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Original research article

Treatment planning study of Volumetric Modulated Arc Therapy and three dimensional field-in-field techniques for left chest-wall cancers with regional lymph nodes

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ABSTRACT

Aim: This study aims to investigate whether there are dosimetric advantages to using VMAT (Volumetric Modulated Arc Therapy) for left-sided chest-wall patients over the three-dimensional conformal field-in-field (FinF) technique.

Background: There is a lack of dosimetric studies dedicated for chest-wall patients. Potential dosimetric advantage could be obtained using VMAT due to complex geometry of PTVs (Planning Target Volumes) and OARs (Organs at Risk) in chest-wall and lymph nodes.

Materials and methods: VMAT and FinF plans were generated and evaluated based on DVHs (Dose Volume Histograms) for both PTVs and OARs for 22 left-sided chest-wall patients with involved regional nodes. PTV HIs (Homogeneity Indices) and CIs (Conformity Indices), and EUDs (Equivalent Uniform Doses) for PTVs and OARs were also evaluated for comparisons between VMAT and FinF.

Results: FinF planning met PTV criteria adequately in all cases except two. In these two cases, VMAT was able to meet PTV criteria adequately. VMAT demonstrated significant reduction in left lung $V_{20\text{Gy}}$ in chest-wall patients compared to FinF plans. The volumes of the right lung and right breast receiving 5 Gy were much higher in VMAT than those in FinF for all patients.

Conclusions: Compared to the FinF technique, there is a generally limited benefit using VMAT for left-sided chest-wall patients due to large low-dose-bath to OARs with insignificant improvement in PTV coverage. In case where FinF planning cannot meet dose constraints, VMAT provides a viable option. The use of VMAT planning over the FinF technique in chest-wall cancers should be carefully analyzed on an individual basis.

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1. Background

The tangential beam arrangement has been commonly accepted as the standard external beam radiation technique for breast and chest-wall cancers. In this beam setup, using simple wedges to modulate the beam fluence, significant dose inhomogeneity may be present, especially for large breasted patients.^{1,2} Better dose distribution can be achieved through more sophisticated beam fluence modulation. The field-in-field technique (also known as forward intensity modulated radiation therapy) divides a beam into segments that can result in improved dose homogeneity and conformity to the Planning Target Volumes (PTVs) by applying a systematic way of blocking hot spots.^{3,4} Further improvement can be achieved using intensity modulated radiation therapy (IMRT). The fixed-gantry IMRT (fIMRT) has been under much investigation either in tangential setup⁵ or in multi-beam setup.^{6,7} Its dosimetric improvement over conventional planning methods has been demonstrated. For left-sided breast/chest-wall cancers, greater efforts have been expended aimed at reducing lung and cardiac dose, while still providing adequate PTV coverage and homogeneity.

VMAT (Volumetric Modulated Arc Therapy) has been increasingly gaining popularity in clinical application since its introduction in 2008.⁸ VMAT is an arc-based technique that leads to highly conformal dose distributions through employing beam fluence modulation, variable dose rate, and gantry speed. While VMAT is shown to achieve similar or better PTV coverage and sparing of OARs to that of fIMRT, the major advantages of VMAT are less delivered monitor units (MUs), and reduced total treatment time in the treatment unit.^{9–12}

Recently, there has been growing interest in applying VMAT to treating breast and chest-wall cancers. For the treatment of patients post breast conservative surgery (intact breast), some studies comparing VMAT to fIMRT and the field-in-field (FinF) technique have indicated that VMAT provides an improvement in PTV coverage and dose homogeneity.^{13,14} However, VMAT is not recommended as the dosimetric quality of plans has not been shown to be superior to FinF or fIMRT.^{15,16}

For post-mastectomy patients with regional node involvement, a traditional delivery method is an isocentric technique consisting of tangential beams to treat the primary site and a parallel-opposed pair (POP) to treat supraclavicular/axillary nodes. Due to the thin wall of the chest-wall, PTV heterogeneity can be quite pronounced, and adequate dose coverage for the PTV is difficult to achieve without increased dose to the adjacent organs such as the ipsilateral lung and heart. The need for dose feathering at the junction between the chest-wall tangents and nodal POP presents an additional challenge to achieve dose homogeneity. Scarcity of literature on the comparison of VMAT with FinF precludes clinicians from drawing a definitive conclusion on the best practice. One study stated that VMAT may benefit chest-wall patients, however, only one chest-wall patient was examined.¹³ Another feasibility study showed that both VMAT and tomotherapy provided acceptable treatment plans for chest-wall patients.^{15,16} More study is needed to directly compare VMAT with FinF, as FinF is the most routinely used 3D conformal technique in chest-wall cancer treatment. VMAT also has the potential to reduce lung

and heart dose in left-sided chest-wall treatment. Further reduction in dose to normal tissues is possible when VMAT is applied to the POP treatment of nodal volumes.

1.1. Aim

In this article, we focused on the treatment of the left-sided chest-walls with positive supraclavicular nodes. We presented a comparison of dosimetric analysis of PTVs and OARs, using the following two methods: 3D conformal field-in-field technique and VMAT. We aim to investigate whether there are dosimetric advantages to using VMAT for chest-wall sites compared to using the field-in-field technique.

2. Materials and methods

2.1. Patient selections, dose prescription and objectives

Twenty-two left-sided chest-wall patients of median age 64 (range: 31–88) with positive supraclavicular/axillary nodes were randomly selected for VMAT chest-wall study. Dose prescriptions were 50Gy in 25 fractions for chest-wall target volumes (PTV50) and 45Gy in 25 fractions for supraclavicular nodes (PTV45). The average chest-wall separation was 19.7 ± 2.8 cm. The average volume of PTV50, PTV45 was 255.6 ± 97.8 cm³ and 233.7 ± 71.6 cm³, respectively. The average volume of the lung was: 1171.3 ± 261.5 cm³ (left) and 1361.7 ± 229.1 cm³ (right); the average volume of the heart was 489.5 ± 172.9 cm³. All patients underwent free-breathing CT simulation in the supine position with both arms abducted superiorly using a breast board system (MedTec®). The scan slice thickness was 0.25 cm. The scan volume was defined by the superior border at the level of the mastoid/ear lobe junction and inferior border at 7.0 cm beyond the most inferior extent of the breast/chest-wall wire.

The dosimetric objectives for the coverage of chest-wall and nodal PTVs (PTV50, PTV45, respectively) were as follows: 95% of the volume to be covered by 95% of the prescribed dose. This constraint could be relaxed to 93% volume coverage if 95% could not be achieved. OARs were to receive dose as low as possible. Various levels of importance of dose objectives were assigned to PTVs and OARs. Hot spots (volume was no greater than 2.0 cm³) were not to receive more than 107% of the prescribed dose. Details of dose objectives can be found in Table 1.

2.2. Field-in-field planning technique

In the conventional four field technique treating chest-wall with positive regional nodes, a lateral beam at gantry angle of around 130° and a medial beam at the gantry angle of around 315° were used to cover the chest-wall PTV50. The nodal PTV45s were covered by an anterior/posterior oblique POP pair. The field matching of the POP pair and tangential beams were obtained through a half beam block. Bolus of thickness 0.5 cm was placed on the chest-wall every second fraction of the entire treatment course. Chest-wall planning was performed using the three dimensional conformal field-in-field (FinF) technique applied iteratively to reduce hot spots

Table 1 – Dosimetric planning goals for the patients in this study. ALAP stands for “As Low As Possible”.

Structure	Criteria		Importance
PTV 50 Gy	V _{95%}	95% of volume receives 95% of 50 Gy	High
PTV 45 Gy	V _{95%}	95% of volume receives 95% of 45 Gy	High
Heart	V _{5Gy}	10% of volume receives 5 Gy	Medium
Left lung	V _{20Gy}	25% of volume receives 20 Gy	High
	V _{5Gy}	70% of volume receives 5 Gy or ALAP	Medium
Right lung	V _{5Gy}	10% of volume receives 5 Gy or ALAP	Medium
Spinal cord	Maximum dose	20 Gy	High
Right breast	V _{5Gy}	10% of volume receives 5 Gy or ALAP	Medium

resulting from the previous iteration. The planning is volume based and is normalized to the prescribed dose. Beam isocenter was situated at the junction of the chest-wall PTV and supraclavicular/axillary nodal PTV. Mixed energies of 6 MV and 18 MV could be used if the patient had a large breast/chest-wall separation, typically greater than 24.0 cm.

2.3. VMAT planning in Eclipse®

VMAT planning was performed using Varian’s RapidArc® optimization product (version 10). The calculation grid size was set to 0.25 cm with the heterogeneity correction on. The forward dose calculation algorithm was Anisotropic Analytical Algorithm (AAA version 10). The maximum dose rate and photon energy were 600 MU/min and 6 MV, respectively. The clinical target volumes (CTVs) for chest-wall 50 Gy, and nodal 45 Gy were contoured on CT images. PTVs were generated from the corresponding CTVs by adding 0.5 cm in all directions. If some parts of PTV extended outside the body contour, PTV.eval was generated such that those parts of PTV contour outside the body contour were cut off to be coincident with the chest-wall contour. A PTV_skin structure was created and accounted for the volume of the chest-wall skin to the thickness of 0.3 cm. The PTV_skin dose objective was 5% of the volume to receive 100% of the prescribed dose and 85–95% of the volume was to receive 80% of the prescribed dose. A 0.5 cm bolus was applied on every fraction. Organs at Risk (OARs) such as heart, contralateral breast, ipsilateral and contralateral lungs, and spinal cord were contoured on CT images.

Two 200° co-planar arcs, clockwise (CW) and counter clockwise (CCW) were used for the beam setup. The CW arc started at gantry angle of 300° and ended at 140°. The CCW started at 140° and ended at 300°. The collimator angles were set to 30° and 330° for CW and CCW arcs, respectively, to mitigate the tongue-and-groove effect due to an inter-leaf radiation leakage. The field size defined by the X jaws was 15 cm to accommodate limited MLC leaf travel on a carriage within a single field. The arc geometry tool in Eclipse® TPS was used to ensure the adequate incorporation of all PTVs with respect to the jaw openings of the two arcs. This tool suggests an optimal arc arrangement, taking into account tumor size and location. The location of the isocentre was placed approximately at the center of the combined PTV50 and PTV45. This tool could also conveniently demonstrate how well the PTV target was “seen” by the jaw opening through the display of varying colors on the particular portion of the PTV. Our experience showed that the arc geometry tool facilitated the VMAT arc setup in the planning.

2.4. Plan comparisons

2.4.1. Dosimetric evaluation metrics

The VMAT and FinF plans were analyzed using Dose Volume Histograms (DVHs) produced for PTVs and OARs. To quantitatively describe the dose homogeneity within the PTVs, and dose conformity to the PTVs, Homogeneity and Conformity Indices were introduced. A target homogeneity index (HI)¹⁷ is defined as the ratio of the difference between D_{2%} and D_{98%} divided by the prescribed dose. The HI closer to zero indicates that the target coverage is more homogeneous. A conformity index (CI)¹⁸ is calculated as the ratio between the patient volume receiving no less than 95% of the prescribed dose and the volume of PTV receiving no less than 95% of the prescribed dose. In an ideal situation, the CI is one. Any CI values that deviate from one (typically greater than one) suggest less target conformity. V5 (5 is in the unit of Gy, this is also true for V10, V20 and V30), V10, and V20 for the left lung; V5, V10, V20, and V30 for the heart; and V5 for the right lung and right breast were compared between VMAT and FinF plans. The average cumulative DVHs were calculated through averaging over each individual patient DVHs. The number of MUs for each fraction was also compared between VMAT and FinF plans.

2.5. Radiobiological evaluation metrics

Equivalent Uniform Doses (EUDs) were obtained for PTVs and OARs using the following formula¹⁹:

$$EUD = \left(\sum_{i=1}^N v_i D_i^a \right)^{1/a}$$

where v_i is a fractional target/organ receiving a dose D_i for the ith voxel; N is the number of voxels in a particular structure; and a is a tissue-specific parameter that describes the volume effect. The values of a are determined empirically from clinical data. They are negative for target structures, and positive for normal tissues. In this study, a is taken at –10 for PTVs, 1 for the lung, and 4 for the breast and heart.^{20,21}

The standard Mann–Whitney U test was used to analyze the data. The difference between the two techniques is considered significant if the U value is less than the critical value of U which is determined by p ≤ 0.05, where p represents the p value. The advantage of the Mann–Whitney U test over the student’s t test is that the U test does not require the assumption of normal distribution of the dosimetric parameters.

3. Results

Fig. 1 shows representative axial dose distributions between VMAT and FinF for a chest-wall patient. The isodose 25 Gy (represented by the yellow isodose line) covered less volume of the lung in VMAT than in FinF, while the isodose 10 Gy (represented by the brown isodose line) covered more volume of the lung in VMAT than in FinF. VMAT produced dose distributions that were more conformal to regional nodes than FinF was.

3.1. Dosimetric results

Coverage of chest-wall PTV50 and nodal PTV45 and dose constraints of OARs were adequate using FinF in all patients except two, in whom satisfactory PTV50 coverage was not achievable.

Fig. 2 shows the average DVHs calculated from 20 patients (FinF was adequate) for PTV50, PTV45, lungs, heart and right breast for VMAT and FinF. Table 2 summarizes the plan comparison parameters for VMAT and FinF techniques treating the left chest-wall with regional nodes. The HI for both PTV50 and PTV45 were not statistically different. The CI calculated from VMAT plans was closer to one than that calculated from FinF plans, which indicated that VMAT produced more conformal target coverage than FinF did. VMAT showed statistically significant higher V5 but lower V20 to the left lung than FinF

did. VMAT gave higher V5 to the heart but not different for V10, V20 and V30 than FinF. Again VMAT demonstrated significantly larger low-dose volume (V5) to the right lung and right breast than FinF.

Fig. 3 shows the DVHs calculated from the two left chest-wall patient (FinF is not adequate). DVHs for PTV50, PTV45, heart, right breast, left and right lungs are displayed for VMAT versus FinF. Table 3 presents the plan parameter comparison for these two patients between VMAT and FinF. PTV50 was well covered in the VMAT plan compared to the FinF plan. PTV45 was also well covered in the VMAT plan. Although the FinF plan met the PTV criterion that 95% of the prescribed PTV45 dose (45 Gy) covered 95% of the PTV45 volume, there existed some volume (small albeit) of PTV45 receiving the dose significantly less than 45 Gy. The left lung V20 was slightly lower in VMAT than that in FinF.

3.2. EUD results

Table 4 shows that EUDs of PTV50 and PTV45 between VMAT and FinF were statistically similar. The average EUD for the left lung in VMAT was not statistically higher than that in FinF while the right lung and right breast received much less dose than in VMAT. The heart EUD in VMAT was not statistically different from that in FinF.

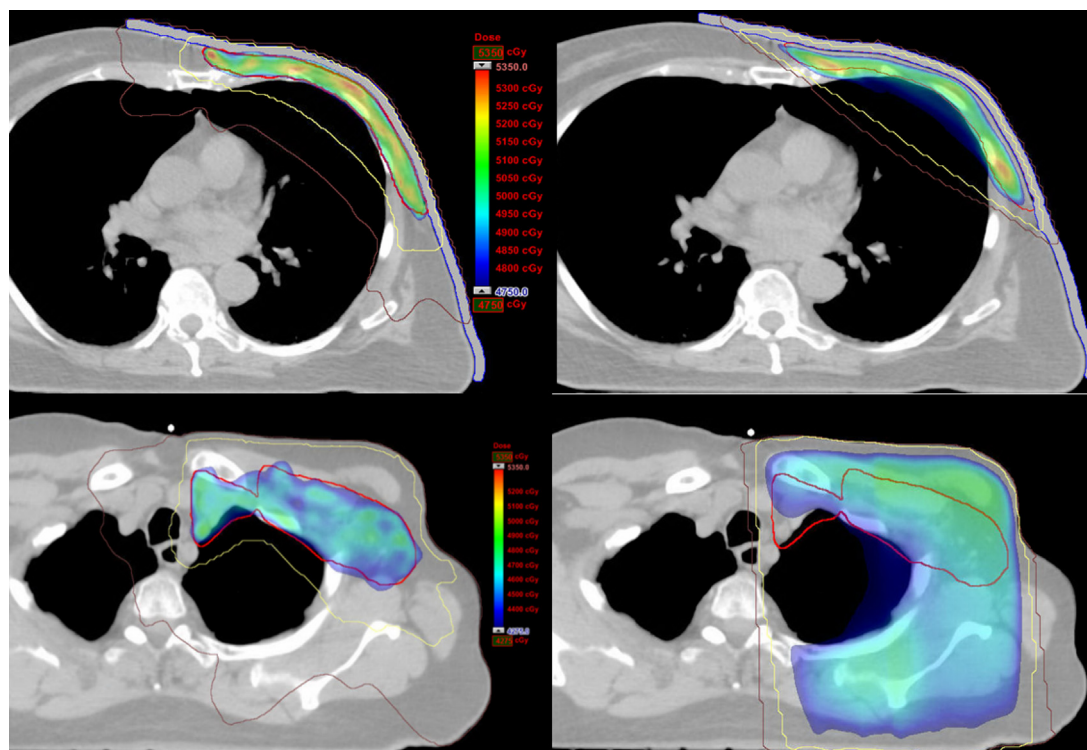


Fig. 1 – Comparison of dose distributions between VMAT and FinF. The color wash threshold was set to 107% and 95% of the PTV prescribed dose. 25 Gy (yellow) and 10 Gy (brown) isodose lines are displayed to represent low dose bath. The top row shows chest-wall PTV50s from VMAT (left) and FinF (right), the dose scale being from 53.5 Gy to 47.5 Gy with a 0.5 Gy step. The bottom row shows nodal PTV45s from VMAT (left) and FinF (right), the maximum and the minimum doses shown on the dose scale are 53.5–42.75 Gy, respectively. Between the maximum and minimum doses, the dose scale is from 52 Gy to 44 Gy with a 1.0 Gy step.

Table 2 – Plan comparison parameters between VMAT and field-in-field (FinF) techniques treating the left chest-wall for the twenty patients. Mann–Whitney U test was used. NSD and SD represent “not statistically different” and “statistically different”, respectively.

Structures	Parameters	VMAT		FinF		Mann–Whitney U test
		Average	St dev	Average	Std	
PTV50	Homogeneity index	0.121	0.022	0.125	0.047	NSD
	Conformity index	1.46	0.21	2.96	0.75	SD
PTV45	Homogeneity index	0.142	0.056	0.151	0.036	NSD
	Conformity index	1.41	0.36	3.61	0.68	SD
Left lung	V5	75.2%	8.6%	43.1%	10.8%	SD
	V10	40.3%	4.1%	32.7%	8.1%	NSD
	V20	15.5%	5.2%	27.8%	8.5%	SD
Heart	V5	17.2%	6.9%	4.2%	2.2%	SD
	V10	3.3%	2.9%	1.7%	1.1%	SD
	V30	0.5%	0.7%	1.1%	0.8%	NSD
Right lung	V5	0.1%	0.1%	0.5%	0.8%	NSD
Right breast	V5	16.9%	8.6%	1.1%	0.5%	SD
MUs		12.6%	14.9%	0.5%	2.1%	SD
		657	58	431	35	SD

Table 3 – Plan parameters comparison between VMAT and FinF plans for the two left chest-wall patients with regional nodes. Average values were calculated. Statistical analysis was not performed due to only two patients.

Structures	Parameters	VMAT (average)	FinF (average)
PTV50	Homogeneity index	0.144	0.85
	Conformity index	1.32	1.92
PTV45	Homogeneity index	0.139	0.53
	Conformity index	1.76	2.13
Left lung	V5	74.2%	37.9%
	V10	48.1%	29.4%
	V20	20.1%	23.2%
Heart	V5	23.9%	3.2%
	V10	8.4%	1.0%
	V30	3.8%	0.4%
Right lung	V5	1.1%	0.3%
Right breast	V5	24.6%	0.0%
MUs		44.0%	0.0%
		616	441

Table 4 – Comparison of EUD averages and standard deviations for PTV and OARs between VMAT and FinF for the twenty two left chest-wall patients. The dose is expressed in Gy. Mann–Whitney U test was used. NSD and SD represent “not statistically different” and “statistically different”, respectively.

Structure	VMAT		FinF		Mann–Whitney U test
	Average	St dev	Average	St dev	
PTV50	50.7	0.3	48.2	5.1	NSD
PTV45	45.6	0.8	44.7	3.3	NSD
Left lung	11.0	1.8	14.2	3.4	NSD
Heart	7.9	1.6	11.2	4.3	NSD
Right lung	3.8	0.9	0.4	0.1	SD
Right breast	5.8	1.5	1.6	0.5	SD

4. Discussion

Jin et al.¹⁵ compared the dosimetry for twenty left-sided breast cancer patients for five different radiotherapy planning techniques including VMAT and FinF. They reported VMAT and FinF had similar homogeneity index (HI) and conformity index (CI); V5 of the left lung was much higher in VMAT than that in FinF; no significant difference was found between VMAT and FinF in the left lung V20 and the heart V5; the right breast received much higher dose in VMAT. They concluded that VMAT was not recommended for left-sided breast

treatment. Popescu et al.¹³ studied 5 patients. Among those 5 patients, 3 were breast patients, one underwent mastectomy and one was an inflammatory patient. They compared VMAT with IMRT and the modified wide tangent (MWT) technique for locoregional radiotherapy for left-sided breast cancer, including internal mammary nodes. For the MWT technique, three patients were planned using FinF and the remaining two used wedged pair. They obtained the average DVHs of five patients for PTVs and OARs. Their results indicated that VMAT achieved better PTV coverage than did the MWT technique. DVHs of OARs were similar to those in Jin’s study. Badakhshi et al.¹⁶ studied the feasibility of VMAT in 12 breast cancer patients

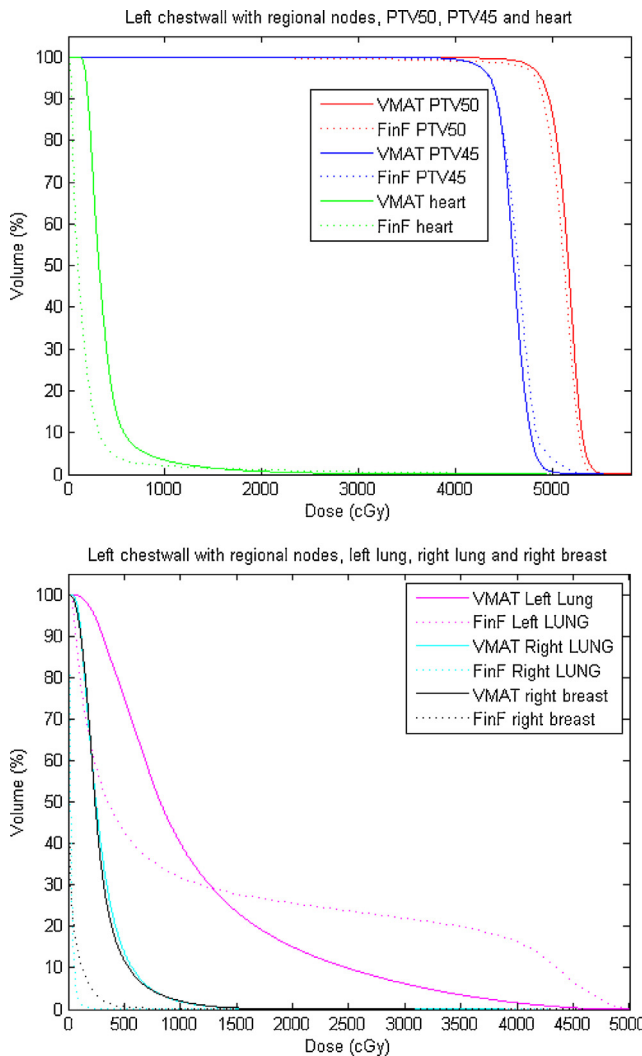


Fig. 2 – Average DVHs calculated from the twenty left chest-wall patients. Comparison of PTV50, PTV45, heart, left lung, right lung and right breast between VMAT and FinF.

(8 left breast cancer and 4 right breast cancer) and compared it with 3D-CRT. They concluded that VMAT, although demonstrated a slightly better conformity index, was inferior to IMRT and 3D-CRT with regard to dose distribution to OARs, especially at the low dose level.

The above studies drew conclusions based on the averaged dose distribution either from left-sided breast patients or from patients including breast and chest-wall sites. For example, Popescu et al.¹³ drew conclusions from a group of 3 breast patients, one chest-wall patients and one inflammatory patient. The averaged results across all patients might not be adequate to determine the best method of treatment planning for patients with different anatomical features. This article addresses the lack of dedicated study on left-sided chest-wall patients.

Plans of 20 left chest-wall patients with regional nodes showed that PTV coverage in VMAT and FinF was statistically similar with VMAT demonstrating better dose conformity to

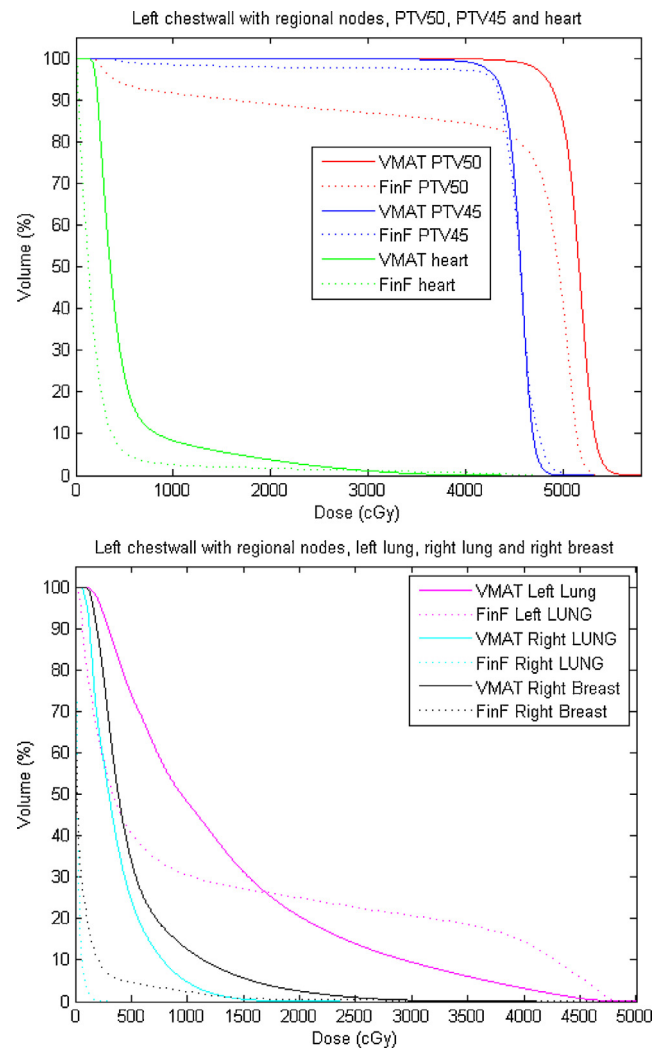


Fig. 3 – Average DVHs calculated from two left chest-wall patients. Comparison of PTV50, PTV45, heart, right breast, left lung and right lung between VMAT and FinF.

target volumes. V5 for the left lung and heart was significantly higher in VMAT than in FinF. However, VMAT produced less V20 for the left lung in chest-wall patients. This is readily understood since VMAT can deposit dose more conformal to the thin chest-wall PTV than FinF can, hence, less volume of the left lung is irradiated with high dose. V10, V20 and V30 of the heart were not distinguishable between VMAT and FinF plans. V5 of the right lung and right breast were significantly higher in VMAT than in FinF. For the remaining two left chest-wall patients, the satisfactory coverage for the PTV50 was difficult to achieve using FinF due to the thin size and a strongly concave shape of the PTV50 volume extending to the midline of the patient's chest. In these cases, VMAT demonstrated its advantage by adequately covering PTV50 and PTV45. It is noted that a better PTV coverage in VMAT was achieved at the expense of higher V5 for the lungs, hearts and right breast. This example demonstrated that although the majority of left chest-wall patients may not benefit from VMAT, there existed a subpopulation where FinF could not provide adequate coverage of the PTV. Whether

patients should be treated with VMAT over FinF depends on the clinician's comprehensive evaluation of each individual patient.

Due to wide variations of locations and shapes of PTVs and OARs, it is natural to think that some patients may benefit from VMAT while others may not. This may help explain mixed recommendations from the literature.^{13–16} It may not be apparent simply through visual inspection of patient anatomy, shape and location of PTVs, whether a particular patient will benefit from VMAT. Hence, FinF planning should remain the standard technique for chest-wall treatments. However, when FinF fails to meet the dosimetric criteria, VMAT provides a viable option for planning.

It is noted that this study is not aimed to provide a large number of patient cases, but merely indicated that a subset of patients exist that may benefit from VMAT planning. Hence, statistical analysis of the left-sided chest-wall patients are not presented due to limited number of patients. Future study may include more cases to demonstrate the advantage of this approach.

In radiation delivery, part of the PTV may be missed by the beam due to intra-fractional breathing motion. This issue is alleviated in tangential beam setup by adding an approximately 2.0 cm of flash beyond the chest-wall contour. However, there is no readily available method to add flash in VMAT planning. Since the purpose of this study is dosimetric analysis, no motion was accounted for in the planning. If the VMAT plan proceeds to be used in clinical delivery, ways to address this issue include an artificially expanded PTV¹⁴ or use of the deep inspiration breath-hold technique,^{22,23} although some literature indicates that treatment delivery in a free breathing mode is adequate as breast/chest-wall motion is in the range of 0.3 cm or less.^{24,25}

Although radiation pneumonitis as a complication of breast/chest-wall cancer treatment only affects 1% of patients,²⁶ it is well-recognized as one of the plan quality indicators requiring assessment. While lung V5 was greatly increased in all VMAT patients, there was a significant reduction in V20, a widely accepted predictor of radiation pneumonitis. From this, it can be assumed, patients will have less chance of developing radiation pneumonitis using VMAT compared with FinF. It should be noted, however, that some studies have found close correlation between high percentage normal lung volume exceeding 5 Gy of dose (V5) and pneumonitis.^{27,28}

All plans in VMAT demonstrated much higher MUs than FinF. In addition, all patients were exposed to high volume of low-dose bath to the right lung and right breast. This raises a concern about radiation induced secondary cancer malignancy. The EUDs of the right lung and heart from VMAT were much higher than those in FinF as shown in Table 4. Chen et al.²⁹ estimated that the risk of developing contra-lateral cancer is 2–11%. The risk of contra-lateral breast cancer is estimated to be 3–5%, depending on whether hormone therapy is used.³⁰ Hence, the risk for a woman to develop a contralateral cancer is increased in VMAT plans as the EUD dose is increased by 3–5-folds. This should be one of factors considered when applying VMAT to treating chest-wall cancers, especially for younger patients who are expected to live much longer.

In practice, planning and treatment delivery time is an important factor to consider in any clinic. Based on the experience at the authors' clinic, VMAT decreased planning time (roughly 90 min for FinF planning versus 75 min for VMAT). In terms of treatment delivery, beam ON to beam OFF time is similar between the two modalities. Actual patient appointment times will vary based on imaging modalities.

5. Conclusion

Our study indicates that compared to the field-in-field technique, there is generally limited benefit to using VMAT for left-sided chest-wall patients, due to large low-dose-bath (5 Gy) to Organs at Risk and normal tissues with insignificant improvement in PTV coverage. In case where FinF planning has not been able to meet dose constraints, VMAT has proven useful. Whether a patient is treated with VMAT should be carefully analyzed on an individual basis.

Conflict of interest

None declared.

Financial disclosure

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