotherapy. Med Phys. 2008;35:1464–1475.

11. Qiu J-J, Chang Z, Wu QJ, et al. Impact of volumetric modulated arc therapy technique on treatment with partial breast irradiation. Int J Radiat Oncol Biol Phys. 2010;78:288–296.

12. Popescu CC, Olivotto IA, Beckham WA, et al. Volumetric modulated arc therapy improves dosimetry and reduces treatment time compared to conventional intensity-modulated radiotherapy for locoregional radiotherapy of left-sided breast cancer and internal mammary nodes. Int J Radiat Oncol Biol Phys. 2010;76:287–295.

13. Nicolini G, Clivio A, Fogliata A, et al. Simultaneous integrated boost radiotherapy for bilateral breast: a treatment planning and dosimetric comparison for volumetric modulated arc and fixed field intensity modulated therapy. Radiat Oncol. 2009;4:27.

14. Johansen S, Cozzi L, Olsen DR. A planning comparison of dose patterns in organs at risk and predicted risk for radiation induced malignancy in the contralateral breast following radiation therapy of primary breast using conventional, IMRT and volumetric modulated arc treatment techniques. Acta Oncol. 2009;48:495–503.

15. Simone B, Simone CB, Dan TD, et al. Lack of radiation-induced pulmonary toxicity 25 years after treatment with breast conservation therapy or mastectomy for early-stage breast cancer: results from the NCI randomized trial. Int J Radiat Oncol Biol Phys. 2011;81:S6–S7.

16. Stranzl H, Zurl B. Postoperative irradiation of left-sided breast cancer patients and cardiac toxicity. Strahlenther Onkol. 2008;184:354–358.

17. Yuksel D, Surenkok S, Ilgan S, et al. The effects of tangential radiotherapy on lung clearance in breast cancer patients. Radiother Oncol. 2005;77:262–266.

18. Spriuitt KH, Dahle M, Cuijpers JP, et al. Flattening filter free vs flattened beams for breast irradiation. Int J Radiat Oncol Biol Phys. 2013;85:506–513.

19. Kuo YC, Chiu YM, Shih WP, et al. Volumetric intensity-modulated Arc (RapidArc) therapy for primary hepatocellular carcinoma: comparison with intensity-modulated radiotherapy and 3-D conformal radiotherapy. Radiat Oncol. 2011;6:76.