Treatment Planning Comparison of Volumetric Modulated Arc Therapy With Trilogy and Halcyon for Bilateral Breast Cancer

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Research

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Abstract

Background: To evaluate the dosimetry of Halcyon in treatment of bilateral breast cancer with volumetric modulated arc therapy.

Methods: On CT images of 10 patients with bilateral breast cancer, four Halcyon plans with different setup fields were generated and dosimetric comparisons were conducted among the four plans to select an optimal setup field mode. The four setup-field plans were referred to as CBCT-H, CBCT-L, MV-H, MV-L. Whole and partial arc plans on Trilogy and Halcyon referred to as T-4arc, T-8arc, H-4arc and H-8arc were designed. The dosimetric differences between whole and partial arc plans in the same accelerator were compared to understand the most suitable field setting mode. The better Halcyon plan was selected to the further dosimetric comparison of the plan quality and delivery efficiency between Trilogy and Halcyon.

Results: CBCT-H plans increased D_{mean}, D_2 and V_{107} of planning target volume (PTV) and V_5 and D_{mean} of the heart, left ventricle (LV) and lungs compared to other plans. No significantly dosimetric differences were observed in PTV and organs at risk (OARs) among CBCT-L, MV-H and MV-L. The mean dose and low dose volume of heart, lungs and liver were significantly decreased in T-8arc plans. In terms of V_5, V_{20}, V_{30}, V_{40} and D_{mean} of the heart, V_{20}, V_{30}, V_{40} and D_{mean} of the LV, V_{30}, V_{40}, D_{max} and D_{mean} of the left anterior descending artery (LAD), V_5 and V_{40} of lungs, H-8arc was significantly higher than H-4arc (p<0.05). Compared to Trilogy's plans, Halcyon's plans reduced the high-dose volume of the heart and LV, but increased the mean dose of the heart. For the dose of the LAD and the V_{20}, V_{30} of lungs, there was no statistical difference between the two accelerators. Compared with Trilogy, plans on Halcyon significantly increased the skin dose, but also significantly reduced the delivery time.

Conclusion: For Halcyon, the whole-arc plans has more dosimetric advantages in bilateral breast cancer radiotherapy. Although the mean dose of the heart and the skin dose are increased, the dose of the cardiac substructure and other OARs are comparable to the Trilogy, and the delivery time is significantly reduced.

Background

Breast cancer is one of the most common malignant tumors in women. Postoperative radiotherapy can significantly reduce the recurrence rate of tumors, reduce mortality, and prolong the survival time of patients with breast cancer [1]. Bilateral breast cancer is relatively rare, accounting for about 2.1% of all patients with breast cancer [2]. Because of the larger target area and more complex shape, it is more difficult to design the treatment plan for bilateral breast cancer.

The Halcyon linear accelerator (LINAC) is a new machine from Varian company, which offers a single 6 MV flattening-filter-free (FFF) X-ray with a jawless design. Halcyon has many differences from conventional C-arm LINACs, such as jawless, dual-layer multi-leaf collimator (MLC), faster gantry rotation

and daily image guided radiotherapy (IGRT). Comparable dose distribution and excellent delivery efficiency have been shown on Halcyon in radiotherapy for head and neck, brain, unilateral breast, and cervical cancers [3-7]. Trilogy is a conventional C-arm LINAC with jaw and Millennium MLC.

It's proved volumetric modulated arc therapy (VMAT) can improve the quality of the plan and the delivery efficiency in bilateral breast cancer [8-10]. Previous study found that the partial-arc VMAT plans significantly reduced the cardiopulmonary dose compared to the whole-arc VMAT plans in unilateral breast radiotherapy [11]. Similarly, partial-arc VMAT plans were feasible in bilateral breast radiotherapy [12]. These studies were based on conventional C-arm LINAC with jaw. To our knowledge, the application of Halcyon in the VMAT plans for bilateral breast cancer have not been reported. It is unknown whether the partial-arc VMAT plan is applicable on Halcyon. In Halcyon 1.0, high-quality/low-dose megavoltage cone beam computed tomography (MV CBCT) or orthogonal MV radiograph pair could be selected for image guided, and the four setup-fields delivered different monitor units (MUs). It is important to choose an optimal setup field.

The aim of the study was to select an optimal setup field and the suitable arc mode of VMAT plans for Halcyon in bilateral breast radiotherapy, and analyze the plan quality and delivery efficiency by comparing the dosimetric differences between the Halcyon and Trilogy to guide the clinical application in bilateral breast radiotherapy.

Materials And Methods

Patient Selection and Volume Delineation

From September 2006 to December 2018, CT image datasets of 10 patients diagnosed with bilateral breast cancer and received bilateral breast radiotherapy at Shandong Cancer Hospital were selected. The clinical target volume (CTV) includes all bilateral breast tissue, excluding local lymph node region. The planning target volume (PTV) was generated by expanding a 5-mm margin from the CTV and was shrinked to 5 mm below the skin on the skin side. The organs at risk (OARs) include the total lung, heart, left ventricle (LV), left anterior descending artery (LAD) and liver. The skin is defined as the 3mm region below the body outside of the PTV. The normal structures were defined as the body minus the PTV (B-P).

Treatment Planning

In Halcyon version 1.0, all imaging setup fields are taken using digital megavoltage imaging (DMI) panels. When designing a Halcyon plan, four different setup fields could be selected. For the 10 patients, we designed four VMAT plans with different setup fields on Halcyon: high-quality MV cone beam CT (the gantry rotates clockwise from 260° to 100° and delivering 10 monitor units, simply called CBCT-H); low-dose MV CBCT (delivering 5 MUs in a clockwise gantry rotation from 260° to 100°, simply called CBCT-L); high-quality orthogonal MV radiograph pair (images acquired with 0° and 90° and delivering 2 MUs for each field, simply called MV-H) and low-dose orthogonal MV radiograph pair (images acquired with 0° and 90° and delivering 1 MU for each field, simply called MV-L). For the four plans, two anticlockwise

160° to 200°and two clockwise 200° to 160° rotation arcs were used. First, the dosimetric differences between the four plans were compared to find the optimal setup mode.

Then, four VMAT plans were designed for the 10 patients. On Trilogy, whole and partial arc plans were generated. The whole-arc plan consisted of two anticlockwise 160° to 200°and two clockwise 200° to 160° rotation arcs. The partial-arc plan consisted of total 8 partial arcs. For unilateral breast, four 100° around arcs were generated. In the two plans, the medial x-jaw was set to the minimum site (−2 cm) to minimize the irradiated volume of the lungs and heart. 6 MV X ray was used and the dose rate was set to 600 MU/min. The whole and partial arc plans designed on the Trilogy were referred to as T-4arc and T-8arc respectively. Two whole and partial arc plans, referred to as H-4arc and H-8arc, were designed on Halcyon with the same arc angle as T-4arc and T-8arc mentioned above. In Halcyon plans, 6 MV FFF X ray was used and the maximum dose rate was 800 MU/min. Low-quality MVCBCT was selected for image guided.

The prescription dose was 50 Gy in 2-Gy fractions. All plans were designed with the Eclipse version 15.5 treatment planning system (Varian Medical Systems, Palo Alto, CA, USA) using analytic anisotropic algorithm (AAA). The normalization of dose was 95% volume of PTV achieved 100% prescription dose. All plans used the same optimization parameter setting, with the goal of minimizing the dose to the lungs, heart and LAD while ensuring the PTV dose coverage. No dose constraint was applied to the skin and LV during the optimization.

Dosimetric Evaluation

The dose statistics of the plans were based on dose-volume histogram (DVH) analysis. For PTV, the dose of 2% and 98% volume (D_2, D_{98}), the volume receiving 107% and 110% of the prescribed dose (V_{107} and V_{110} and the mean dose (D_{mean}) were analyzed. The conformity index (CI) and the homogeneity index (HI) of the PTV were calculated according to the following formula:

$$CI = \frac{TV_{PV}{}^2}{TV \times PV}$$

TV_{PV} represents the volume of the PTV wrapped by the prescription dose, the TV represents the volume of the PTV, and the PV represents the total volume wrapped by the prescription dose. Larger CI values indicate the better conformity of target [13].

$$HI = \frac{D_2 - D_{98}}{D_p} \times 100\%$$

D_2 and D_{98} represents the irradiated dose of 2% and 98% volume of the PTV respectively. D_p represents the prescribed dose. Lower HI values indicate the better uniformity of target [14].

For OARs, the V_X and mean doses were analyzed. V_X represents the irradiated volume of X Gy dose.

The number of MUs was analyzed for all plans. The delivery time of T-4arc, T-8arc, H-4arc and H-8arc was recorded. The delivery time was recorded from the first field beam on to the last field beam off, excluding the positioning time.

Statistical Analysis

All data were statistically analyzed using the Statistical Package for Social Sciences v20.0 software (SPSS Inc., Chicago, IL, USA). First, A one-way analysis of variance (ANOVA) using Bonferroni's multiple comparisons test were applied to compare the four different setup-field plans on Halcyon. Second, whole and partial arc plans on same LINAC were compared to determine the most suitable field mode for the machine. The Mann-Whitney U rank and test was used. The better Halcyon plan was selected to the further comparison. Third, a statistical comparison of the better Halcyon plan and the Trilogy plan was implemented to analyze the dosimetric differences between the two machines using Mann-Whitney U rank and test. The differences were considered statistically significant when $p < 0.05$.

Results

Dose Comparisons for Different Setup-field Plans

Table 1 shows the dose parameters for the four different setup-field plans on Halcyon. Among the four plans, no significant differences were observed in the D_{98}, V_{110}, CI and HI of the PTV. Compared to CBCT-L, CBCT-H plans increased D_{mean}, D_2 and V_{107} of PTV. No significant differences were observed in all dosimetric indicators of PTV among CBCT-L, MV-H and MV-L. For OARs, CBCT-H plans increased V_5 and D_{mean} of the heart, LV and lungs compared to other plans. No significant differences were observed in V_{20}, V_{30}, V_{40} of heart and V_{10}, V_{20}, V_{30}, V_{40} of LV and lungs between the four plans. For LAD, CBCT-H increased V_5 compared to MV-L, but no significant differences were observed in other dosimetric parameters among the four plans. For skin, liver and MUs, there were no statistical differences between the four plans. For B-P, CBCT-H increased V_5 compared to CBCT-L and MV-L, but no significant differences were observed in other dosimetric parameters among the four plans. Figure 1 shows the dose distributions of the four different setup-field plans on Halcyon.

Table 1 Dosimetric analysis for four different setup-field plans on Halcyon

	CBCT-H	CBCT-L	MV-H	MV-L	*p*	*p*<0.05
PTV						
D_{mean}(Gy)	52.40±0.29	52.02±0.18	52.22±0.21	52.13±0.29	0.012	a
D_{98}(Gy)	48.51±0.21	48.54±0.31	48.54±0.30	48.59±0.35	0.949	
D_{2}(Gy)	54.29±0.60	53.59±0.31	53.83±0.39	53.65±0.48	0.006	a,c,
V_{107} (%)	16.11±12.81	3.55±2.77	7.91±6.72	7.49±10.83	0.030	a
V_{110} (%)	0.8±1.6	0.01±0.03	0.05±0.10	0.03±0.07	0.093	
CI	0.86±0.02	0.86±0.02	0.86±0.02	0.86±0.02	0.959	
HI	11.56±1.32	10.09±1.09	10.59±1.07	10.11±1.42	0.055	
heart						
V_{5}(%)	55.02±9.25	30.45±6.16	33.19±8.43	29.37±7.70	0.000	a,b,c
V_{10}(%)	14.93±4.23	10.15±2.90	13.28±4.40	12.23±3.90	0.047	a
V_{20}(%)	3.85±1.76	2.69±1.33	3.65±2.05	3.56±1.72	0.464	
V_{30}(%)	1.06±0.59	0.75±0.47	1.04±0.74	1.08±0.70	0.615	
V_{40}(%)	0.12±0.12	0.08±0.12	0.11±0.14	0.13±0.16	0.863	
D_{mean}(Gy)	7.06±0.74	5.64±0.57	6.04±0.94	5.66±0.87	0.001	a,b,c
LV						
V_{5}(%)	57.92±11.20	35.74±9.32	39.93±11.56	35.96±10.37	0.000	a,b,c
V_{10}(%)	21.24±7.09	16.14±5.93	19.05±6.78	17.88±6.38	0.376	
V_{20}(%)	7.80±3.29	5.80±2.74	7.31±3.57	7.13±3.29	0.560	
V_{30}(%)	2.61±1.31	1.86±1.00	2.49±1.52	2.59±1.49	0.560	
V_{40}(%)	0.34±0.23	0.21±0.16	0.36±0.32	0.40±0.37	0.478	
D_{mean}(Gy)	8.26±1.25	6.77±1.12	7.32±1.47	6.94±1.40	0.028	a,c
LAD						
V_{5}(%)	97.45±5.08	84.61±13.44	85.06±12.65	80.58±14.49	0.020	c
V_{10}(%)	68.42±18.09	63.24±17.19	65.43±16.81	64.14±17.98	0.918	

V_{20}(%)	48.25±21.34	43.11±19.10	46.90±19.53	45.24±20.15	0.946	
V_{30}(%)	21.29±13.82	14.27±10.90	20.78±15.04	21.63±15.04	0.593	
V_{40}(%)	0.38±0.46	0.14±0.32	0.44±0.54	0.55±0.64	0.328	
D_{max}(Gy)	39.48±3.21	38.85±3.06	39.66±3.29	39.77±3.49	0.922	
D_{mean}(Gy)	19.20±4.74	17.19±4.03	18.51±4.57	18.21±4.96	0.803	
Lungs						
V_5(%)	57.73±8.87	43.70±4.06	46.63±7.39	43.71±6.64	0.000	a,b,c
V_{10}(%)	26.51±3.40	22.91±2.58	25.22±3.21	24.20±2.59	0.064	
V_{20}(%)	14.9±2.90	13.18±2.54	14.72±2.65	14.22±2.42	0.471	
V_{30}(%)	9.09±2.41	8.01±2.11	9,02±2.23	8.64±2.02	0.680	
V_{40}(%)	4.17±1.60	3.54±1.38	4.07±1.47	3.87±1.37	0.780	
D_{mean}(Gy)	10.36±1.09	9.08±0.84	9.63±1.04	9.29±0.86	0.027	a
liver						
D_{mean}(Gy)	6.91±1.49	6.02±1.10	6.46±1.46	6.31±1.39	0.539	
skin						
V_{30}(%)	74.56±7.62	74.15±7.63	73.42±7.96	73.26±7.84	0.979	
V_{40}(%)	41.26±9.18	40.42±8.81	39.69±9.20	39.23±8.53	0.960	
V_{45}(%)	17.66±4.86	16.83±4.25	15.73±4.18	15.3±3.75	0.604	
V_{50}(%)	0.28±0.21	0.27±0.23	0.14±0.11	0.13±0.13	0.116	
D_{mean}(Gy)	36.13±1.94	35.97±1.89	35.76±1.97	35.68±1.88	0.952	
B-P						
V_5(%)	32.91±4.48	27.62±2.75	28.90±3.46	28±3.38	0.008	a,c
V_{10}(%)	19.93±2.25	18.43±1.89	19.35±1.99	19.02±2.08	0.436	
V_{20}(%)	13.30±1.54	12.58±1.43	13.07±1.43	12.93±1.46	0.737	
V_{30}(%)	8.86±0.85	8.47±0.89	8.75±0.86	8.67±0.80	0.773	
V_{40}(%)	5.03±0.36	4.86±0.40	4.96±0.42	4.92±0.38	0.802	

V_{50}(%)	0.83±0.12	0.76±0.12	0.78±0.12	0.75±0.14	0.483
D_{mean}(Gy)	7.96±0.73	7.35±0.62	7.53±0.68	7.41±0.66	0.191
MUs	936.5±68.2	1036.1±103.8	956.6±73.4	986.2±76.5	0.053

PTV, planning target volume; V_x, volume receiving at least x% of the prescribed dose; D_x, dose received by the x% of the volume; CI, conformity index; HI, homogeneity index; V_X, volume receiving at least x Gy; LV, left ventricle; LAD, left anterior descending artery; MU, monitor unit; CBCT-H, plan with high-quality MV CBCT; CBCT-L, plan with low-dose MV CBCT; MV-H, plan with high-quality MV pair; MV-L, plan with low-dose MV pair; a: CBCT-H vs CBCT-L; b: CBCT-H vs MV-H; c: CBCT-H vs MV-L; d: CBCT-L vs MV-H; e: CBCT-L vs MV-L; f: MV-H vs MV-L

Dose Comparisons for Different arc plans on identical LINAC

Table 2 shows the PTV dosimetric parameters of the four whole and partial arc plans on Halcyon and Trilogy LINACs. For PTV, there were no statistically significant differences in D_{mean}, D_2, D_{98}, V_{107}, V_{110} and HI between whole and partial arc plans on Trilogy (p<0.05). T-4arc showed better conformity than T-8arc (p<0.05). On Halcyon, D_2, V_{107}, V_{110} and HI of PTV in H-8arc were higher than those in H-4arc (p<0.05). D_{98} and CI in H-4arc plans were higher than those in H-8arc plans, and the differences were statistically significant. There was no statistical difference in D_{mean} of PTV between the two plans on Halcyon.

Table 3 shows the dosimetric parameters of organs at risk. On Trilogy, T-8arc plans significantly reduced the V_5 and D_{mean} of heart, V_5 of LV, V_5, V_{10} and D_{mean} of lungs, D_{mean} of liver and total MUs compared to T-4arc. T-4arc plans reduced the V_{40} of LV and lungs compared with T-8arc. No significant differences were observed in the dose of LAD and skin and the delivery time. On the Halcyon, lung doses (V_5 and V_{40}), heart doses (V_5, V_{20}, V_{30}, V_{40} and D_{mean}), and LV (V_{20}, V_{30}, V_{40} and D_{mean}) and LAD (V_{30}, V_{40}, D_{max}, and D_{mean}) doses were significantly reduced in 4arc plans compared to 8arc plans (p<0.05). H-8arc plans significantly reduced the number of MUs compared with H-4arc plans. No significant differences were observed in the dose of skin and the delivery time. Figure 2 shows the mean dose-volume histograms for the four plans.

According to the results above, T-8arc and H-4arc plans showed better dosimetry on the respective LINAC. Because of the poor dosimetry, H-8arc was not used for further statistical comparison. Next, H-4arc was statistically analyzed with T-4arc and T-8arc respectively to reflect the dosimetric differences between the two LINACs.

Table 2 Dosimetric parameters of PTV for whole and partial arc plans on Trilogy and Halcyon

PTV	T-4arc	T-8arc	H-4arc	H-8arc	P<0.05
D_{mean}(Gy	51.79±0. 24	51. 55±0. 27	52. 02±0. 18	52. 20±0. 22	c,d
D_2(Gy)	53.53±0.42	53.07±0.55	53.59±0.31	54.16±0.47	b,c
D_{98}(Gy)	48.40±0.40	47. 98±0. 55	48. 54±0. 31	48. 14±0. 41	b,c
V_{107}(%)	3.16±2.44	1.42±2.24	3.55±2. 77	11.11±8. 38	b,c
V_{110}(%)	0.03±0.05	0.01±0.03	0.01±0.03	0.41±0.49	b
CI	0.87±0.02	0.82±0.04	0.86±0.02	0.83±0.03	a,b,c
HI(%	10.27±1.54	10.18±2.06	10.09±1.09	12.04±1.39	b

PTV, planning target volume; Dx, dose received by the x% of the volume; Vx, volume receiving at least x% of the prescribed dose; CI, conformity index; HI, homogeneity index; T-4arc, whole-arc plans on Trilogy; T-8arc, partial-arc plans on Trilogy; H-4arc, whole-arc plans on Halcyon; H-8arc, partial-arc plans on Halcyon; a: T-4arc vs T-8arc, b: H-4arc vs H-8arc, c: T-8arc vs H-4arc, d: T-4arc vs. H-4arc

Dose Comparisons for the plans between Trilogy and Halcyon

For PTV, significant difference was observed in D_{mean} between T-4arc and H-4arc. There were no statistically significant differences in D_2, D_{98}, V_{107}, V_{110}, and CI, HI between the two plans. Compared with T-8arc plan, H-4arc significantly increased D_{mean}, D_2 and V_{107} of PTV. Better D_{98} and CI were observed in H-4arc. No statistically significant differences were observed in V_{110} and HI between T-8arc and H-4arc plans. The results are shown in Table 2.

For the doses of heart and substructures, H-4arc plans increased V_5 and D_{mean} of the heart, but reduced V_{30} and V_{40} of heart and LV (p<0.05). No statistically significant differences were found in the V_{10} and V_{20} of heart, V_{10}, V_{20} and D_{mean} of LV, and all dosimetric parameters of LAD between H-4arc and two Trilogy plans. H-4arc plans showed the lowest values in heart and LV doses (V_{20}, V_{30}, V_{40}) and LAD doses (V_{30}, V_{40}, D_{max}, D_{mean}) compared to the two Trilogy plans, but the results showed no statistical significance (p>0.05). Table 3 shows the results. T-8arc plans significantly reduced the V_5, V_{10} and D_{mean} of lungs and D_{mean} of liver compared to T-4arc and H-4arc plans, and no statistically significant differences were found in these indexes between the latter two plans. For V_{20}, V_{30}, and V_{40} of lungs, there were no statistically significant differences between H-4arc and two Trilogy plans (p>0.05). H-4arc plans increased the skin doses (V_{30}, V_{40}, V_{45}, V_{50}, and D_{mean}) compared to two Trilogy plans.

T-4arc plans showed the largest number of MUs compared to T-8arc and H-4arc plans, and no statistically significant difference was found between the latter two plans. The average delivery time of T-4arc, T-8arc,

and H-4arc were 6.05 ±0.57, 6.04 ±0.89, and 2.18 ±0.15 minutes, respectively. H-4arc plans showed the shortest delivery time and was statistically different from the two Trilogy plans. Table 3 shows the results.

Table 3 Dosimetric parameters of OARs and delivery efficiency for whole and partial arc plans on Trilogy and Halcyon

	T-4arc	T-8arc	H-4arc	H-8arc	p<0.05
heart					
V_5（%）	20.36±6.15	13.70±4.88	30.46±6.16	49.16±4.50	a,b,c,d
V_{10}（%）	8.53±3.33	7.98±3.66	10.15±2.90	15.01±6.36	-
V_{20}（%）	3.43±1.47	4.04±2.44	2.69±1.33	5.79±3.96	b
V_{30}（%）	1.11±0.56	1.84±1.69	0.75±0.47	2.67±2.76	b,c
V_{40}（%）	0.19±0.19	0.62±0.90	0.08±0.12	1.10±1.76	b,c
D_{mean} (Gy）	4.94±0.62	3.93±1.05	5.64±0.57	7.06±1.61	a,b,c,d
LV					
V_5（%）	34.19±10.26	23.90±7.57	35.74±9.32	48.98±14.84	a,c
V_{10}（%）	17.53±6.61	15.54±6.57	16.14±5.93	22.88±9.80	-
V_{20}（%）	7.59±3.02	9.11±5.24	5.80±2.74	11.98±7.67	b
V_{30}（%）	2.68±1.32	4.65±3.98	1.86±1.00	6.50±6.20	b,c
V_{40}（%）	0.50±0.53	1.64±2.02	0.21±0.10	2.92±4.13	a,b,c
D_{mean} (Gy）	6.92±1.33	6.02±2.01	6.77±1.12	9.16±2.97	b
LAD					
V_5（%）	85.66±14.54	75.99±11.42	84.61±13.44	89.27±8.74	-
V_{10}（%）	61.56±16.52	63.63±16.88	63.24±17.20	67.47±16.55	-
V_{20}（%）	43.26±17.70	47.53±21.76	43.11±19.10	52.92±21.70	-
V_{30}（%）	24.22±15.50	25.72±20.54	14.27±10.90	31.15±18.19	b
V_{40}（%）	1.14±1.51	6.51±15.43	0.14±0.32	9.77±15.91	b
D_{max} (Gy）	40.44±4.23	41.93±4.17	38.85±3.06	42.52±4.35	b
D_{mean} (Gy）	18.13±4.68	18.96±6.30	17.19±4.03	21.34±5.82	b
lungs					
V_5（%）	45.12±3.12	30.42±3.52	43.7±4.06	49.07±4.72	a,b,c
V_{10}（%）	23.85±2.62	19.37±2.60	22.91±2.58	25.47±2.92	a,c

V_{20} (%)	13.38±2.21	12.35±2.56	13.18±2.54	15.77±3.02	-
V_{30} (%)	7.92±1.75	8.54±2.25	8.01±2.11	10.56±2.98	-
V_{40} (%)	3.15±1.11	5.03±1.87	3.54±1.38	6.04±2.53	a,b
D_{mean} (Gy)	9.12±0.73	7.51±0.95	9.08±0.84	9.15±2.97	a,c
skin					
V_{30} (%)	67.29±8.73	68.91±8.23	74.15±7.63	75.20±6.93	c,d
V_{40} (%)	31.26±7.87	32.37±8.53	40.42±8.81	41.46±7.34	c,d
V_{45} (%)	7.93±3.72	9.28±3.68	16.83±4.25	17.45±3.33	c,d
V_{50} (%)	0.03±0.05	0.01±0.03	0.27±0.23	0.49±0.45	c,d
D_{mean} (Gy)	33.88±1.97	34.32±1.92	35.97±1.89	36.27±1.61	c,d
liver					
D_{mean} (Gy)	5.67±1.48	3.58±1.10	6.02±1.10	6.66±1.50	a,c
MU	1170.8±97.3	1051.5±70.1	1036.1±103.8	831.6±45.2	a,b,d
delivery time (min)	6.05±0.57	6.04±0.89	2.18±0.15	2.16±0.37	c,d

V_X, volume receiving at least x Gy; LV, left ventricle; LAD, left anterior descending artery; MU, monitor unit; T-4arc, whole-arc plans on Trilogy; T-8arc, partial-arc plans on Trilogy; H-4arc, whole-arc plans on Halcyon; H-8arc, partial-arc plans on Halcyon; a: T-4arc vs T-8arc, b: H-4arc vs H-8arc, c: T-8arc vs H-4arc, d: T-4arc vs. H-4arc

Discussion

The design of treatment plan for synchronous bilateral breast cancer radiotherapy is difficult because of the large target range and the requirement of reducing the cardiopulmonary dose as much as possible. Compared to conventional LINACs, Halcyon has shown comparable dosimetric distribution and excellent delivery efficiency in radiotherapy for tumors in multiple body parts. To the best of our knowledge, this is the first report on the dosimetry of Halcyon for bilateral breast cancer.

Image guided must be took before each patient is treated on Halcyon. Four different setup fields delivered different MUs can be selected. In this study, the dosimetric differences of four setup-field plans were firstly compared. Our study showed that CBCT-H plans, which delivered 10 MUs in each treatment fraction, increased V_5 and D_{mean} of heart, LV, and lungs and V_5 of LAD and B-P. No statistically significant differences were observed in dosimetry among CBCT-L, MV-H and MV-L plans. In cases of delivering more MUs in each treatment fraction, the low-dose MV CBCT plans did not increase the doses to OARs

compared to MV-L and MV-H plans. Therefore, we inferred that low-dose MV CBCT was the optimal setup-field mode. Flores-Martinez et al. [6] compared four different setup-field plans for unilateral breast cancer, in their opinion low-dose MV CBCT was the most suitable technique for patients treated on Halcyon. The result was the same as ours. Our and Flores-Martinez's study were all based on Halcyon 1.0. In Halcyon 2.0, KV CBCT was introduced, which displayed the lower dose and faster acquisition.

Second, the differences between whole and partial arc plans in the same LINAC were compared. The results showed that partial-arc plans on Trilogy showed more dosimetric advantage, especially in low-dose volumes of the heart, left ventricle, and lungs and the mean doses of the heart, lungs, and liver. This is because during designing a partial-arc plan, it is possible to artificially choose the arc degree that irradiates less volume of OARs. Rotating the collimator angle and fixing the jaw can further reduce the influence of the leakage between the MLC on the dose of the OARs, which can minimize the dose of the OARs. Boman et al. [11] compared the dosimetric differences between the whole and partial arc VMAT plans of unilateral breast cancer including regional lymph node irradiation, and the results showed that partial-arc plans significantly reduced the dose of the ipsilateral lung and the V_5 of the heart, but increased the V_5 of contralateral breast. The result is similar to ours, but the cases of our study are bilateral breast cancer which does not involve the dose of the contralateral breast. Comparing the two plans of the Halcyon, the results were contrary to the Trilogy's, and the whole-arc plans showed better dosimetry. For PTV, in addition to the mean dose, the whole-arc plan was better than partial-arc plan in terms of the maximum dose, minimum dose, conformity and uniformity. For OARs, the partial-arc plan increased the dose to the heart, left ventricle, LAD, and lungs. The results showed that partial-arc plans have no advantage for Halcyon, which may be related to the jawless setting on Halcyon. According to the results above, when designing the treatment plan for bilateral breast cancer, we can choose a more suitable arc setting according to the corresponding LINAC.

Based on the results above, we mainly compared the dosimetric differences between Halcyon's whole-arc plan and Trilogy's two plans. All plans meet clinical requirements. For PTV, apart from the mean dose, there were no statistical differences in other dosimetric parameters between the two partial-arc plans on Halcyon and Trilogy. Compared with the T-8arc plan, H-4arc showed worse D_{mean}, D_2 and V_{107}, and better D_{98} and CI of PTV. In short, the plans of the two machines are comparable in terms of target dose.

Darby et al. [15] found a linear relationship between the mean dose of the heart and the incidence of ischemic heart disease, and the incidence increased by 7.4% for 1Gy increase in the mean dose. Therefore, the mean dose of the heart is often used as a reference for cardiac toxicity. However, the dose of cardiac substructure also needs to be considered in radiotherapy. Some studies believe that LAD and LV are important parts of the heart related to radiation-induced heart disease [16,17]. In this study, for low-dose irradiated volumes of the heart and LV, partial-arc plans on the Trilogy showed the lowest values, while for high-dose irradiated volumes, the whole-ac plans on the Halcyon showed the lowest values. For the mean dose of the heart, the partial-arc plans on the Trilogy showed the lowest value, and the whole-arc plans on the Halcyon showed the highest value. This may be related to the additional radiation dose

to the heart from each MV CBCT scan. For all dosimetrc parameters of LAD, there is no statistical difference between whole-arc plans on Halcyon and the two plans on Trilogy.

For lungs, the partial-arc plans on the Trilogy reduced the low-dose irradiated volume (V_5, V_{10}) and the mean dose, but increased the high-dose irradiated volume (V_{40}). There was no statistical difference in the comparison of V_{20} and V_{30} in lungs between all plans of the two LINACs. For all dosimetric parameters of lungs, there was no statistical difference between the two whole-arc plans on the two LINACs. Fiorentino et al. [18] retrospectively analyzed the VMAT plans of 16 patients with bilateral breast cancer. For lungs, the average values of D_{mean}, V_5 and V_{20} were 11.8 ± 2.3 Gy, 78.9 ± 15.3% and 15.7 ± 5%, respectively. No acute and late complication above grade 2 were observed during the 24 months follow-up. In our study, the mean dose, V_5 and V_{20} of lungs in all plans are lower than their study.

The plans on Halcyon increased the skin's dose compared to the two plans on Trilogy. O'Grady et al. [19] found 6X FFF fields on Halcyon increased superficial dose compared to FF fields for breast cancer radiotherapy, and in vivo measurements, phantom measurements, and planning comparison all demonstrated this. The results were the same as ours. Because the rays are softened after flattening filter is removed, the 6MV X-rays in FFF mode are equivalent to lower-energy rays, resulting in a shallower depth of the dose built-up area, thereby increasing the superficial dose. Studies about Monte Carlo (MC) have shown that the influence of contamination electrons in the FFF mode is greater, which further leads to an increase in surface dose [20,21]. Barsky et al. [5] retrospectively analyzed 34 breast cancer cases treated on the Halcyon, and the results showed that breast cancer cases were well tolerated on Halcyon, and the acute toxicity was comparable to the published reports of conventional LINACs. No grade 3 or higher acute toxicities occurred, and grade 2 dermatitis occurred in only 6 patients. For the liver, studies have shown that when the mean dose of the whole liver is <30-32 Gy, the incidence rate of radiation liver injury is <5% [22]. In this study, the mean dose of liver was less than 7Gy in all plans. We believed that all plans are safe in terms of liver protection.

Previous studies have demonstrated that Halcyon could reduce the treatment time significantly compared to conventional LINACs [3-7]. Our study proved the same results in radiotherapy for bilateral breast cancer. This may be related to the Halcyon's faster gantry and MLC speed and higher dose rate. The shortening of treatment time can reduce intra-fraction movement, improve patient comfort, and increase machine throughput.

In summary, our study could provide a reference for radiotherapy of bilateral breast cancer on Halcyon. VMAT plans on Halcyon can meet clinical requirements in radiotherapy for bilateral breast cancer. The low-dose MV CBCT could be selected as an optimal setup mode. For Halcyon, the whole-arc plans are more excellent than partial-arc plans. Although Halcyon increase the mean dose of the heart and the dose of the skin compared to the conventional LINAC, it is comparable to the Trilogy in dose of the cardiac substructure and other OARs, and significantly reduces the delivery time.

Abbreviations

LINAC: linear accelerator; FFF: flattening-filter-free; MLC: multi-leaf collimator; IGRT: image guided radiotherapy; VMAT: volumetric modulated arc therapy; MV CBCT: megavoltage cone beam computed tomography; MUs: monitor units; CTV: clinical target volume; PTV: planning target volume; OARs: organs at risk; LV: left ventricle; LAD: left anterior descending artery; B-P: body minus the PTV; DMI: digital megavoltage imaging; AAA: analytic anisotropic algorithm; CI: conformity index; HI: homogeneity index; ANOVA:one-way analysis of variance; CBCT-H: plan with high-quality MV CBCT; CBCT-L: plan with low-dose MV CBCT; MV-H: plan with high-quality MV pair; MV-L: plan with low-dose MV pair; T-4arc: whole-arc plans on Trilogy; T-8arc: partial-arc plans on Trilogy; H-4arc: whole-arc plans on Halcyon; H-8arc: partial-arc plans on Halcyon; Monte Carlo (MC)

Declarations

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Availability of data and materials

The data are available upon request.

Ethics approval and consent to participate

This study was approved by the Research Ethics Board of the Shandong Cancer Hospital.

Written informed consent was waived by the Institutional Review Board.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TS and YY designed the study. GZ collected the CT data. XL and TS designed the treatment plans. QQ and CL analyzed the data. TS and XL wrote the paper. All authors read and approved the final

manuscript.

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Figures

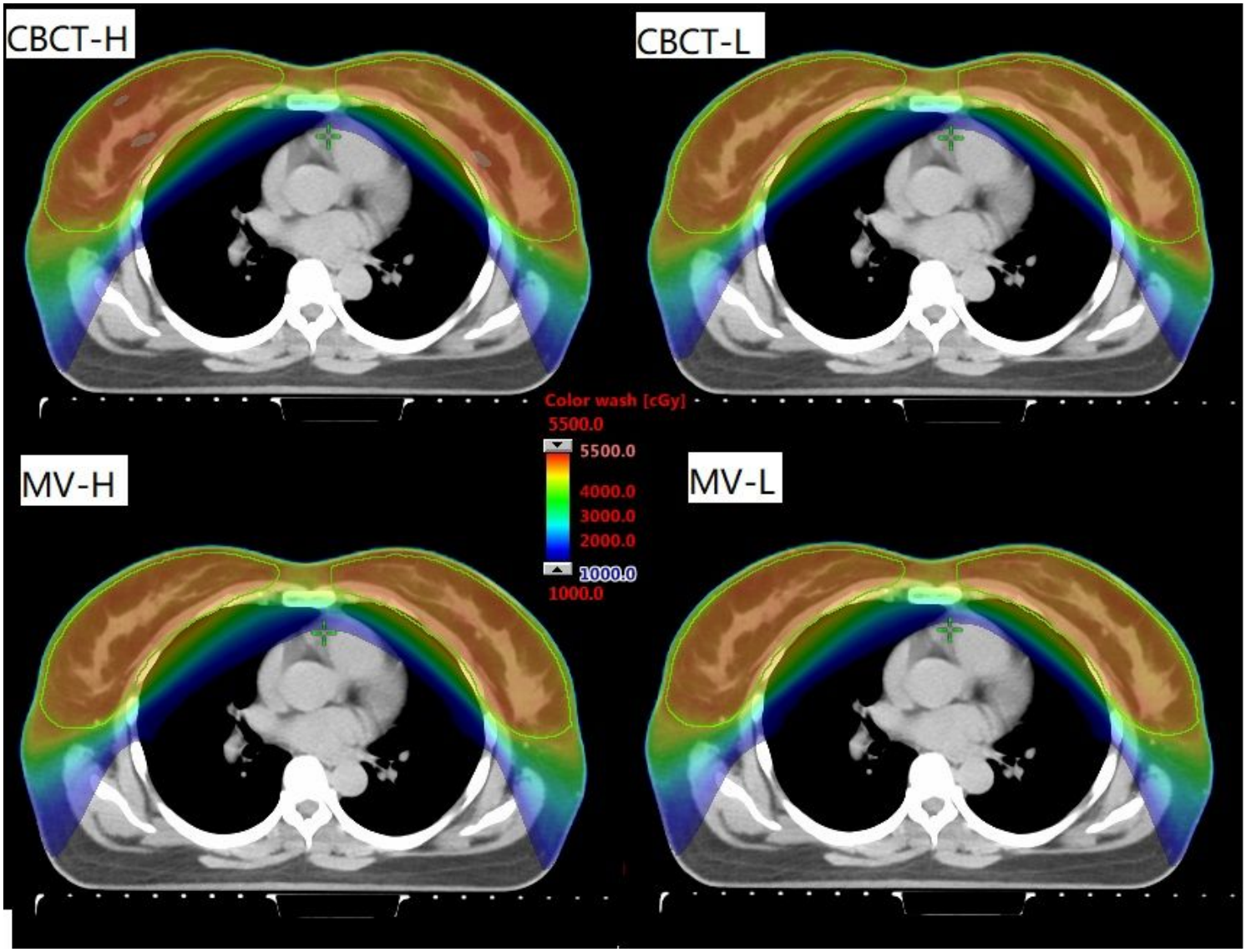

Figure 1

Dose distributions of the four different setup-field plans on Halcyon. CBCT-H, plan with high-quality MV CBCT; CBCT-L, plan with low-dose MV CBCT; MV-H, plan with high-quality MV pair; MV-L, plan with low-dose MV pair

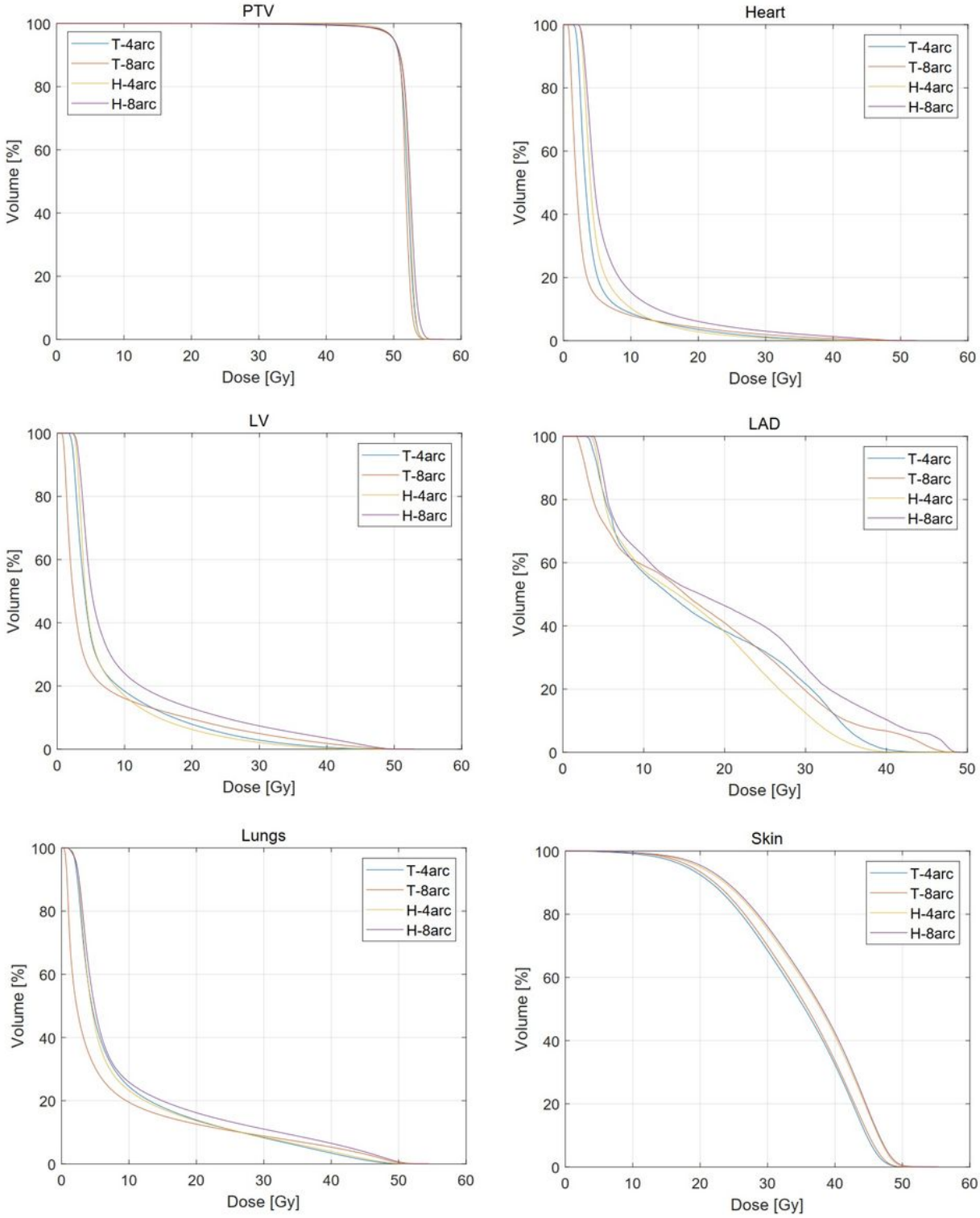

Figure 2

The mean dose-volume histograms for the four plans. PTV, planning target volume; LV, left ventricle; LAD, left anterior descending artery; T-4arc, whole-arc plans on Trilogy; T-8arc, partial-arc plans on Trilogy; H-4arc, whole-arc plans on Halcyon; H-8arc, partial-arc plans on Halcyon;