A comparative dosemetric study of bilateral breast cancer after modified radical mastectomy with HT and VMAT

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Research

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Abstract

Background: The purpose of this study was to compare the dosimetric differences in helical tomotherapy (HT) and volumetric modulated arc therapy (VMAT) plans of bilateral breast cancer after modified radical mastectomy.

Methods: Ten patients with synchronous bilateral breast cancer (SBBC) who received modified radical mastectomy were selected for study. Two radiotherapy treatment plans, including HT and VMAT, were created for each patient. The prescribed doses of bilateral breast cancer and dual target volumes were given 25 times at 50Gy. The dosemetric parameters of planning target volume (PTV) and organs at risk (OARs) between HT and VMAT plans were compared and evaluated.

Results: For PTV, HT had a higher V95 than that of VMAT plans (99.23 ± 0.61 % vs 98.17± 1.08 %, p=0.024). The conformity index (CI) between two techniques was statistically equivalent (0.812 ± 0.03 vs 0.793 ± 0.04, p=0.322) and the homogeneity index (HI) was reduced from 0.127 to 0.105 (p=0.007) when compared with that of VMAT. For OARs, HT had significantly lower D_{max} for spinal cord and V5 for heart when compared with those of VMAT plans (16.68 Gy and 20.93% vs 38.82 Gy and 30.26%, respectively) (p<0.001). HT plans showed significantly lower V5, V10 and V20, that resulted in lower D_{mean} for the lungs (13.38 Gy vs 14.28Gy, p=0.013). However, VMAT showed specific advantages on V10, V20 and V30 for the heart and V5 and V10 for the liver when compared with those of HT plans (p<0.01). The D_{mean} for the heart and liver between the two techniques was not significantly different (p>0.05). HT plans also showed greater monitor units (MUs) and beam on time.

Conclusion: HT had better PTV coverage and HI and showed better protections for the spinal cord and lungs compared with those of VMAT plans. HT plans effectively reduced the low-dose volume (V5) of the heart, while VMAT plans reduced V10, V20 and V30 for the heart. Both HT and VMAT plans exhibited similar D_{mean} for the heart and liver. The treatment efficiency of VMAT is higher than that of HT plans, and therefore, physicians need to choose a reasonable radiotherapy plan according to patient's conditions.

Background

Breast cancer is the most common malignancy among women worldwide. Treatment with adjuvant radiotherapy reduces the risk of local recurrence by half, and mortality by one-sixth [1]. Treatment combination of surgical removal of the tumor or total mastectomy with postoperative chemotherapy and breast or chest wall radiotherapy, is the standard treatment mode for advanced breast cancer [2, 3]. Several clinical studies have shown that the use of traditional three-dimensional conformal radiotherapy (3DCRT) following modified radical mastectomy, is rather difficult when also attempting to protect organs at risk (OARs) [4]. The use of reverse intensity modulation radiation therapy (IMRT) can obtain better planning target volume (PTV) coverage and reduce radiation damage to OARs such as heart, and the lungs [5, 6]. Synchronous bilateral breast cancer (SBBC) is a relatively rare disease that has an incidence

rate of < 5% compared with all other breast cancers [7]. Although the incidence of SBBC is lower compared with unilateral breast cancer, its overall survival is significantly worse [8, 9].

We defined SBBC as a cancer that is simultaneously diagnosed in both breasts, or within a period of 6 months from the diagnosis date of the first tumor. After modified radical mastectomy, SBBC radiotherapy requires a wider distribution of target volume, that is considerably closer to both heart and the lungs. Moreover, target volume is also closer to the skin when compared with other treatment sites. For multiple target volumes, the overlapping doses of the radiation field cause uneven dose distribution in the target volume that is prone to cold and hot spots, making the planning and design difficult. Meanwhile, the prescribed doses of the bilateral target volume are required to be simultaneously met, which decreases target coverage and increases the irradiated volume of the OARs, leading to increased side effects of the radiotherapy.

To decrease the dose of OARs and achieve a more homogeneous dose distribution, breast irradiation techniques that incorporate new technologies, such as HT and VMAT with image-guided radiotherapy (IGRT), are clinically used. Different dosimetric studies have shown that HT and VMAT techniques improve PTV coverages, thus allowing better dose homogeneity compared to traditional techniques such as 3DCRT and tangential half-field technique in the treatment of SBBC[10, 11, 12]. For complex treatment volumes such as SBBC, VMAT and HT techniques show better dosimetric advantages compared to IMRT technique [13, 14, 15]. In our study, aiming at dual-target characteristics of bilateral breast cancer, HT and VMAT techniques are used to design two radiotherapy plans. PTV coverage, conformal index (CI) and homogeneity index (HI) are compared between two techniques. Irradiated dose and volume of OARs and monitor units(MUs)and beam on time are also compared. The purpose of this study is to compare dosimetric differences and treatment efficiency between HT and VMAT plans to provide a reference for clinical applications.

Methods

Patients

The study included ten patients who were diagnosed with SBBC and received bilateral radiotherapy after breast modified radical mastectomy at the Third Affiliated Hospital of Kunming Medical University from January 2017 to March 2021. All patients had invasive ductal carcinomas without breast reconstruction or contraindication of radiotherapy. The mean age of patients was 48 years (range from 35 to 69 years) and the study group included any of the following conditions: tumor diameter > 5cm, axillary lymph node metastasis ≥ 4, axillary lymph node metastasis 1–3, and positive cutting edge. The radiotherapy was usually carried out after 4 to 6 weeks chemotherapy. The study was approved by the Research Ethics Committee of the Third Affiliated Hospital of Kunming Medical University.

Position fixation and CT simulation positioning

The patients were immobilized in a supine position with both arms raised on a carbon fiber breast board, and planning CT (sensation open, SIEMENS) was conducted. A metal marking point was placed at the intersection of the positioning laser to mark a line for postural repetition during treatment, and for the surgical scar and chest wall area with lead wire. CT acquisition was with 5 mm slice thickness extending from the cricothyroid membrane to the lower edge of the liver.

Target and normal tissue delineation

The scanned images were imported into Philips Pinnacle 3 doctor workstation. The breast clinical target volume (CTV) includes bilateral chest wall, and upper and lower clavicle lymphatic drainage areas. The following were considered bilateral chest wall range: upper boundary to bilateral sternoclavicular joints, lower boundary to 2cm below the submammary skin fold, inner boundary to sternocostal joint, outer boundary to anterior edge of latissimus dorsi, anterior boundary to skin, and posterior boundary to anterior costal edge. The following were considered the range for bilateral upper and lower clavicle drainage areas: upper boundary to the cricothyroid notch, lower boundary to the level of the first intercostal space, the inner boundary to the side of the trachea, and the outside to the medial edge of the humeral head. PTV (PTV_L on the left and PTV_R on the right) was obtained by 0.5cm expansion in all directions from the CTV that were also restricted to extend to the skin and lungs. OARs included spinal cord, heart, lung tissues, and liver, and 0.5cm a thick compensation membrane was placed on the bilateral chest wall area. The same doctor outlined the target volume and OARs for the ten patients and that were reviewed by the same chief physician to ensure the consistency of the outline structure.

Planning procedure

HT and VMAT plans were designed in the Tomotherapy version 5.0.5.18 treatment planning system (Accuray Planning Station, Madison, WI, USA) and the Monaco version 5.1 treatment planning system (Elekta AB, Stockholm, Sweden), respectively. Six MV photon beams were used for the two plans and all plans were designed by the same physicist and approved by the same associate senior physicist.

HT plans were calculated by applying the beam data from an Accuray TOMO HD with strong modulated beam. A 2.512cm field width (FW) and a 0.287 pitch were used in the plan. The modulation factor (MF) was initially set to 3 and was adjusted throughout the optimization. The advantage of the HT technology is its capacity to simultaneously treat multiple target volumes and maintain a good dose distribution and uniformity in the target volume near normal tissues when they need to be avoided.

VMAT plans were calculated by applying the beam data from an Elekta Versa HD linear accelerator, including multi leaf collimator (MLC) (80 leaf pairs with a 0.5cm leaf width, maximum leaf speed of 6.5cm/s, variable dose rate up to 600MU/min). The bilateral target volumes were designed with a single field isocenter. Geometric centers of the bilateral target areas (PTV_L and PTV_R) were respectively moved to the junction of the dual target area and the lung tissue to form two isocenters (ISO_L and ISO_R). A single isocenter (ISO) was constructed by medially and posteriorly moving ISO_L and ISO_R to the same point while keeping the same collimator and gantry angles in each partial arc. The angle between the start and

end positions of the gantry was set at approximatively 230°, according to the position, shape, and contour of the target volumes. A dual arc(1 arc clockwise and 1 arc counterclockwise) was set with a gantry range from 115–245° (Fig. 1). Monte Carlo algorithm was used for all dose calculation with a 0.3cm grid size. The sequencing parameters for the applied optimization were maximum control points/arc of 160 and a min. seg. width of 0.6cm, and a medium fluence smoothing factor was also applied. Both two plans were set at 95% of PTV (including PTV_L and PTV_R) to receive a prescribed dose of 50Gy and OARs that meet clinical requirements as predetermined optimization goals. A step-by-step optimization was used in the optimization process. Prior entering the second step of calculation, the tomographic dose distribution curve and the dose volume histogam (DVH) were repeatedly viewed, and the optimization and adjustment were repeated until the first step optimization could better meet the optimization goal.

The prescribed dose of bilateral breast PTV was given a conventional split pattern of 50 Gy/25 F, 5 times/week, 2 Gy/time, and the plan required 100% of the prescribed dose to cover 95% of the target volume. For the OARs, the planning objectives were $D_{max} \leq 40$ Gy to the spinal cord, $V_5 \leq 80$ % and $V_{20} \leq 30$ % to the lungs, $D_{mean} \leq 5$ Gy to the heart and $D_{mean} < 10$ Gy to the liver.

Dosimetric evaluation parameters

After the plans had been completed, two plans were compared and evaluated based on the dosimetry parameters and DVHs. For PTV, V95 was the coverage of the target volume, and CI was evaluated as proposed by Baltas et al. [16]:

CI = (Vt,ref/Vt)×(Vt,ref/Vref)

In which Vt,ref is the volume which receives at least 95% of the prescribed dose in PTV, Vt is the whole PTV volume, and Vref is the whole volume receiving at least 95% of the prescribed dose. The closer the CI value is to 1, the better conformity is.

HI was calculated according to ICRU 83 [17]:

HI = (D2-D98)/D50

Where the values of D98 and D2 (dose received by the 98 and 2% of the volume) are defined as metrics for minimum and maximum doses, and D50 is the average dose. A smaller HI value represents a better homogeneity.

The relevant parameters of OARs, including D_{max}, D_{mean} and V5, V10, V20 and V30 (percentage of organ receiving at least 5, 10, 20 and 30 Gy, respectively)were evaluated from DVHs.

The Average cumulative DVH for PTV, OARs, and healthy tissue, were built from the individual DVH for the qualitative visualization of the results. These histograms were obtained by averaging the corresponding

volumes over the whole patient's cohort for each dose bin of 0.05Gy. The delivery parameters were recorded in terms of MUs and beam on time.

Statistical analysis

The statistical analyses were performed using the SPSS software version 25 (IBM Corp) and the data are represented by the mean ± standard deviation (SD). The Shapiro-Wilk tests were used to test the data normal distribution within a group due to the small number of patients. A paired test-test was performed to compare the different techniques for normal distributed data. The Wilcoxon signed-rank test was used for non-normality distributed data. The differences were reported to be statistically significant when $p < 0.05$.

Results

Figure 2 shows most of the conceived structures, together with a typical dose distribution for a patient case. In A and B (axial), the blue colored region indicates PTV. HT reduced the region in low-dose (5 GY) for the heart but also that of the region in low-middle-dose (5, 10, and 20 GY) and lungs compared with VMAT plans.

The average DVH for all PTVs, spinal cord, lungs, heart, and liver, are shown in Fig. 3. Tables 1 and 2 summarize numerical findings from DVH, delivery, and pre-treatment dosimetry analyses. Data are presented as averages for the investigated patients and errors indicate inter-patient variability at a 1 standard deviation level.

Table 2
Dosimetric parameters of the OARs with HT vs. VMAT

Structure	parameter	HT		VMAT		p value
		mean	SD	mean	SD	
Spinal cord	D_{max} (Gy)	16.68	0.47	38.82	1.25	0.000
Lung L	V5 (%)	64.09	6.93	76.00	2.48	0.000
	V10 (%)	38.37	2.21	40.40	1.21	0.000
	V20 (%)	23.84	1.32	22.82	1.65	0.017
	V30 (%)	16.39	0.89	14.25	0.52	0.000
	D_{mean} (Gy)	13.83	1.82	13.72	0.83	0.877
Lung R	V5 (%)	55.17	3.60	71.41	2.72	0.000
	V10 (%)	35.00	2.02	42.25	1.78	0.000
	V20 (%)	22.79	1.34	26.44	1.56	0.000
	V30 (%)	15.86	0.97	17.07	0.90	0.009
	D_{mean}(Gy)	13.02	1.85	14.68	1.26	0.014
Lungs	V5 (%)	60.23	4.65	73.57	2.50	0.000
	V10 (%)	36.55	2.47	41.42	1.08	0.000
	V20 (%)	23.37	1.31	24.75	1.57	0.003
	V30 (%)	16.03	0.88	15.80	0.57	0.472
	D_{mean} (Gy)	13.38	1.30	14.26	0.97	0.013
Heart	V5 (%)	20.93	1.16	30.26	1.55	0.000
	V10 (%)	6.81	1.19	2.77	0.19	0.000
	V20 (%)	2..77	0.32	0.48	0.09	0.000
	V30 (%)	1.09	0.03	0.07	0.01	0.005[b]
	D_{mean} (Gy)	4.75	0.61	5.06	0.51	0.066
Liver	V5 (%)	38.81	2.46	25.23	1.04	0.000
	V10 (%)	10.40	1.30	9.47	1.00	0.008

Abbreviations: HT: helical tomotherapy, VMAT: volumetric-modulated arc therapy, SD: standard deviation

Structure	parameter	HT		VMAT		p value
		mean	SD	mean	SD	
	V20 (%)	1.17	0.80	2.75	0.42	0.002
	V30 (%)	0.32	0.05	0.44	0.08	0.008
	D_{mean} (Gy)	4.64	0.83	4.54	0.24	0.677

Abbreviations: HT: helical tomotherapy, VMAT: volumetric-modulated arc therapy, SD: standard deviation

PTV dose evaluation

Table 1 data are reported for PTV. HT had a higher PTV coverage for V95 than that of VMAT plans. HT showed a higher D98 compared to VMAT plans. HT achieved a significantly lower homogeneity index (HI) than that of the VMAT plans. No significant differences were detected between HT and VMAT plans for the D50, D2, D_{mean} and CI of the PTV.

Table 1 Dosimetric parameters of the PTV with HT vs. VMAT

parameter	HT		VMAT		P value
	mean	SD	mean	SD	
V95(%)	99.48	0.61	98.17	1.08	0.024
D98 (Gy)	49.38	0.24	48.13	0.22	0.000
D50(Gy)	52.58	0.41	52.44	0.40	0.446
D2(Gy)	54.90	0.71	54.78	0.55	0.597
D_{mean}(Gy)	52.59	0.54	52.26	0.33	0.160
CI	0.812	0.03	0.793	0.04	0.322
HI	0.105	0.01	0.127	0.02	0.007

Abbreviations: HT: helical tomotherapy, VMAT: volumetric-modulated arc therapy, SD: standard deviation

OARs dose evaluation

Table 2 data are reported for OARs. HT plans showed significantly lower conformity spinal doses (D_{max}), heart doses (V5), lungs doses (V5, V10, V20 and D_{mean}), and liver doses (V20 and V30) compared to VMAT plans. Moreover, VMAT plans had specific advantages for V10, V20, and V30 for the heart and for lower V5 and V10 for the liver when compared with HT plans. HT and VMAT plans showed similar D_{mean}

values for the heart (4.75 ± 0.61 Gy vs 5.06 ± 0.51 Gy, p = 0.066) and similar D_{mean} values for the liver (4.64 ± 0.83 Gy vs 4.54 ± 0.24 Gy, p = 0.677).

Abbreviations

HT: helical tomotherapy; VMAT: volumetric-modulated arc therapy; SBBC: synchronous bilateral breast cancer; PTV: planning target volume; OARs: organs at risk; VX: body volume receiving a dose of X Gy; DX:: dose received by X% of the volume; HI: homogeneity index; CI: conformity index; D_{max}: maximum dose; D_{mean}: mean dose;3DCRT: three-dimensional conformal; MUs: monitor units; IMRT: intensity-modulated radiation therapy; IGRT: image-guided radiotherapy; CTV: clinical target volume;TPS: treatment planning system; FW: field width; MF: modulation factor; MLC: multi leaf collimator; DVH: dose volume histogam.

Declarations

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Availability of data and materials

The data and materials related to patients' personal information are not readily available; readers who require access to data can contact the authors.

Authors' contributions

Study concepts: XH Liu, X Chenl. Study design: XH Liu, YX Xia, X Chen. Radiotherapy planning: XH Liu, YX Xia. Data acquisition: X Chen. Data analysis and interpretation: XH Liu, L Chang. Manuscript preparation, editing and review: XH Liu,X Chen, YX Xia. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the local ethics committee of the Third Affiliated Hospital of Kunming Medical University review board as KYLX202119.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

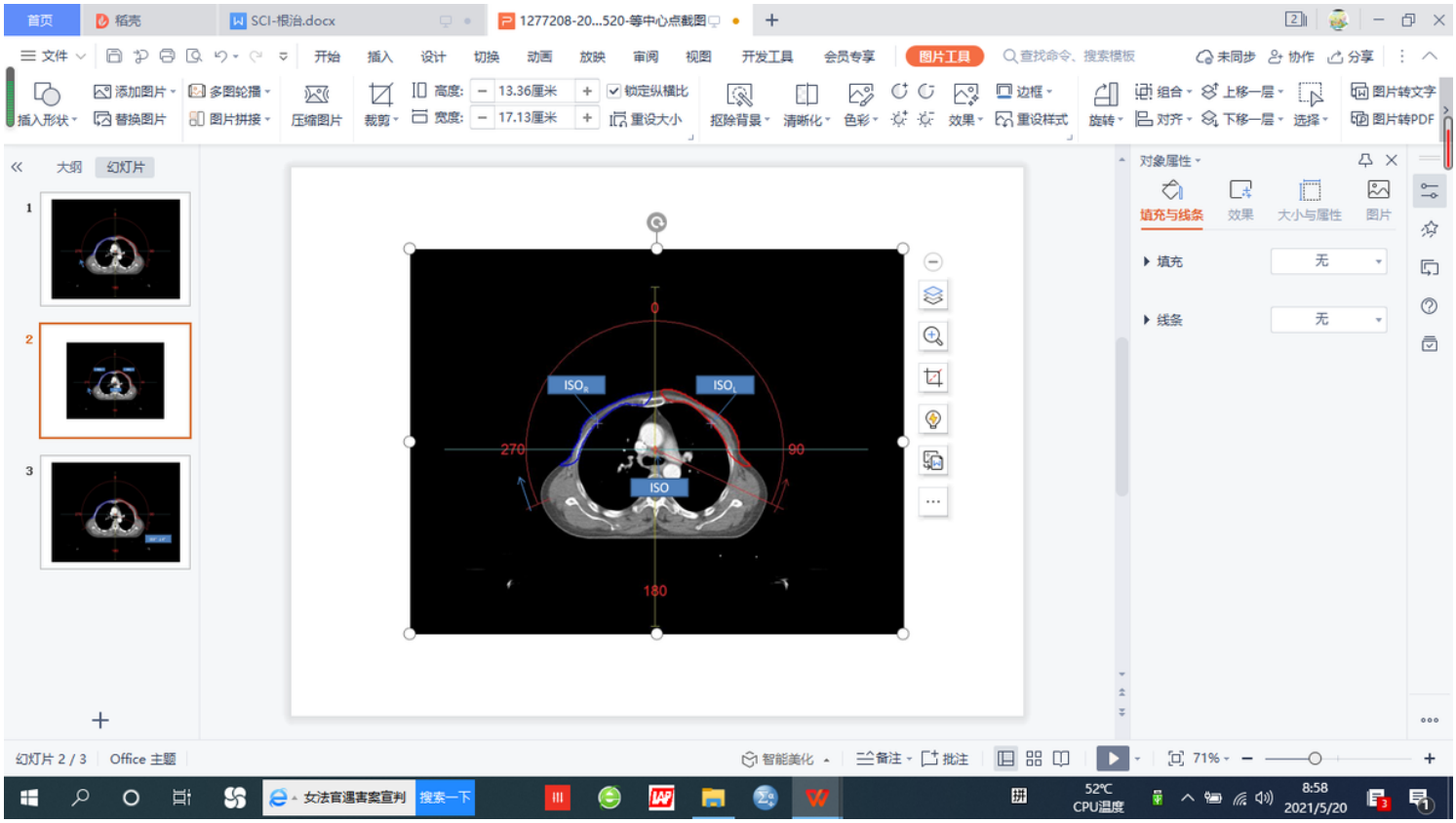

Figure 1

One arc clockwise, one arc counterclockwise (115-245°) and ISO for VMAT plan

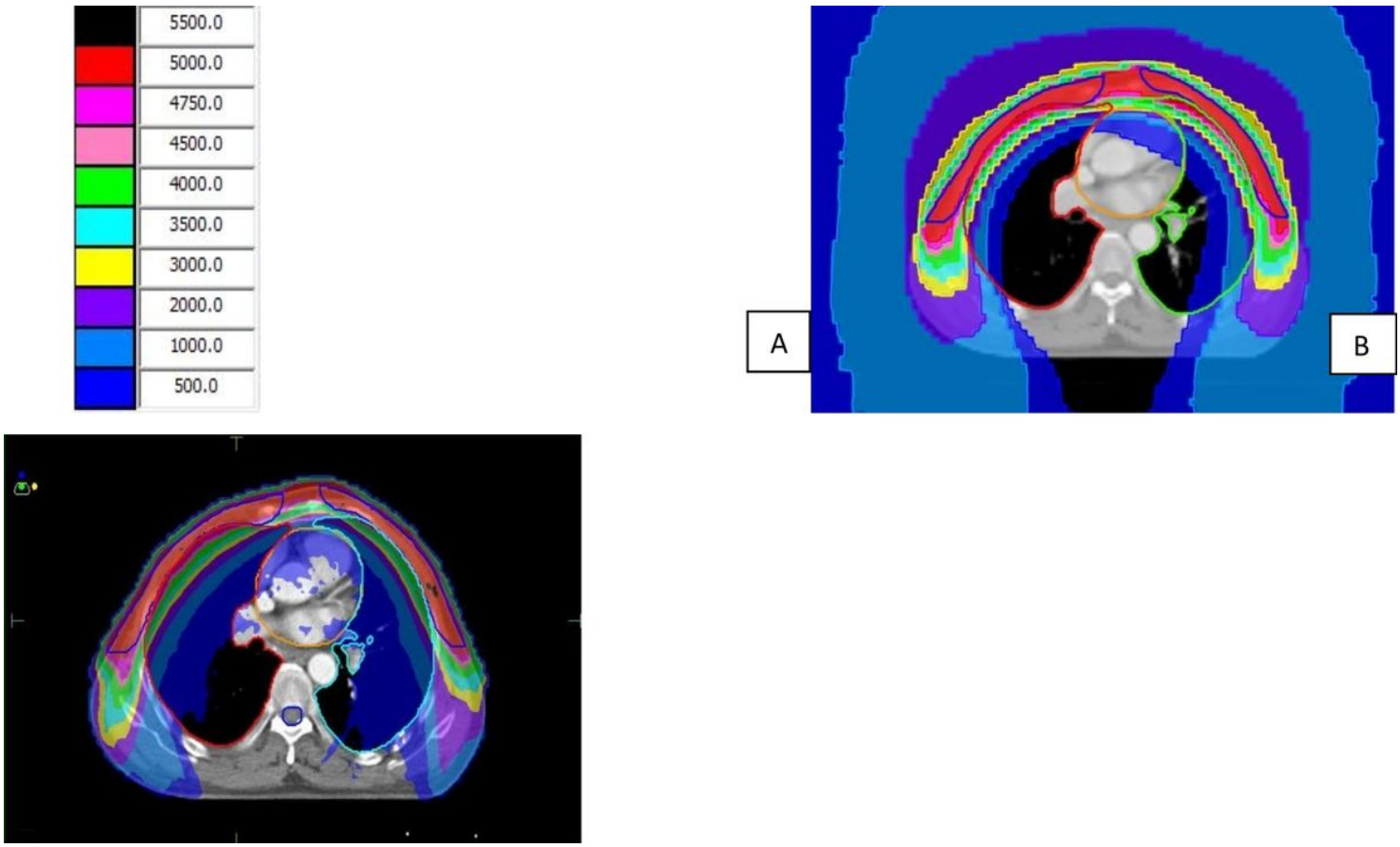

Figure 2

An example of dose distributions on axial views for one case with the blue colored region indicating PTV. A. HT plan. B. VMAT plan.

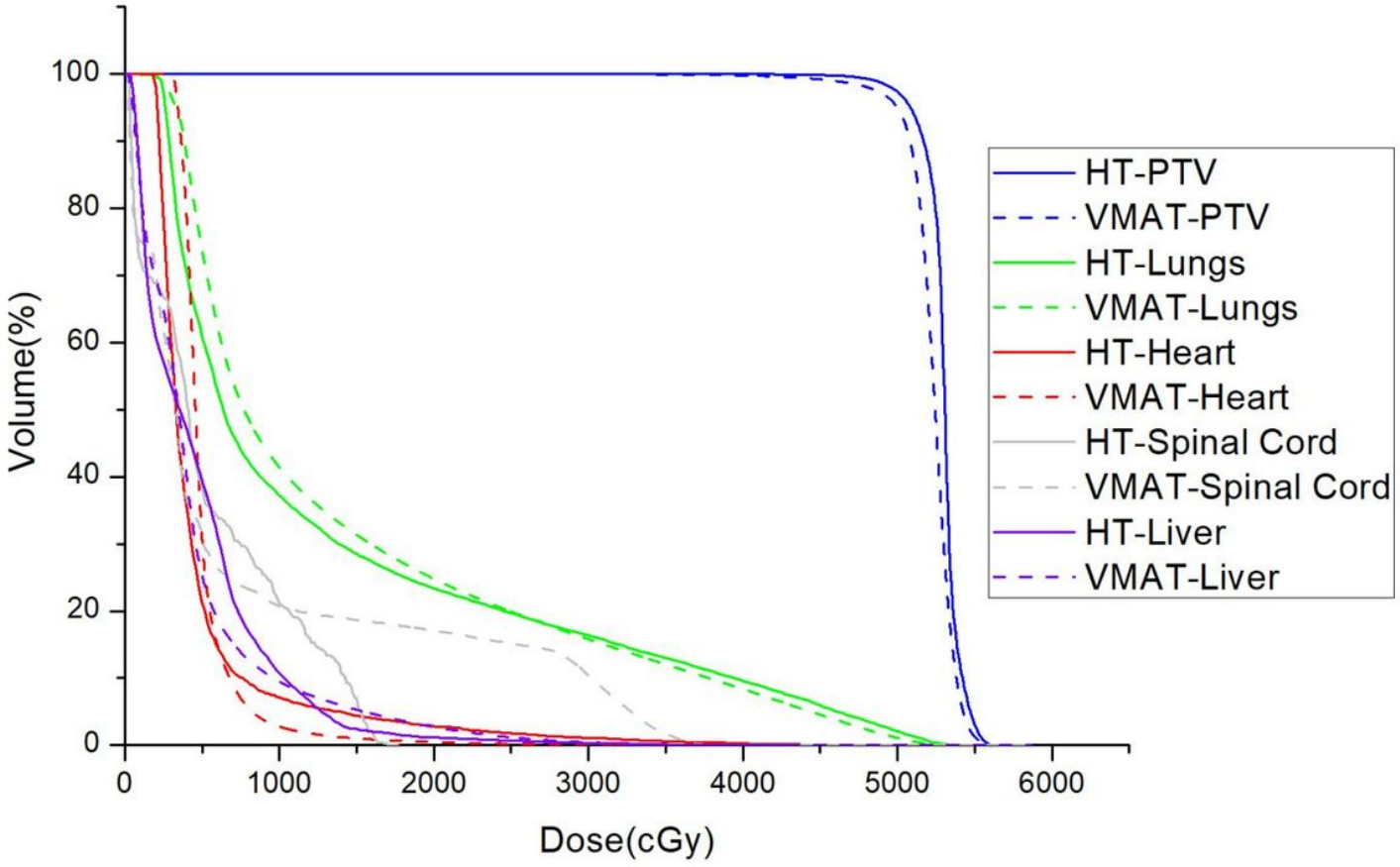

Figure 3

Mean DVHs of PTV and OAR for two radiotherapy plans.