An Innovative VMAT Technique for Left-sided Breast Cancer Patients With Postmastectomy Radiotherapy (PMRT) Evaluated by Ratio of Heart Volume in Tangent Line (RHVTL)

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Research

Keywords: VMAT, PMRT, left-sided breast cancer, dosimetry, RHVTL

Posted Date: July 7th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-578136/v1

Abstract

For patients with left-sided breast cancer (LBC), postmastectomy radiotherapy (PMRT) has been shown to improve the overall survival and many advanced planning techniques was adopted in PMRT. We aim to use an innovative VMAT technique to enhance the conformity of PTV and reduce the scattering dose of surrounding OARs, thereby reducing the long-term toxicity of the heart as well as ipsilateral lung (IL). The study further analyzes the more appropriate treatment planning techniques for personalized LBC patients with PMRT. 35 LBC patients were retrospectively selected undergoing PMRT. The PTV included lymph nodes, chest walls, excluding internal mammary nodes, where 95% of PTV receiving the prescription dose of 50Gy (2Gy/fraction) with three different techniques, VMAT, IMRT, Hybrid VMAT. Furthermore, the ratio of Heart Volume in Tangent line and heart volume (RHVTL) was proposed to evaluate the relative antonymy position between patient's heart and PTV, which hypothetically represents the complexity of treatment planning. The data from this study showed that for LBC patients undergoing PMRT, the CI from VMAT was 0.85 (IMRT and H-VMAT were 0.77 and 0.83), the heart D mean was 502.9cGy (IMRT and H-VMAT were 675.6cGy and 687cGy) and the V20 of IL was 21.3 as the lowest of the three techniques, but the dose of the contralateral breast (CB) and contralateral lung increased noticeably. In H-VMAT and IMRT, the mean heart dose was significantly related to RHVTL, with R-values of 0.911 and 0.892 respectively, while the values in VMAT was 0.613, thus the VMAT technique was relatively unaffected by the difficulty of treatment plan. For RHVTL values exceed than 0.06, the mean heart dose under VMAT technique raised by 98.7cGy compared to the RHVTL value of less than 0.06, but H-VMAT and IMRT increased by 233cGy and 261.58cGy individually. This study illustrates that separated fields and adjacent fields in VMAT technique obtained the optimal conformality and lowest doses of heart in three techniques for LBC with PMRT. Thus, based on the results of our preliminary study, the VMAT technique is highly recommended when RHVTL is exceeded 0.06.

Introduction

In the comprehensive treatment of breast cancer, Postmastectomy Radiotherapy (PMRT) can significantly improve the total survival rate and local control rate of patients and reduce the risk of local recurrence [1–5]. For treatment planning, PMRT for left-sided breast cancer shows more challenges mainly because planning target volume (PTV) includes regional nodes and supraclavicular lymph nodes. To achieve individualized radiotherapy, treatment planning and long-term toxicity reaction in each patient should also be taken seriously [6–13]. Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) have been increasingly used to improve plan quality for PMRT and shown to achieve better conformity and homogeneity of PTV, but more scattering doses are obtained in critical organs especially for ipsilateral lung and heart [14–18]. While many studies have discussed the benefit of IMRT and VMAT for PMRT, the efficiency of IMRT has been reported to show more monitor units (MUs) and longer delivery time [19, 20]. In this study, we have developed unique VMAT and Hybrid VMAT (H-VMAT) techniques that produce more conformal target volume coverage, excellent homogeneity in the planning target volume, and the acceptable dose of organs at risk for the PMRT patients. Adjusting jaw in this

VMAT technique also has been developed leading to a significant reduction of scattering dose in the critical organs. The advantages of three techniques have been described, dosimetry parameters and treatment efficiency of these plans have been evaluated. This study hypothetically further analyzes the complexity of planning techniques for LBC patients undergoing PMRT. The choice of different techniques could be evaluated by the ratio of heart volume in tangent line and heart volume (RHVTL) illustrated the patient's anatomical structures on computed tomography images. The purpose of this study is to find the more appropriate treatment techniques to achieve personalized radiotherapy in terms of the different sections of RHVTL.

Method And Materials

Patient characteristics

This study retrospectively enrolled thirty-five left-sided breast cancer patients with median age of 53 (range 28–69 years) undergoing PMRT. All patients are selected from April 2020 to March 2021 at a single institution. The patients are received the treatment 50Gy(2Gy/25fractions) using various planning techniques (mostly VMAT technique). The RT images and structures of patients are used for dosimetry evaluation. The patients underwent a planning computed tomography (Siemens Definition AS Open, Germany) in free-breathing with 0.3cm slice thickness and were positioned supine with their arms over the head using a customized vacuum bag. All plans are generated on Eclipse 15.5 (Varian Medical Systems, USA).

Contours

The RT structures are strictly based on consensus definitions from RTOG breast cancer Atlas contoured by the same radiation oncologist with 12 years of experience at our institution, included chest wall and comprehensive nodal (supraclavicular, infraclavicular, axillary lymph node). Organs at risk (OARs) contoured by the RT_Mind (MedMind Technology Co., Ltd, China) generated by AI algorithm for all patients. The tangent line has been contoured as two boundary sides of PTV, and the heart volume in tangent line have been measured for plan evaluation and correlation study as the Fig. 1. Shown below.

Treatment Planning

The patients were treated on Varian Trilogy linear accelerators (Varian Medical Systems, USA) using 6MV photons. A 5mm bolus was placed to cover the chest wall region to meet the 95% target coverage especially near the skin surface in 15 factions. Other 10 factions have not placed the bolus to decrease the side effects of skin caused by high doses of radiation. However, in this study, the virtual 5mm bolus was placed for 25 factions to conveniently compare dosimetric parameters in treatment planning. We conducted three treatment plans:

The VMAT plans were designed as four partial arcs which include two separated fields and two adjacent fields. Arc 1 and Arc 2 were commonly set from 295° to 20° and reversed, Arc 3 and Arc 4 were set from 40° to 150° and reversed. The beam eye view and collimator angles are set as Fig. 2.

The IMRT plan content ten fields which are 3 covering lymph nodes (20°,40° and 160°), 6 covering chest walls PTV(290°,315°,340° and 90°,120°,150°)and 1 bridging (150°). Collimators are fitted on specific PTV at different angles. To effectively protect OARs, all the fields are used the Fixed Jaw technique, and adjusting the jaws could be a valid way of protecting the heart and ipsilateral lung specifically.

Furthermore, hybrid VMAT includes five fields, two tangential fields covering PTV-CW with 70% dose, two separated partial arcs covering around 30% dose of PTV-CW from 295° to 20° and 40° to 150°, one arc from 150° to 295° covering PTV-IMNs. For all three planning techniques, dose of OARs was minimized as low as possible with the same restrictions shown below in Table 1.

Table 1
The dose- volume constraints for planning target volume and organs at risk

PTV/OAR	Dose–volume constraints
PTV	D95%>5000 cGy
	CI > 0.75
Heart	V20 < 15%
	D mean < 800 cGy
Ipsilateral Lung	V5 < 60%
	V20 < 25%
	V30 < 15%
	D mean < 1400 cGy
Contralateral Lung	V5 < 60%
	D mean < 1400 cGy
Contralateral Breast	D0.1cc < 2000 cGy
	D mean < 500 cGy

Plan Evaluation

To illustrate the quality of treatment planning, DVH could be more straightforward method. The plans are all set as 5000cGy cover 95% volume, the conformity index (CI) was calculated as

$$CI = \frac{V\_PTVrefs}{V\_PTV} \times \frac{V\_PTVref}{V\_refs}$$

Where V_PTVref is the volume of reference isodose (100%) inside the PTV; and V_PTV is the volume of PTV and V_ref is the reference isodose (100%). Homogeneity index (HI) was calculated as

$$HI = \frac{D2\% - D98\%}{D50\%}$$

Where D2%, D98% and D50% are the doses received by 2%, 98% and 50% of the PTV, D105% and D1cc have been evaluated in this study.

To compare delivery efficiency, total monitor units (MUs), beam on time and actual delivery time were also analyzed. Actual delivery time has been measured on Varian Trilogy linear accelerators including BOT and operation time (gantry rotation time and collimator rotation time).

Statistical analysis

All data was extracted from TPS and recorded in Excel. Pearson correlation analysis was used to evaluate the effects between the dosimetry parameters and patients' characteristics as the R value. A pair two-tailed t-test was performed to calculate the P-value (SPSS, version 25, Chicago, IL, United States), $P \leq 0.05$ were considered statistically significant.

Results

Table 2. summarizes the dosimetric comparison results for VMAT, H-VMAT, and IMRT treatment techniques. For PMRT patients with left breast cancer using VMAT technique, the CI was 0.85 (IMRT and H-VMAT were 0.77 and 0.83), the heart Dmean was 502.98cGy (IMRT and H-VMAT were 675.6cGy and 687cGy), and the V20 for the ipsilateral lung was the lowest of the three methods (VMAT, IMRT and H-VMAT were 20.9, 28.4 and 27.8 respectively), but the dose of breast and contralateral lung increased significantly. In Table 3, for H-VMAT technique, the heart V20 and the ratio of heart volume in tangent line (RHVTL) and heart volume were significantly related, with an R-value of 0.911, while in VMAT and IMRT, the values were 0.892 and 0.613 individually, the same results shown in heart V30 and Dmean. Hence, the VMAT technique was relatively unaffected when the RHVTL has a larger value. Figure 3 shows the dose distributions of three planning methods of one patient in horizontal planes. The blue wash represents the 10% dose and the red wash is 100% of the prescription dose. It represents that in VMAT technique, heart dose is significantly lower, but the contralateral lung received more dose mostly 10% prescription dose. The PTV using VMAT technique has shown more conformal, and the worst case is using IMRT technique. Figure 4 shows DVH of three techniques and the main OARs and PTV has compared. Furthermore, the significant difference shown in the beam on time and actual delivery time, VMAT has the lowest time on both two times about 108.1s and 159.5s, IMRT and H-VMAT were 255.5s and 368.3s, 110.5s and 181.4s respectively. Figure 5 demonstrated the relationship between RHVTL in six sections. It shows heart Dmean varying significantly following by the increasing RHVTL value. Statistically, while H-VMAT and IMRT technique have the appropriate mean heart dose (584.1cGy and 577.28cGy) in the range of RHVTL 0-0.06, the heart Dmean rapidly increased when RHVTL is larger than 0.06 (817.1cGy and 838.8cGy),

slightly lower than dose limitation of heart and clinically acceptable. For RHVTL values exceed than 0.06, the heart D mean under VMAT technique raised by 98.7cGy compared to the RHVTL value of less than 0.06, but H-VMAT and IMRT increased by 233cGy and 261.58cGy individually. Hence, VMAT technique should be highly recommended when RHVTL is exceeding 0.06.

Table 2
The dosimetric parameters for left-sided breast cancer PMRT using VMAT, H-VMAT, IMRT and the P value for different planning techniques.

	Mean ± SD			**P-VALUE**		
	VMAT	IMRT	H-VMAT	VMAT VS IMRT	IMRT VS H-VMAT	VMAT VS H-VMAT
PTV						
CI	.85 ± 0.24	.77 ± 0.36	.83 ± 0.03	<.001	<.001	.002
HI	.10 ± 0.04	.095 ± 0.05	.09 ± 0.1	.03	.782	.057
V105(%)	44.09 ± 5.7	33.25 ± 5.44	46.47 ± 9.45	<.001	<.001	.481
D1cc (cGy)	5481.9 ± 28.65	5497.6 ± 54.6	5495 ± 74.92	<.001	.875	.440
HEART						
V20(%)	5.0 ± 3.25	11.46 ± 5.0	12.2 ± 5.3	<.001	.209	<.001
V30(%)	1.7 ± 1.4	8.13 ± 3.8	8.1 ± 3.8	<.001	.968	<.001
D mean (cGy)	502.9 ± 139.2	675.6 ± 177.5	687 ± 177.1	.001	.677	<.001
IL						
V5(%)	50.7 ± 3.8	48.0 ± 5.1	49.6 ± 4.7	.02	.118	<.137
V20(%)	20.9 ± 2.3	28.4 ± 3.3	27.8 ± 4.3	<.001	.523	<.001
V30(%)	23.5 ± 1.5	21.9 ± 2.5	21.3 ± 4.3	<.001	.597	<.001
D mean (cGy)	1136.1 ± 79.3	1403.8 ± 115.0	1324.8 ± 156.1	<.001	.042	<.001
CL						
V5(%)	37.7 ± 10.0	3.7 ± 2.7	23.0 ± 8.6	<.001	<.001	<.001
V20(%)	2.0 ± 2.8	.04 ± 0.07	.08 ± 0.16	<.001	.199	.013
D mean (cGy)	481.0 ± 106.8	136.2 ± 86.2	368.6 ± 163.5	<.001	<.001	.009
CB						
V5(%)	51.6 ± 24.6	13.2 ± 11.0	8.71 ± 12.4	<.001	.175	<.001
D mean (cGy)	508.1 ± 151.7	212.9 ± 140.0	292.8 ± 120.1	<.001	.003	<.001

	Mean ± SD			P-VALUE		
MU	773.8 ± 94.3	2112.7 ± 298.7	735.1 ± 83.4	<.001	<.001	.058
BOT	108.1 ± 11.4	255.5 ± 33.2	110.5 ± 11.8	<.001	<.001	.382
AD-TIME	159.5 ± 11.5	368.3 ± 33.6	181.4 ± 11.7	<.001	<.001	<.001

Table 3
The correlation of planning target volume, heart, and ipsilateral lung dose parameters with HVTL, RHVTL and LVTL.

	Correlation Coefficient		
	VMAT	IMRT	H-VMAT
PTV			
CI vs PTV (cc)	.490	.300	.312
HI vs PTV (cc)	.109	.330	.185
HEART			
V20 vs RHVTL	.613*	.892**	.911**
V30 vs RHVTL	.633*	.841**	.871**
D mean vs RHVTL	.340	.761**	.851**
V20 vs HVTL(cc)	.615*	.842**	.889**
V30 vs HVTL(cc)	.632*	.831**	.822**
D mean vs HVTL(cc)	.557*	.738*	.823**
L LUNG			
V5 vs Lung L(cc)	− .249	− .255	.274
V20 vs Lung L(cc)	− .012	− .153	.188
V30 vs Lung L(cc)	− .070	− .011	.292
D mean vs Lung L(cc)	− .111	− .128	.166
V5 vs LVTL (cc)	.241	− .284	− .348
V20 vs LVTL(cc)	.339	.377	.499
V30 vs LVTL(cc)	.176	.487	.547*
D mean vs LVTL(cc)	.275	.374	.524*

Discussion

The difficulty of PMRT treatment planning has been shown mainly because of complex PTV geometry structures and uncertainly relative position of OARs and PTV. In our study, three techniques have been compared for PMRT patients and all methods provide an acceptable dose coverage to the target volume. While no specific technique could be superior in all criteria, the VMAT technique could significantly reduce IL and heart dose and achieve a good balance between planning target coverage and OARs sparing.

However, IMRT and H-VMAT have lower dose in CB and CL. The importance of radiation-related occurrence rate in surrounding OARs should be illustrated.

The study from Darby et al. reported that reducing the mean heart dose 1 Gy could proportionally avoid a 7.4% rate of the risk of an acute coronary event [1]. Hence, one of the most critical objectives in planning breast cases could be keeping the mean heart dose as low as possible. Jacobse et al. show that myocardial infarction (MI) rate linearly affected by mean heart dose and decreasing whole heart mean dose is excepted contribute better cardiovascular healthy [5]. In multivariate analysis study of Chung et al including 1742 patients followed by 5–12 years indicated that mean heart dose increased 1 Gy, the risk of breast cancer treatment-related heart disease events significantly increased as adjusted hazard ratio: 1.23 [9]. In addition, diabetes mellitus (DM) and history of heart disease (HTN) were found to be adverse risk factors as hazard ratios: 1.92 and 2.51 respectively. The dosimetry comparisons have been evaluated in different techniques over the last decades. Popescu et al. compared IMRT, 3DCRT, and VMAT planning techniques and reported mean heart dose of the VMAT technique is 10.9 Gy (range 9.2 to 11.0) [7]. Xie et al. demonstrated nine left-sided PMRT patients including six advanced techniques and non-coplanar VMAT has the lowest mean heart dose as 7.4 ± 1.2 Gy [21]. Kuo et al. investigated the plans using the VMAT technique achieved 95% prescription dose to 95% volume have 7.5 ± 1.1 Gy for left-sided breast cancer [16]. Furthermore, their study based on 95% covering 95% of the prescription dose, our study shows the novel VMAT technique demonstrated that the mean heart dose is 5.0 ± 1.4 Gy for left-sided FB cases lower than all the reported study above with 95% covering 100% prescription dose condition.

However, the dose of VMAT technique for contralateral breast and contralateral lung significantly higher than IMRT and H-VMAT. The influence of dose to the contralateral breast in breast cancer has been illustrated by Stovall et al. The study shows that radiotherapy did not play a vital role in the development of second breast primary, but younger patients are more likely to have a long-term risk of developing breast cancer [27]. McDuff SGR et al. evaluated the patient who younger than 45 years old and harbor certain rare ATM variants should be noticed the risk of developing contralateral breast cancer [28]. However, inconsistency of published data limits the precise recommendations for contralateral breast cancer dose. Choi et al. propose that the number of 747 breast cancer patients with IMNs-PTV can significantly increase radiation exposure to the lungs, but the incidence and severity of radiation pneumonitis were minimal and acceptable [8]. Chung et al. demonstrated that despite the large volume of lungs receiving a low dose, the incidence of grade 3 of radiation pneumonitis is significantly low [9]. Wen et al. illustrated that study including 515 patients shows the risk of symptomatic radiation pneumonitis could be evaluated only by V20 and V30 [14].

The main limitation of this study for left breast cancer undergoing PMRT is not using deep inspiration breath hold (DIBH) to generate a planning image instead of using Free-breathing scanning technique. DIBH technique is highly recommended in Wiant et al. study including 25 patients, the mean heart dose using DIBH is 1.4 Gy and 3.0 Gy using free-breathing for whole breast cancer [19]. The study from Kim et al involved 69 patients mean heart dose decrease from 3.7 Gy to 1.8 Gy, reduced around 51% [30] and 48 patients involved in the study of Dong et al. shows that heart D mean reduced from 5.4 Gy to 3.6 Gy [7].

However, the DIBH technique has shown a longer beam-on time and treatment time which could lead to uncertainty of treatment delivery. Poeta et al demonstrated the 4 partial arcs split-VMAT plan could significantly reduce treatment delivery time from 8.9 mins to 5.4 mins compared to conventional treatment and each partial arc around 30 seconds which similar to our study (average partial arc approximately 27 seconds) [20]. Base on their feedback from treatment delivery, most patients were able to comfortably hold their breath for more than 20s, the feasibility of our technique should be further analyzed. While CI (0.85 vs 0.61) and delivery time (2.6mins vs 5.4mins) of our VMAT technique is superior to using split-VMAT, our study shows more mean heart dose (5.0 Gy vs 2.9 Gy). The heart and other critical organs dose of our technique using DIBH could be evaluated in further study. In order to decrease the uncertainty of delivery, H-VMAT could be recommended when RHVTL is lower than 0.06. Tangential fields as a base plan with a larger margin could to some extend improve PTV coverage in terms of tumor motion during treatment.

The evaluation of the planning complexity of left-sided breast cancer has been discussed. The measurement of Heart Volume in Tangent Line and the ratio of HVTL and heart volume have been first proposed in this study. The unique VMAT technique could be more unaffected by a relative position of anatomy. But for a more conventional method like IMRT and 3DCRT, the relationship between RHVTL and mean heart dose have a significantly high value. So, in our institution, we generally use unique VMAT when the traditional techniques meet the difficulty achieving target coverage and normal tissue constraints. However, in order to obtain a more reliable pattern, more data will be needed for analysis and validation. The value of RHVTL exceeding 0.06 may not be the most appropriate cut-off value for the determination of personalized planning techniques. More advanced criteria should be further illustrated.

Conclusion

The study found that the methods of VMAT separated Fields and adjacent Fields resulted in the optimum CI and a relatively low dose of heart and left lung in three techniques, but increased dose of contralateral lung and breast. When RHVTL is larger than 0.06, it is recommended that VMAT techniques can significantly reduce the dose of the heart and ipsilateral lung. While the dose differences between the OAR are small when RHVTL is lower than 0.06, the total actual delivery time using IMRT technique will be longer than VMAT and H-VMAT. Hence, in the case of free-breathing treatment, H-VMAT and VMAT should be more appropriate choices in terms of different RHVTL value.

Abbreviations

LBC: left-sided breast cancer; PMRT: postmastectomy radiotherapy; IL: ipsilateral lung; RHVTL: Heart Volume in Tangent line and heart volume; LVTL: Lung Volume in Tangent Line; CB: contralateral breast; PTV: planning target volume; IMRT: Intensity-modulated radiotherapy; VMAT: volumetric modulated arc therapy; MUs: monitor units; H-VMAT: Hybrid VMAT; CT: computed tomography; CI: conformity index; HI: Homogeneity index; DVH: dose-volume histogram; DIBH: deep inspiration breath hold; BOT: beam on time; AD-TIME: actual delivery time.

Declarations

Ethical Approval and Consent to participate

Institutional scientific and ethics board has approved this study. This article does not contain any studies with human participants performed by any of the authors.

Consent for publication

All study participants provided informed written consent for publication.

Availability of supporting data

All datasets provided in this study are included in the article or supplementary material.

Competing interests

All authors declare that they have no competing interests.

Funding

This study was supported by Shenzhen Science and Technology Innovation Commission Project (ZDSYS20190902092855097，KCXFZ20200201101050887) and Shenzhen City San Ming project (SZSM201612041).

Authors' contributions

ZZ and ML conceived idea, analyzed data and wrote the manuscript. PY, ZP and XL helped with statistical analysis. PF and ZT helped with editing the manuscript. YJ and YW checked results and critically revised the manuscript. All authors contributed to the article and approved the submitted version.

Acknowledgements

This study was supported by Peking university Shenzhen Hospital and Shenzhen-Peking University-Hong Kong University of Science and Technology Medical Center, China.

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Figures

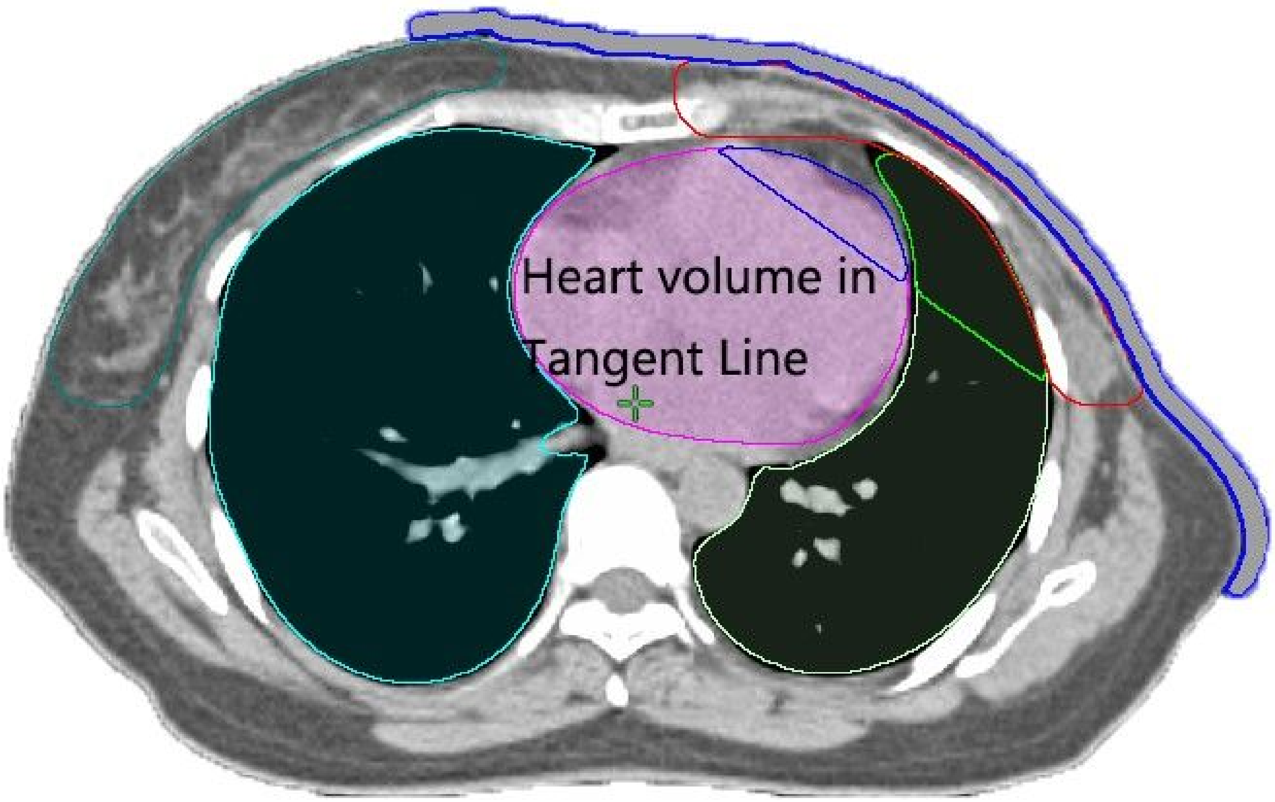

Figure 1

The demonstration of Heart Volume in Tangent Line (HVTL) measurement

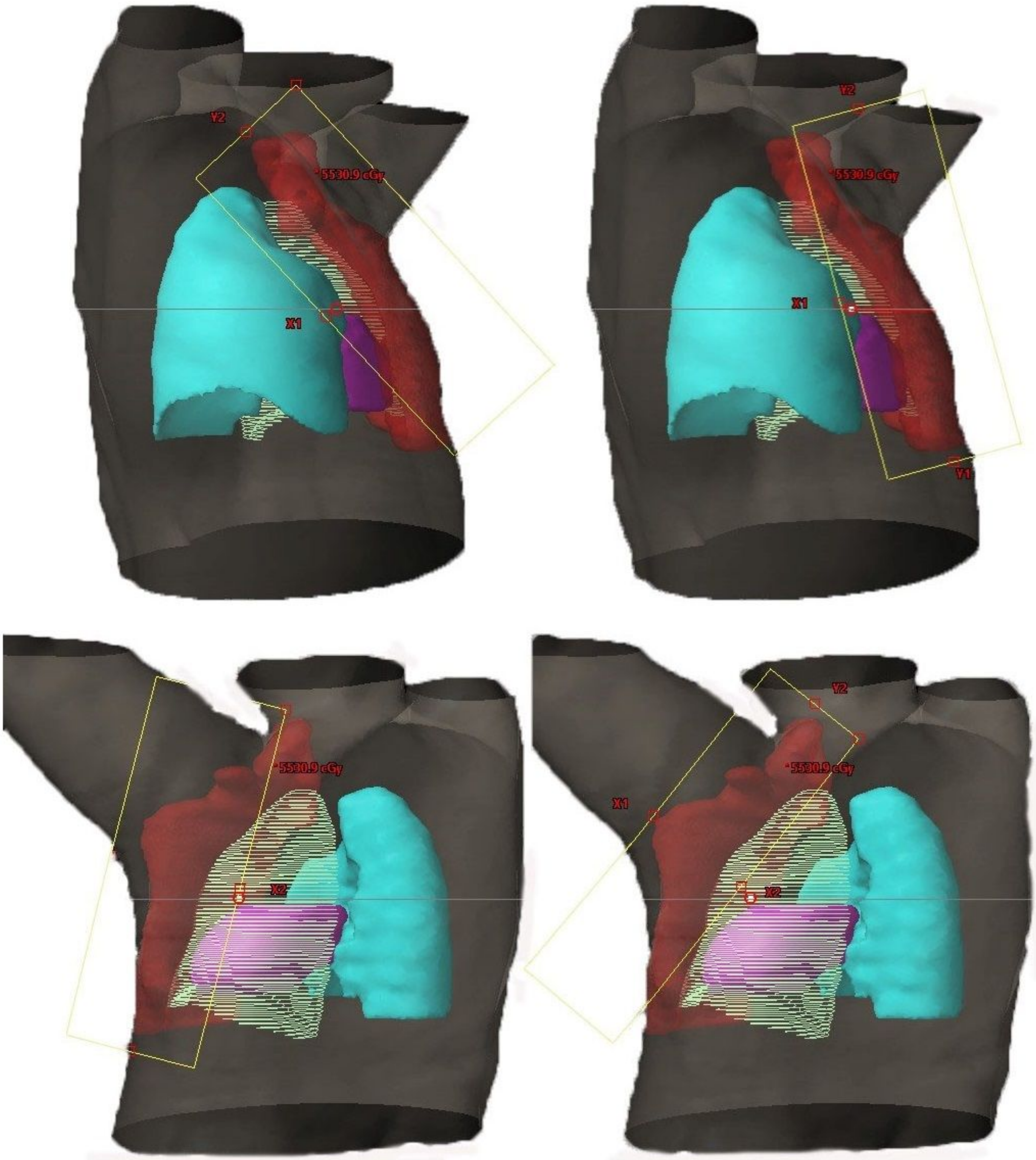

Figure 2

The beam eye view of beginning setup in four partial Arc VMAT treatment

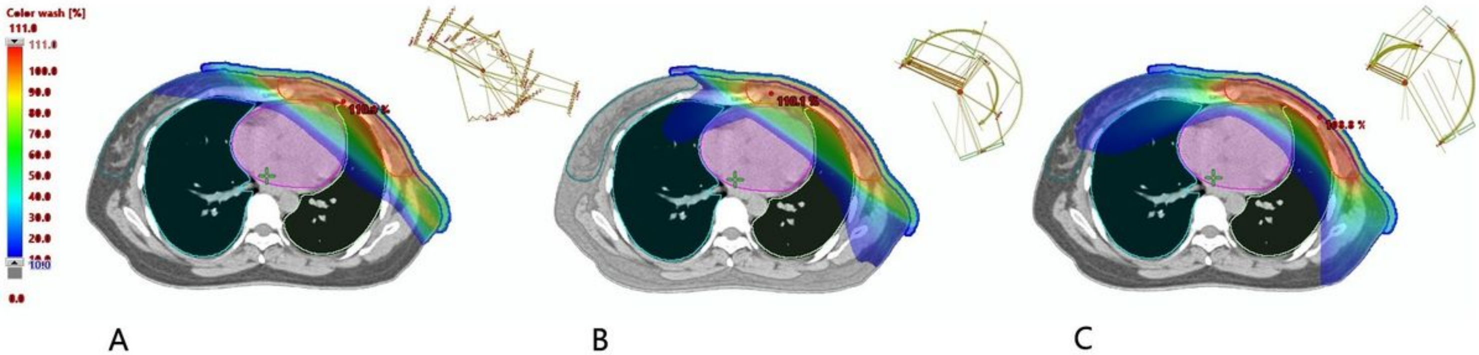

Figure 3

The dose distributions of three techniques: IMRT(A), H-VMAT(B) and VMAT(C) (from left to right) and the demonstrations of three techniques of fields angles setup.

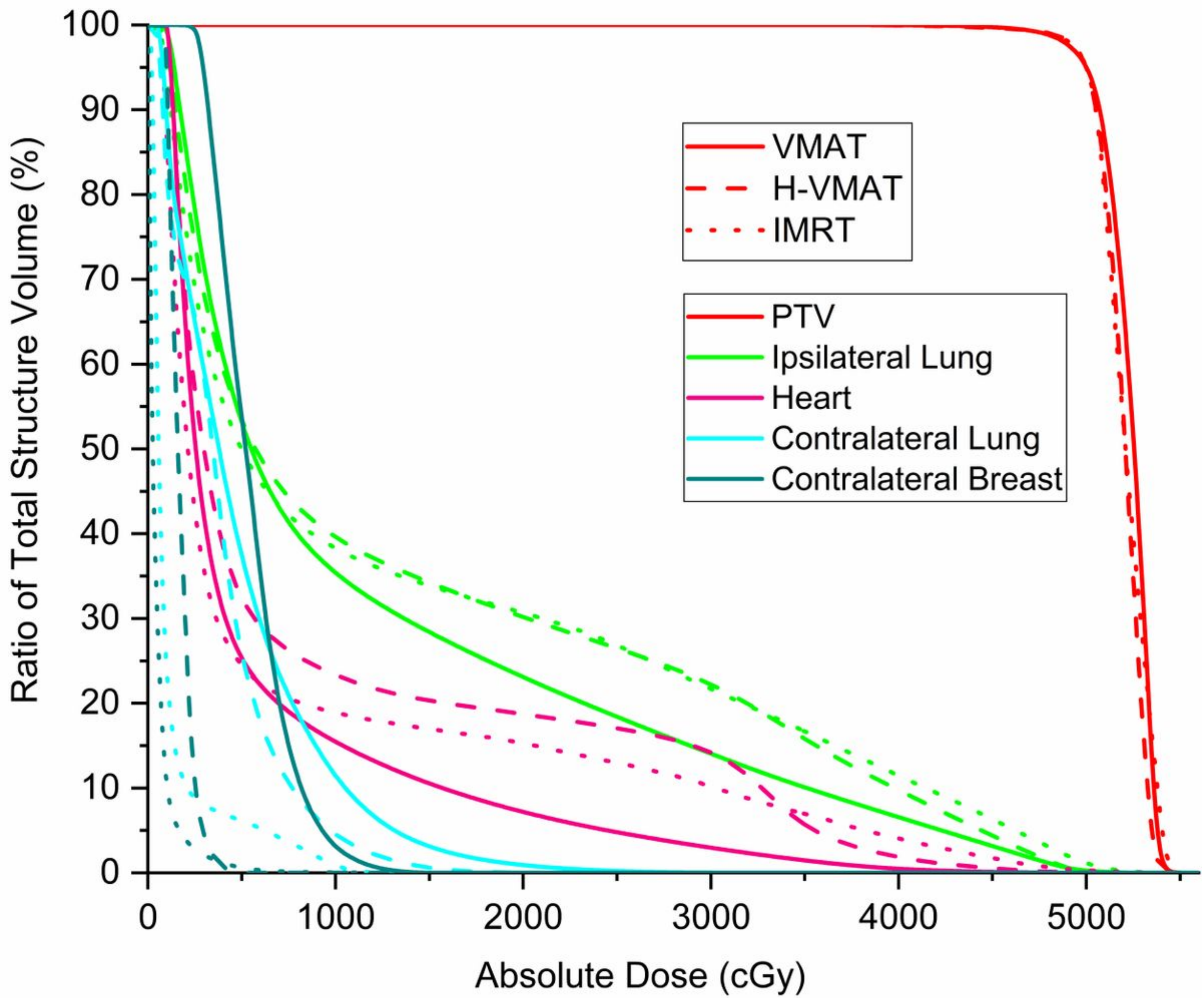

Figure 4

The comparison of dose-volume histogram (DVH) of three different techniques (VMAT, H-VMAT and IMRT). Structures: red, planning target volume; green, Ipsilateral Lung; pink, heart; blue, contralateral Lung; dark blue, contralateral breast.

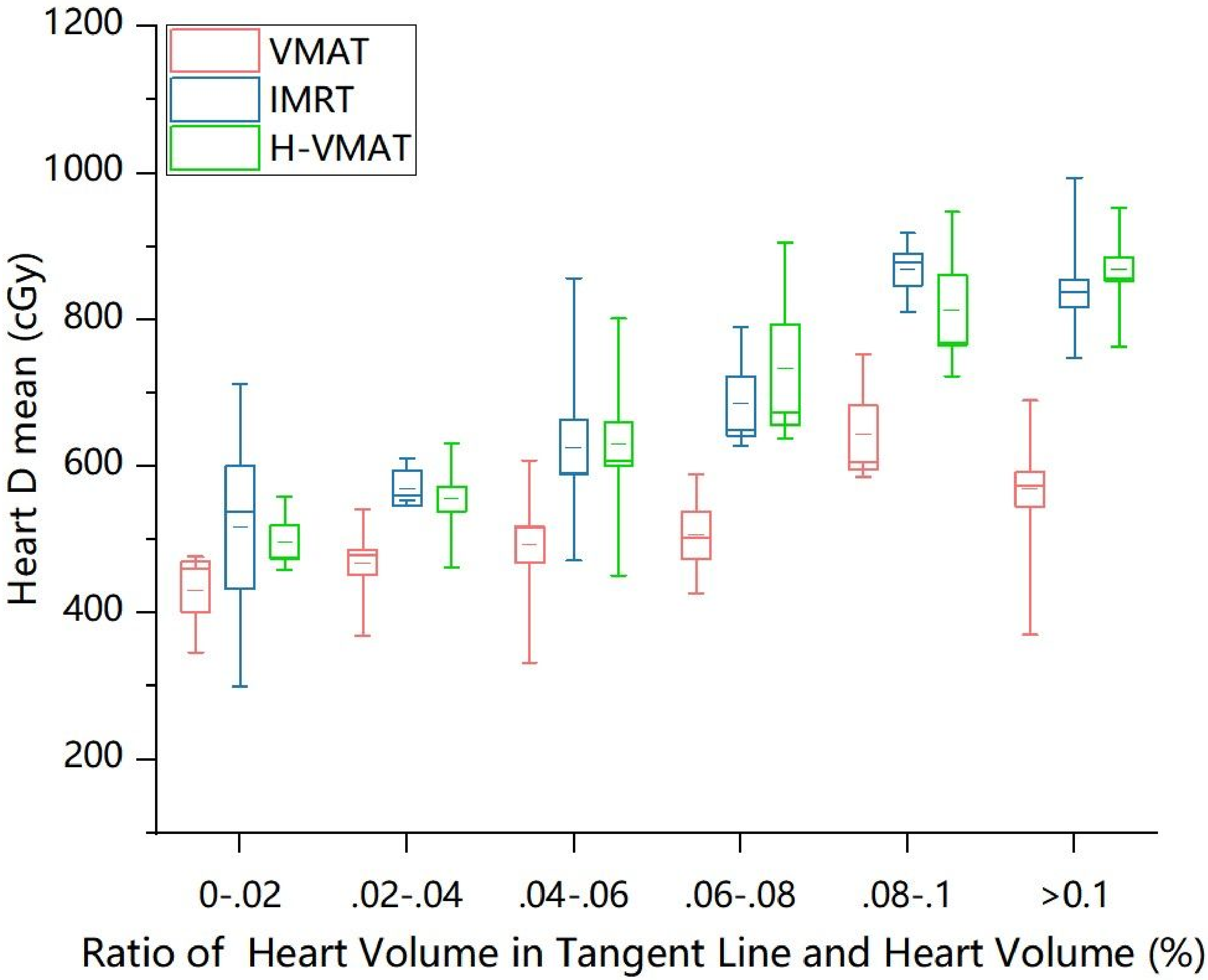

Figure 5

The relationship between ratio of Heart Volume in Tangent Line and Heart volume and mean heart dose in six sections. The small straight lines represent the average mean heart dose, the upper, lower, and middle error bars show the maximum, minimum and medium mean heart dose respectively.