

Non-coplanar volumetric modulated arc therapy for locoregional radiotherapy of left-sided breast cancer including internal mammary nodes

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Background. Non-coplanar volumetric modulated arc therapy (ncVMAT) is proposed to reduce toxicity in heart and lungs for locoregional radiotherapy of left-sided breast cancer, including internal mammary nodes (IMN).

Patients and methods. This retrospective study included 10 patients with left-sided breast cancer who underwent locoregional radiotherapy after breast-conserving surgery. For each patient, the ncVMAT plan was designed with four partial arcs comprising two coplanar arcs and two non-coplanar arcs, with a couch rotating to 90°. The prescribed dose was normalized to cover 95% of planning target volume (PTV), with 50 Gy delivered in 25 fractions. For each ncVMAT plan, dosimetric parameters were compared with the coplanar volumetric modulated arc therapy (coVMAT) plan.

Results. There were improvements in conformity index, homogeneity index and V_{55} of total target volume (PTVall) comparing ncVMAT to coVMAT ($p < 0.001$). Among the organs at risk, the average V_{30} , V_{20} , V_{10} , V_5 , and mean dose (D_{mean}) of the heart decreased significantly ($p < 0.001$). Furthermore, ncVMAT significantly reduced the mean V_{20} , V_{10} , V_5 , and D_{mean} of left lung and the mean V_{10} and V_5 and D_{mean} of contralateral lung ($p < 0.001$). An improved sparing of the left anterior descending coronary artery and right breast were also observed with ncVMAT ($p < 0.001$).

Conclusions. Compared to coVMAT, ncVMAT provides improved conformity and homogeneity of whole PTV, better dose sparing of the heart, bilateral lungs, left anterior descending coronary artery (LAD), and right breast for locoregional radiotherapy of left-sided breast cancer with IMN, potentially reducing the risk of normal tissue damage.

Key words: non-coplanar; volumetric modulated arc therapy; left-sided breast cancer; internal mammary nodes

Introduction

Adjuvant radiotherapy after breast-conserving surgery has been proven to be effective in reducing the risk of recurrence and death from breast cancer.¹⁻² In radiotherapy for breast cancer, internal mammary nodes (IMN) and supraclavicular nodes (SCN) are often included in planning target volume

(PTV) to improve local control.³⁻⁶ However, irradiation of IMN inevitably increases the dose delivered to heart and lungs, raising the risk of radiation pneumonitis and cardiac mortality.⁷ Indeed, approximately 1%–5% of patients with breast cancer develop radiation pneumonitis after radiotherapy as predicted by the normal tissue complication probability model.⁸ In a study of 61 patients with

early breast cancer who received radiotherapy, approximately 12.5% developed > grade 1 radiation pneumonitis at 12 months.⁹ Additionally, cardiac diseases, such as ischemic heart disease is another major concern associated with radiotherapy in breast cancer¹⁰⁻¹² and controversies remain concerning IMN irradiation.^{7,13} Therefore, reducing the dose to organs at risk during irradiation of nodal regions is crucial for improving the benefits of treatment while reducing associated toxicity.

Several techniques are used for locoregional breast irradiation. While modified wide tangential beam with forward planning used to be the most common technique¹⁴, intensity-modulated radiotherapy (IMRT) was introduced for radiotherapy of left-sided breast cancer with IMN with the development of technology.¹⁵ Conformity and homogeneity were improved and the proportion of volume receiving 30 Gy (V_{30}) for the heart and the proportion of volume receiving 20 Gy (V_{20}) for the left lung was reduced with IMRT using inverse optimization compared to conventional planning. The recently implemented volumetric modulated arc therapy (VMAT) technology for left-sided breast cancer with IMN can achieve similar PTV coverage and organ-at-risk (OAR) sparing compared to IMRT.¹⁶⁻¹⁸ Helical tomotherapy (HT) is another potential solution; however, beam delivery is time consuming compared with conventional linear accelerator.¹⁹ Furthermore, HT does not provide significant improvement to the mean dose delivered to heart compared with VMAT.²⁰ However, new technologies such as IMRT, VMAT, and HT can reduce the dose to OARs compared with wide tangential beams and it remains important to explore approaches that can improve OAR sparing.

Non-coplanar VMAT (ncVMAT) can extend beam angle arrangements and is therefore potentially better in sparing OARs.²¹ With non-coplanar techniques, different fixed fields or arcs do not employ the same geometric plane, which significantly increases the space of solution for optimizing. This can be realized with a C-arm linear accelerator by rotating the treatment couch around the isocenter. The implementation of ncVMAT has already been studied in partial-breast, complicated whole-breast radiotherapy, and postmastectomy radiotherapy.²²⁻²⁴ However, no studies to date have reported the utility of non-coplanar technique in the treatment of left-sided breast cancer after breast-conserving surgery including the internal mammary and supraclavicular nodal regions. In the present study, ncVMAT plans using four arcs were designed to explore the feasibility of ncVMAT for

locoregional radiotherapy of left-sided breast cancer. Additionally, dosimetric parameters, such as target coverage, conformity index, homogeneity index, and OAR sparing ability, were compared between ncVMAT and coplanar VMAT (coVMAT).

Patients and methods

Patient selection

The present retrospective study was approved by the institutional review board, and informed consent was waived. Ten patients with left-sided breast cancer and IMN after breast-conserving surgery were included in the study. The mean patient age was 52 (range, 34–68) years. The planning computed tomography (CT) data were acquired by a Brilliance CT Big Bore (Philips Healthcare, Best, The Netherlands) using 5-mm thick slices. Both arms of patients were above the head scanning in the supine position. The clinical target volume (CTV) comprised the whole breast, SCN, and IMN. The PTV was generated by expanding a 5-mm margin to CTV, with the exclusion of the most superficial 5-mm area. Therefore, breast planning target volume (PTVbreast), supraclavicular nodes planning target volume (PTVscn), and internal mammary nodes planning target volume (PTVimn) were separately delineated for the breast, SCN, and IMN, respectively, which were then combined to generate the total target volume (PTVall). The volume of PTVall varied from 582.6 cc to 1166.1 cc with an average value of 874.8 cc (standard deviation 191.6 cc). The OARs were also contoured on the planning CT images, which included left and right lungs, heart, left anterior descending coronary artery (LAD), right breast, esophagus, spinal cord, left humeral head, and left brachial plexus.

Treatment planning

All plans were designed with the Pinnacle treatment planning system (version 9.1, Philips Healthcare, Eindhoven, Netherlands) and 6-MV X-ray delivered by an Elekta Versa HD accelerator (Elekta Oncology Systems, Crawley, UK). The multi-leaf collimator (MLC) width was 5 mm at the isocenter, and the treatment couch could rotate from -90° to 90° . The prescribed dose was 50 Gy delivered in 25 fractions for all patients.

All patients were planned with both ncVMAT and coVMAT for comparisons. The ncVMAT was optimized with four arcs, comprising two coplanar arcs and two non-coplanar arcs. The two co-

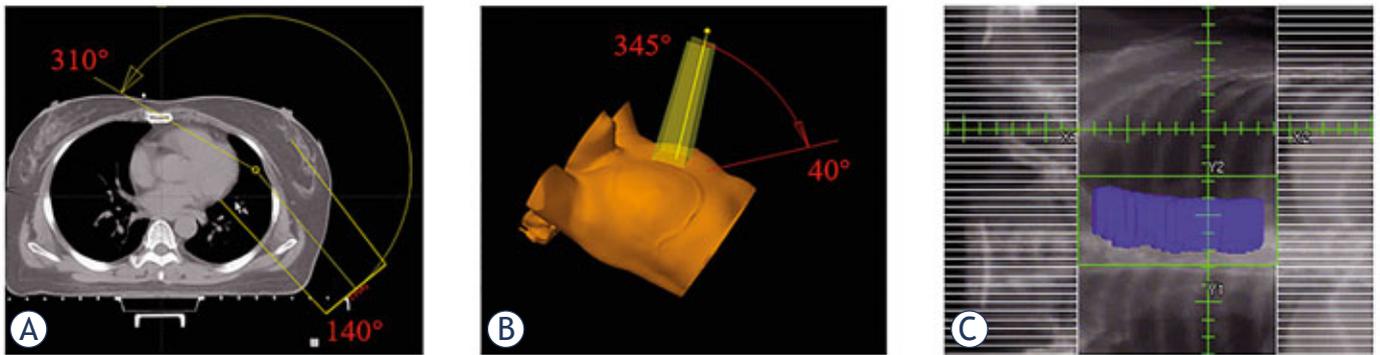


FIGURE 1. Illustration of the arc angle for coplanar arc (A), non-coplanar arc (B), maximum jaw position for non-coplanar arc (C). (Slate blue, internal mammary nodes planning target volume [PTVimn])

planar arcs ranged from 310° to 140° with both clockwise and counterclockwise rotation illustrated in Figure 1 A, and the collimator angles were adjusted slightly according to the shape of each PTV. The non-coplanar arc angle varied from 345° to 40° (both clockwise and counterclockwise) with the couch rotating to 90° shown in Figure 1 B. According to the anatomic location of IMN, the extra dose to heart and bilateral lungs is not avoidable and usually increases with increasing PTVimn coverage. Thus, two non-coplanar arcs were designed to deliver the dose to the internal mammary chains. This was realized by limiting the maximum position of the jaw for non-coplanar arc as shown in Figure 1 C. To protect patients from collision with gantry and to spare the heart, the maximum arc angle was set to 40° in the inferior direction. Additionally, the maximal arc angle in the superior direction was 345° to protect the jaw and arms from irradiation. The four arcs were optimized with an inverse optimizer in the planning system. For coVMAT plans, identical coplanar arc angles (310° to 140°) were used, with two coplanar arcs used for optimization, for all patients.

All plans were normalized to cover at least 95% of the PTVall with the prescribed dose 50 Gy, and the proportion of volume receiving more than 55 Gy (V_{55}) in PTVall was limited to as low as possible while meeting the constraints of the heart and lungs. For the OARs, the proportion of volume of left lung receiving more than 20 Gy (V_{20}) was restricted to lower than 30%,²⁵ and the mean dose of left lung was required to be lower than 15 Gy. The dose constraints for heart were $V_{20} < 15\%$ and mean dose lower than 10 Gy.²⁶ The dose delivery to right lung, and right breast were limited with $V_5 < 10\%$ and mean dose lower than 2-3 Gy. The maximum dose of LAD was restricted to be lower than 55 Gy,

and the mean dose of LAD was limited to be lower than 25 Gy. For all patients, the optimization of parameters was similar between ncVMAT and coVMAT planning, with minor adjustments.

Plan evaluation

Several parameters such as conformity index (CI) and homogeneity index (HI) of PTV were evaluated to compare the ncVMAT and coVMAT plans. CI was based on Paddick's formula:²⁷ $CI = (TVPV)^2 / (TV \times PV)$, where TV is PTV volume, PV is the volume covered by the prescribed dose, and TVPV is the volume of PTV covered by the prescribed dose. A CI value close to 1 represents better conformity. HI was defined as follows:²⁸ $HI = D_{5\%} / D_{95\%}$, where $D_{5\%}$ and $D_{95\%}$ are doses to 5% and 95% of the target volume, and a smaller HI indicates better homogeneity. Prescription dose coverage V_{50} and hot spot V_{55} for PTVall, PTVbreast, PTVscn, and PTVimn were individually evaluated.

Regarding OARs, mean dose (D_{mean}) and proportions of volume receiving 5 Gy (V_5), 10 Gy (V_{10}), and 20 Gy (V_{20}) were calculated for the left lung. Additionally, D_{mean} , V_5 , V_{10} , V_{20} , and V_{30} for the heart; D_{mean} , V_5 , and V_{10} for the right lung and right breast; D_{mean} and maximum dose (D_{max}) for the LAD, esophagus, and left brachial plexus; D_{mean} and V_{30} for left humeral head; D_{mean} , D_{max} , and V_{30} for the thyroid gland; and D_{max} for the spinal cord were also evaluated. Monitor units (MU) for each plan were also calculated, and treatment delivery time was estimated by the treatment planning system.

All statistical analyses were performed with SPSS (version 19.0, IBM, New York, USA). If the data was normally distributed, independent samples *t* test was utilized for the analysis of data; otherwise, nonparametric Wilcoxon signed-rank test

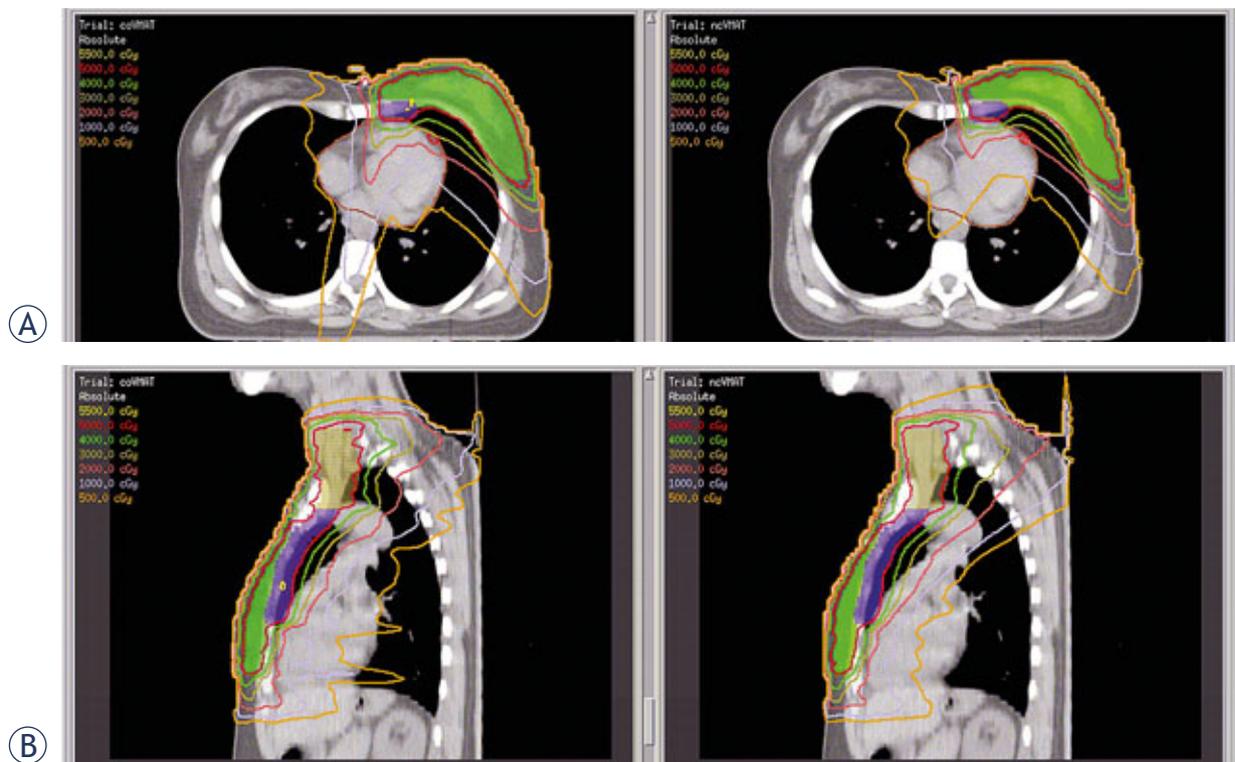


FIGURE 2. Comparison of transverse (A) and sagittal (B) distribution between coplanar volumetric modulated arc therapy [coVMAT] (left) and non-coplanar volumetric modulated arc therapy [ncVMAT] (right). (Color wash: green, breast planning target volume [PTVbreast]; slate blue, internal mammary nodes planning target volume [PTVimn]; olive, supraclavicular nodes planning target volume [PTVscn]; Contour: red, descending coronary artery [LAD]; brown, heart).

was used to compare parameters for significance. Results with a p value of < 0.05 were considered statistically significant.

Results

Figure 2 shows an example of dose distribution by ncVMAT and coVMAT, demonstrating that the dose lines from 500 cGy to 4000 cGy with ncVMAT provided better conformity for PTVbreast and PTVimn. A similar difference could also be observed in the dose-volume histogram of PTV and selected OARs (Figure 3). In this particular patient, ncVMAT provided better sparing of the LAD, heart, bilateral lungs, and right breast and better homogeneity for PTVimn.

Dosimetric evaluation of PTV

All plans were normalized to cover 95% of PTVall with the prescribed dose of 50 Gy. The dosimetric parameters of PTVbreast, PTVscn, PTVimn, and PTVall are shown in Table 1. The mean coverage

was approximately 95% for PTVbreast, PTVscn, and PTVimn, and there was no significant difference between ncVMAT and coVMAT ($p > 0.05$). Additionally, the proportion of volume receiving 110% prescribed dose V_{55} in PTVbreast, PTVscn, PTVimn, and PTVall decreased significantly comparing ncVMAT with coVMAT ($p = 0.005$). Furthermore, improved CI and HI of PTVall were achieved with ncVMAT compared to coVMAT.

Heart

In breast cancer radiotherapy, the heart should be preferentially spared. As summarized in Table 2, the average heart V_{30} , V_{20} , V_{10} , and V_5 declined significantly when using ncVMAT ($p < 0.01$). The mean dose to the heart was significantly reduced from 11.16 ± 3.45 Gy to 9.22 ± 2.98 Gy ($p < 0.001$), and the heart D_{mean} showed a decrease of 17.4%.

Lungs

As shown (Table 2), the left lung mean V_{20} , V_{10} , and V_5 declined significantly when compared ncVMAT

with coVMAT ($p < 0.001$). The contralateral lung mean V_5 and V_{10} also improved with ncVMAT ($p < 0.005$). Both the mean lung doses (MLDs) of the left and right lungs were reduced when compared with ncVMAT with coVMAT ($p < 0.001$), respectively. These results demonstrated that ncVMAT provided an improved sparing strategy for bilateral lungs when compared with coVMAT.

Right breast and LAD

The evaluation of dosimetric parameters of the right breast and LAD (Table 3) showed that the mean contralateral breast V_{10} and V_5 , and D_{mean} declined with ncVMAT ($p < 0.001$). Accordingly, the right breast V_{10} was close to 0 when planned with ncVMAT. The LAD D_{max} and D_{mean} were also improved with ncVMAT, when compared with coVMAT. The reductions in LAD D_{max} and D_{mean} were both statistically significant comparing coVMAT with ncVMAT ($p < 0.001$).

Other OARs

The evaluation of other OARs included in the study is shown in Table 3. Briefly, the D_{mean} of esophagus increased slightly with ncVMAT when compared with coVMAT ($p < 0.001$) and there was also a small decrease in the V_{30} , D_{max} , and D_{mean} of the thyroid gland, and D_{max} and D_{mean} of left brachial plexus with ncVMAT ($p < 0.05$). In addition, there were no significant differences in the V_{30} and D_{mean} of left humeral head, the D_{max} of spinal cord and esophagus ($p > 0.05$). Moreover, all dosimetric parameters of these OARs were clinically acceptable.

MU and treatment delivery time

The average MU values were 797 ± 149 and 803 ± 132 MU for ncVMAT and coVMAT, respectively, which were not significantly different ($p > 0.05$). The average treatment delivery time increased from 233 ± 25 s with coVMAT to 370 ± 31 s (include rotating the couch, approximately 60 s) with ncVMAT. The time was significantly increased with ncVMAT ($p < 0.001$).

Discussion

In the present study, ncVMAT was designed for locoregional radiotherapy of left-sided breast cancer including irradiation of IMN. For coVMAT, the heart was inevitably irradiated to cover the PTVimn

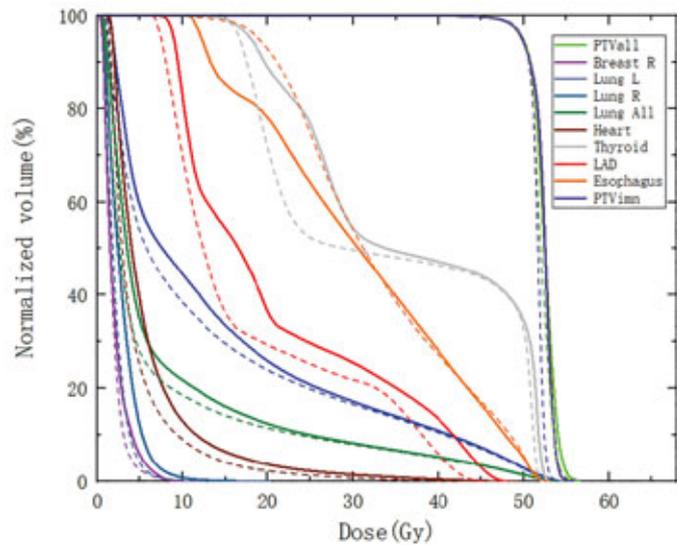


FIGURE 3. Dose-volume histogram of planning target volume (PTV) and selected organs-at-risk (OARs) (Solid line, coplanar volumetric modulated arc therapy [coVMAT]; dashed line, non-coplanar volumetric modulated arc therapy [ncVMAT]).

which was deeply located and anatomically adjacent to the heart. This was observed in Figure 2 A (left) as several sharp peak dose lines across the heart. As the dose constraints were very strict for lungs and the contralateral breast, the beam only irradiated the internal mammary chains, primarily via the vertical direction. By rotating the treatment couch to 90° , the beam irradiated internal mammary chains, more through the ipsilateral breast, the prethoracic muscles and bones, and also through

TABLE 1. Comparison of dosimetric parameters between coplanar volumetric modulated arc therapy (coVMAT) and non-coplanar volumetric modulated arc therapy (ncVMAT) for planning target volume (PTV)

	Parameters	coVMAT	ncVMAT	p
PTVall	CI	0.84 ± 0.04	0.86 ± 0.03	0.028
	HI	1.10 ± 0.02	1.09 ± 0.01	0.019
	V_{55} (%)	6.32 ± 6.35	3.46 ± 3.02	0.011
PTVimn	V_{45} (%)	99.85 ± 0.14	99.85 ± 0.21	0.67
	V_{50} (%)	95.62 ± 0.39	95.67 ± 0.73	0.94
	V_{55} (%)	4.25 ± 4.53	1.08 ± 1.88	< 0.001
PTVscn	V_{50} (%)	95.31 ± 0.43	95.37 ± 0.61	0.681
	V_{55} (%)	1.46 ± 2.89	0.22 ± 0.48	0.001
PTVbreast	V_{50} (%)	95.20 ± 0.52	94.98 ± 0.38	0.054
	V_{55} (%)	8.09 ± 8.84	4.71 ± 4.19	0.028

PTVall= total target volume; PTVbreast = breast planning target volume; PTVimn = internal mammary nodes planning target volume; PTVscn = supraclavicular nodes planning target volume

TABLE 2. Comparison of dosimetric parameters between coplanar volumetric modulated arc therapy (coVMAT) and non-coplanar volumetric modulated arc therapy (ncVMAT) for heart and lung

	Parameters	coVMAT	ncVMAT	p
Heart	V ₅ (%)	61.48 ± 19.63	48.70 ± 18.88	< 0.001
	V ₁₀ (%)	35.50 ± 15.05	26.64 ± 11.97	< 0.001
	V ₂₀ (%)	16.70 ± 8.70	13.07 ± 6.75	< 0.001
	V ₃₀ (%)	8.53 ± 5.28	6.68 ± 3.75	0.001
	Dmean (Gy)	11.16 ± 3.45	9.22 ± 2.98	< 0.001
Left lung	V ₅ (%)	71.67 ± 12.23	59.48 ± 10.51	< 0.001
	V ₁₀ (%)	47.59 ± 8.06	40.48 ± 6.41	< 0.001
	V ₂₀ (%)	26.43 ± 3.95	23.55 ± 3.05	< 0.001
	Dmean (Gy)	15.27 ± 2.03	13.59 ± 1.76	< 0.001
Contralateral lung	V ₅ (%)	9.67 ± 5.35	6.10 ± 4.19	< 0.001
	V ₁₀ (%)	0.87 ± 0.78	0.46 ± 0.50	0.003
	Dmean (Gy)	2.82 ± 0.54	2.43 ± 0.49	< 0.001

the superior and inferior direction of PTV_{imn}. Hence, the conformity of doselines from 500 cGy to 2000 cGy around PTV_{imn} was improved with ncVMAT. We clarify this in the revised manuscript. (Figure 2 A, right). This observation was character-

TABLE 3. Comparison of dosimetric parameters between coplanar volumetric modulated arc therapy (coVMAT) and non-coplanar volumetric modulated arc therapy (ncVMAT) for other organ-at-risk (OAR)

	Parameters	coVMAT	ncVMAT	p
Contralateral breast	V ₅ (%)	9.06 ± 5.22	4.98 ± 2.63	< 0.001
	V ₁₀ (%)	1.53 ± 1.60	0.23 ± 0.27	< 0.001
	Dmean (Gy)	2.62 ± 0.60	2.16 ± 0.41	< 0.001
LAD	Dmax (Gy)	48.90 ± 8.19	46.03 ± 8.20	< 0.001
	Dmean (Gy)	27.39 ± 8.20	23.25 ± 7.16	< 0.001
Left humeral head	V ₃₀ (%)	14.47 ± 16.06	13.50 ± 13.26	0.845
	Dmean (Gy)	19.96 ± 5.11	20.32 ± 5.23	0.737
Esophagus	Dmax (Gy)	51.61 ± 4.64	51.24 ± 3.90	0.052
	Dmean (Gy)	31.22 ± 5.92	33.33 ± 6.09	< 0.001
Left brachial plexus	Dmax (Gy)	54.32 ± 1.05	53.44 ± 0.98	0.004
	Dmean (Gy)	49.77 ± 2.79	49.36 ± 2.74	0.019
Thyroid	V ₃₀ (%)	45.96 ± 8.83	46.10 ± 12.47	0.044
	Dmax (Gy)	54.13 ± 0.77	53.64 ± 0.86	0.009
	Dmean (Gy)	30.79 ± 3.39	29.60 ± 4.71	0.015
Spinal cord	Dmax (Gy)	26.88 ± 5.53	29.38 ± 4.76	0.073

LAD = descending coronary artery

istic of the non-coplanar technique in delivering a higher dose from the superior and inferior direction of the target volume to increase conformity of the target. For the same reason, an improved sparing of the lungs and the contralateral breast was generated with ncVMAT as the beam irradiated more through the middle line. Another possible explanation for an increased sparing of OARs with ncVMAT was that the non-coplanar technique provided more freedom for plan optimization.

Encompassing the IMN is challenging in breast cancer radiotherapy, as it introduces extra irradiation to the heart and lungs. Approaches to reduce toxicity in adjacent OARs compromise the coverage of PTV_{imn}, and 85%²⁹ to 90%³⁰ of the prescribed dose is acceptable in clinical practice. However, the present study investigating the potential utility of ncVMAT in sparing OARs without impacting local control revealed that the coverage of PTV_{imn} was around 95% with both coVMAT and ncVMAT. A tradeoff between target coverage and possible harmful effects is inevitable, and lower coverage of the PTV_{imn} can also be utilized during planning to further reduce the dose to heart and lungs. With ncVMAT, the hot spots V₅₅ for PTV_{imn} were improved, which might provide a potential advantage in protecting anatomically adjacent vessels and nerves from high-dose irradiation.³¹ Moreover, the conformity and homogeneity of PTV_{all} were similar between ncVMAT and coVMAT plans.

Cardiac mortality associated with radiotherapy is a major concern in patients with left-sided breast cancer^{32,33}, who are at higher risk of radiation-induced ischemic heart disease and cardiovascular disease compared to patients with right-sided breast cancer. The rate of major coronary events has been reported to increase by 7.4% with every 1-Gy increase in the dose to the heart.³⁴ Therefore, it is crucial to reduce the dose delivered to heart to the greatest possible extent. In the present study, a reduction of 1.94 Gy in mean heart dose was achieved with ncVMAT; the heart V₃₀, V₂₀, V₁₀ and V₅ were significantly reduced as well. The D_{mean} of the heart with non-coplanar arcs was 9.22 ± 2.98 Gy, which was higher than data reported by Tyran *et al.*¹⁶ and Pham *et al.*³⁵; our data suggested that the dose constraints for bilateral lungs and contralateral breast used in this study were much stricter than the aforementioned studies. Equally, coverage of nodal regions by the prescription dose was reduced in their studies, when compared to a 95% coverage of 50 Gy in this study. Further, ncVMAT was compared with coVMAT with similar optimization parameters without decreasing the cov-

erage of nodal regions, while limiting the dose to lungs and contralateral breast strictly to reduce the risk of harmful effects. Obviously, the dose to the heart could be further reduced if reducing the dose constraints for lungs and contralateral breast while compromising the coverage of nodes. Some studies recommend that certain sensitive areas in heart, injury to which might cause functional damage, should be evaluated separately.³⁶ Marks *et al.* reported that the probability of cardiac perfusion defects increased significantly with the increasing volume of irradiated left ventricle using single-photon emission CT.³⁷ In a retrospective study of patients with breast cancer undergoing radiotherapy from the 1950s to 1990s, Taylor *et al.* found that the irradiation of anterior heart and LAD might have increased the risk of death from cardiac disease.³⁸ Interestingly, improved sparing of $V_{5\gamma}$, V_{10} delivered to the anterior heart, left ventricle, and LAD was possible with ncVMAT in the present study, as illustrated in Figures 2 and 3. With ncVMAT, the maximum and mean doses of LAD were also lower comparing with coVMAT ($p < 0.001$). Although further evidence is necessary to demonstrate radiation-induced dysfunction in different parts of the heart, protection of these related areas still presents potential benefits.

Radiation pneumonitis is a well-known risk of thoracic tumor radiotherapy.³⁹ For breast radiotherapy, moderate symptomatic radiation pneumonitis was not observed if the V_{20} of the ipsilateral lung was $<30\%$, as reported by Lind *et al.*⁴⁰ Furthermore, a high V_{13} indicated a worse recovery after chemotherapy for patients undergoing breast cancer radiotherapy.²⁵ For the ipsilateral lung, Wen *et al.* recommended a $V_{20} < 39.8\%$ and a $V_{30} < 25.7\%$ for patients receiving local-regional irradiation.⁴¹ Thus far, the relationship between V_5 in both the ipsilateral and the contralateral lung, and the risk of radiation pneumonitis for patients after breast cancer radiotherapy is unclear. But according to the experiences in thoracic irradiation treatment, in the present study V_5 was strictly limited to as low as possible.⁴²

In addition to pulmonary and cardiac toxicities induced by radiotherapy, a second primary breast cancer in the long term is another critical concern in young patients with breast cancer.⁴³ Stovall *et al.* reported that the risk of a second primary breast cancer in patients younger than 40 years of age increased with treatment with more than 1 Gy in the contralateral breast.⁴³ Boice *et al.* also illustrated that the risk of a second cancer was associated with age and that patients younger than 45 years

of age had a higher risk of a second cancer after irradiation of the contralateral breast.⁴⁴ Popescu *et al.*⁴⁵ and Xu *et al.*²⁰ demonstrated that VMAT had the ability to reduce irradiation of the contralateral breast compared to IMRT. In the present study, the dose delivered to contralateral breast can be reduced further with ncVMAT. Thus, ncVMAT might be preferred to reduce the risk of a second cancer in young patients.

In the present study, the doses delivered to other OARs were clinically acceptable. Clinicians always face a conflict between effective coverage of the target volume and sparing of the OARs. It remains possible to further reduce the dose delivered to specific OARs with ncVMAT by sacrificing either other OARs or coverage of the target volume, which requires further evaluation on a case-by-case basis. The treatment delivery time, including couch rotation, which was approximately 2.5 min longer with ncVMAT than with coVMAT, was still more efficient than HT (around 1000 s).²⁰ The decline in treatment efficiency with ncVMAT is acceptable to an extent with improving plan quality. Deep inspiration breath-hold (DIBH) is another effective method in reducing dose delivery to the heart.³⁵ The concept was not discussed here because free-breathing is still used in clinical practice, and DIBH was only suitable for patients capable of holding their breath to 70%–80% of the maximum inspiration capacity for a minimum 20–30 s.⁴⁶ For patients incapable of DIBH, ncVMAT is an alternative technique, which better spares the heart and other OARs.

Conclusions

The present retrospective study comparing ncVMAT with normal coVMAT for locoregional radiotherapy of left-sided breast cancer, including IMN revealed that the $V_{5\gamma}$ conformity, and homogeneity for PTVall were improved with similar coverage by introducing of two additional non-coplanar arcs. Regarding the OARs, ncVMAT provided better dose sparing in the heart, bilateral lungs, LAD, and right breast, with no significant differences for most other OARs. In conclusion, ncVMAT is potentially beneficial in reducing the risk of toxicity in left-sided breast cancer.

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