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Dosimetric Evaluation of TF-3DCRT, FIF-Forward IMRT and FF Inversely Optimized IMRT for Breast Conserving Treatment

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Abstract: Objective: To compare the dosimetric characteristic of tangential field 3D conformal (TF-3DCRT, TF), field-in-field intensity-modulated (FIF-IMRT, FIF) and fixed-field inversely optimized intensity-modulated Radiotherapy (FFIO-IMRT, FFIO) for breast conserving treatment, and explore the benefit and efficiency for the three techniques. Materials and Methods: TF-3DCRT, FIF-IMRT and FFIO-IMRT treatment plans were analyzed for 16 breast patients (8 right-sided and 8 left-sided) after breast-conserving surgery. The target and organs at risk (OARs) were contoured by the same physician in the CT images. The prescription dose was 50Gy/25f. TF-3DCRT and FIF-IMRT were designed using Varian Eclipse Ver10.0 planning system, and FFIO-IMRT in the planning system of Pinnacle Ver9.6. Treatment plans were compared according to dose volume histogram (DVH) analysis in terms of PTV homogeneity and conformity indices (HI and CI) as well as OARs dose and volume parameters, and the efficiency was also evaluated. Results: In all cases, the treatment plans showed statistically significant difference between TF-3DCRT, FIF and FFIO-IMRT. The MUs were 244.9±8.3MU vs 285.9±20.3MU vs 534.0±56.2MU ($p<0.001$), the CIs of dose distribution and the target were 0.40±0.12 vs 0.48±0.12 vs 0.57±0.12 ($p<0.01$), and the HIs were 0.20±0.02 vs 0.13±0.02 vs 0.17±0.02 ($p<0.01$). Compared with TF and FFIO, FIF-IMRT showed smaller in the dose of D_2 and volume of V_{107} and V_{110} in the target. FFIO-IMRT generally increased the D_{mean}, V_{10} and V_{20} of ipsilateral lung, the D_1 of contralateral breast and the mean dose of contralateral lung, heart, esophagus, and spinal cord relative to TF and FIF techniques. Conclusion: In breast-conserving RT, FIF-IMRT improved the overall quality of dose distribution and delivery efficiency, and the patients are most likely to benefit from FIF-IMRT.

Keywords: Breast Cancer, Tangential Field, 3DCRT, IMRT, Dosimetry

1. Introduction

Breast cancer deaths in all malignant tumor of the fifth, its incidence in women's common malignant tumor in the second, second only to lung cancer, not only a serious threat to women's health, and destruction of female sexuality and instrument is beautiful, for patients with physical, psychological and social aspects of a huge impact [1]. Breast is the second characteristic of women. Surgery not only requires patients to retain their lives, but also enhances the quality of life, meets women's demands for virtue, and maintains a more harmonious life. This promotes the value of breast-conserving treatment [2]. In order to improve the postoperative beauty effect and quality of life of female patients, the treatment method of early breast cancer retention has become the standard treatment mode and has been widely used in clinical practice [3]. The replacement of total mastectomy with local excision of the tumor depends on the control of the risk of local recurrence in the breast by postoperative radiotherapy. In the comprehensive treatment of breast-conserving breast cancer, radiation therapy occupies an irreplaceable position [4]. It not only significantly improves the local control rate of the tumor, but also improves the long-term survival rate of patients [5]. A large number of foreign prospective data [6] indicate, the combination of radiotherapy and breast cancer postoperative breast-conserving surgery has similar survival rates and recurrence rates as those of modified radical mastectomy. However, the traditional method of radiotherapy for breast site is two tangential field radiation, but the technique has a non-uniform dose distribution in the breast target volume, and high-dose areas are generally distributed outside the target volume such as axillary, brachial plexus tissues and so on, which may result in skin ulcers, upper limb edema and other side effects will make the cosmetic results of breast surgery decreased. Compared with 3DCRT, IMRT has better dose uniformity, better normal tissue protection, and is also used in APBI [7]. The article compares the tangent field 3DCRT, tangential field in field IMRT and fixed field inverse optimized IMRT technique to evaluate and explore these three techniques in improving target dose uniformity and conformity, protecting normal tissues and organ at risky and other dosimetric advantages.

2. Material and Method

2.1. Case Selection and Instrument & Equipment

Randomly selected 16 patients with breast cancer after breast conserving surgery were all treated with radiotherapy. The median age was 48.5 (34-61) years. The primary tumor site was 8 cases on the left side and 8 cases on the right side.

The breast bracket is used for body position fixation. The treatment equipment is a Varian Clinac iX Medical Linear Accelerator equipped with 60 pairs of multileaf collimator systems (the middle 40 pairs of blades have a projection width of 0.5cm at the isocenter and 10 pairs of blades on each side the projection width is 1.0cm at the isocenter), the treatment planning system is Varian Eclipse Ver10.0 and Pinnacle Ver9.6.

2.2. Positioning and Organ Delineation

The patient's arm is free to stretch and fixed with a breast bracket. The free breath CT scan was performed on a Philips 16-row large aperture CT (BrillianceTM Big Bore) with a 0.5cm layer thickness. The scanning range is generally from the mandible to the full thorax, including adjacent normal tissue: the lungs, heart, contralateral breast, spinal cord, and esophagus. On the doctor workstation of the Pinnacle 3 treatment planning system, the same clinical RT physician delineate the patient's skin profile, the volume of the clinical target volume (Clinical Target Volume, CTV), the affected side lung, the healthy side lung, the healthy side of the breast, the heart, the spinal cord and the esophagus (Organ at risk, OARs). Among them, the CTV within the boundaries of the side under the Body to 0.3cm, on this basis, in the direction of up and down, left and right, respectively outward expansion of 0.5cm, direction of outward expansion of 1.0cm, respectively before and after the back line moved to the outer side lung and get PTV (Planning Target Volume). The PTV was mainly used for arranging field and MLC conforming, and the DVH and dose distribution in every layer of the CTV were observed while evaluating the RT plan.

The median volume of CTV obtained is 248.9cm^3 (147.7~489.1cm^3).

2.3. Treatment Planning Designing

The prescription dose of Target Volume is 50Gy/25f, which ensures that the dose distribution of 45Gy can wrap around the outer edge of the lung, and the dose of the contralateral breast is D_{max}≤500cGy, so as to avoid the high dose area in the armpit. The same physicsist designs the TF-3DCRT, FIF-IMRT and FFIO-IMRT plans respectively with Eclipse and Pinnacle treatment planning systems.

2.3.1. TF-3DCRT Planning

To design three dimensional conformal treatment plan of tangential field with Eclipse treatment planning system for each patient case. In the designing plan, the target volume is included in the MLC conformal area as far as possible to minimize the volume of the irradiated lung in the affected side, and to consider the contours of the patient's respiratory motion.

2.3.2. FiF-IMRT Planning

In Eclipse radiotherapy planning system, two tangential fields are considered as the main fields, which can reduce the weight of high dose field in axillary region and decrease the maximum dose of target volume. This action also reduces the coverage dose of target volume.

In order to overcome this shortcoming, the area with dose less than 50Gy in target volume was derived and 1-2 small fields with appropriate deflection angle were added to conform the area, and lead gate was pulled to surround the area, so as to avoid large-scale penetration of the lung field, adjust the weight of the field and MU number.

If DVH and dose distribution are not ideal, then add 1-2 sub-fields according to the above method to implement the conformity of the under-dose area, adjust the angle and weight of sub-fields repeatedly, properly drag MLC blades to block the dose hotspot area, and design the forward static intensity-modulated radiation therapy plan for tangent field, generally adding 1-4 sub-fields can achieve the goal.

2.3.3. FFIO-IMRT Planning

Pinnacle treatment planning system was used to design a static intensity modulated radiation therapy (IMRT) plan for the above cases. In order to avoid putting large healthy breast in front of the target volume, four fields should be arranged around the side of the target volume, and the angle of the field should be adjusted appropriately. The optimal target volume was 95% of the prescription dose, and the average dose of the target volume was taken as the dose normalization point. The optimal type was DMPO. Under the premise of ensuring the target dose to reach the target, the dose of limited areas such as affected lung, healthy lung, breast and axilla should be reduced as much as possible when setting the optimal conditions.

2.4. Data Statistics

According to"ICRU83 report [8]", dosimetric parameters such as conformity index, homogeneity index and maximum dose of organs at risk were defined and evaluated. Definition of conformal index CI [9] as Equation (1):

$$CI = \frac{V_{t,ref}}{V_{ref}} \cdot \frac{V_{t,ref}}{V_t} \tag{1}$$

The CI value is between 0 and 1. The larger the value, the better the conformity. Among them, $V_{t, ref}$ refers to the volume of the target enclosed by 95% prescription dose in the target volume. V_{ref} refers to the volume enclosed by a 95% prescription dose isodose line. V_t as target volume. Definition of homogeneity index HI [8] as Equation (2):

$$HI = \frac{D_2 - D_{98}}{D_{50}} \tag{2}$$

Among them, D_2 is the dose accepted by 2% target volume, D_{98} is the minimum dose accepted by 98% target volume, D_{50} Dose accepted for 50% target volume. The HI value is closer to 0, the better the homogeneity of target volume is. The maximum dose D_{max} was defined as the dose D_1 that endangered 1% of the organ volume.

2.5. Planning Comparison

The dosimetric parameters such as conformity index CI, homogeneity index HI, dose volume histogram (DVH) of target volume and organs at risk and machine MU number were compared.

2.6. Statistical Methods

SPSS 22.0 software was used for statistical analysis. Two paired T test and one-way ANOVA were used for statistical analysis. P<0.01 indicated that the data had very significant difference, P<0.05 indicated that the data had significant difference.

3. Results

Statistical analysis results are listed in Table 1, Table 2, Table 3 and Table 4, respectively. In the tables, p represents the significant difference value of the TF-3DCRT, FIF-IMRT, and FFIO-IMRT plans using one-way ANOVA. p_1, p_2, p_3 represent the significant difference value from paired sample T test between the TF-3DCRT and FIF-IMRT, FIF-IMRT and FFIO-IMRT, FFIO-IMRT and TF-3DCRT. Where the dosage unit is cGy. Relative volume is a percentage value.

3.1. Dose Comparison of Target Volume

The data in Table 1 showed that there was no significant difference in the volume of V_{100} covered by prescription dose in target volume among the three kinds of plans (p>0.05). The maximum dose D_2, high dose regional volume V_{107}, V_{110} paired test and single factor variance test were significantly different among the three kinds of plans (p<0.01), and the mean value comparison was FIF<FFIO<TF.

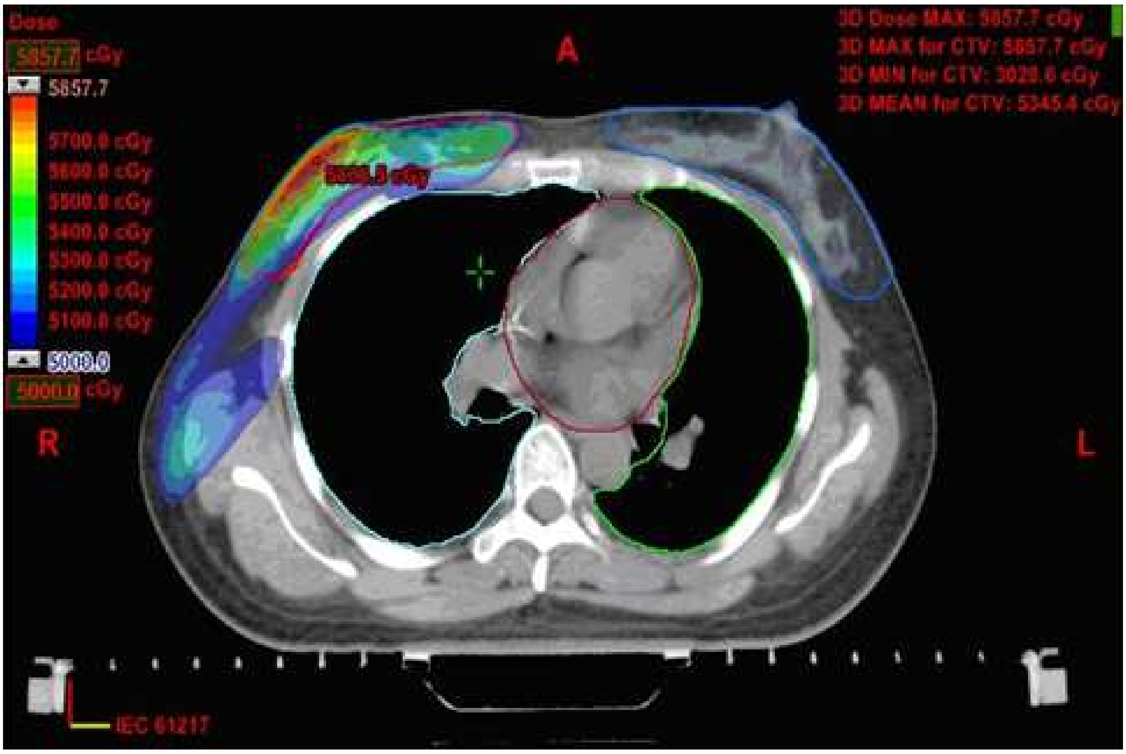

Figure 1. *Axial view on dose distribution of TF-3DCRT.*

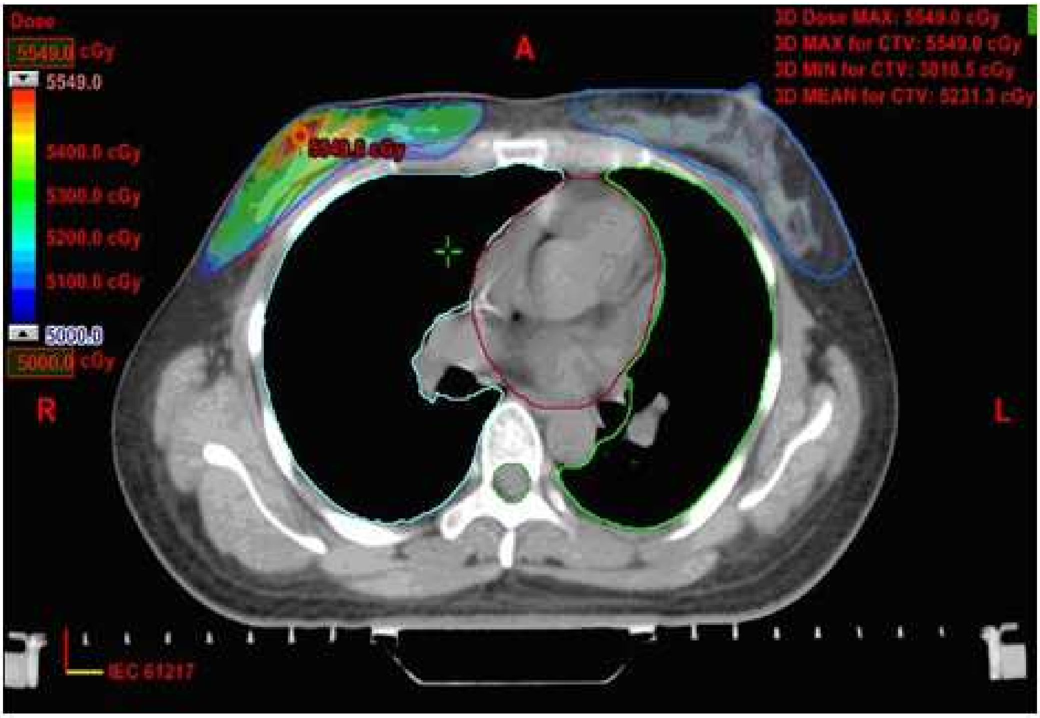

Figure 2. *Axial view on dose distribution of FIF-IMRT.*

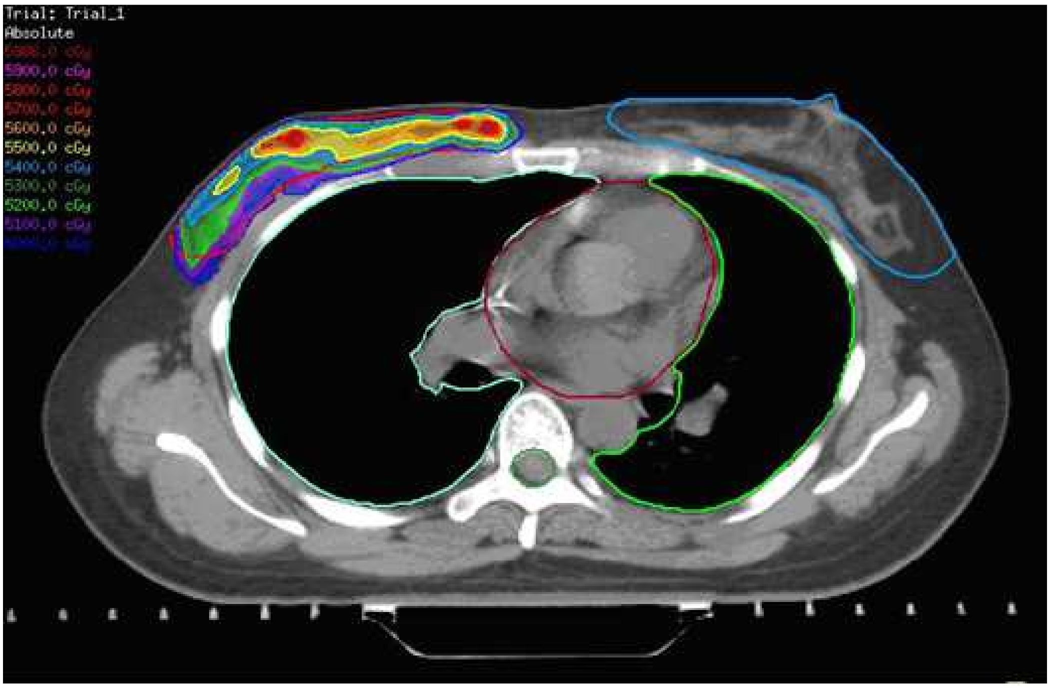

Figure 3. *Axial view on dose distribution of FFIO-IMRT.*

Table 1. *Dose comparison of TVs on three kinds of plans.*

Parameter	TF-3DCRT		FIF-IMRT		FFIO-IMRT		p
	$\bar{x}\pm s$	p_1	$\bar{x}\pm s$	p_2	$\bar{x}\pm s$	p_3	
D_2	5971.96±93.98	<0.001	5599.34±71.43	<0.001	5799.03±27.71	<0.001	<0.001
D_{50}	5575.06±106.01	<0.001	5367.72±90.43	<0.001	5467.27±86.71	<0.001	<0.001
D_{98}	4863.18±53.85	0.244	4881.71±22.05	0.204	4903.81±34.94	0.139	0.040
V_{100}	95.12±0.11	0.090	95.04±0.06	0.148	95.24±0.37	0.462	0.064
V_{107}	70.39±12.11	<0.001	44.11±10.13	<0.001	58.34±8.74	0.001	<0.001
V_{110}	53.26±14.69	<0.001	18.29±11.13	<0.001	33.69±10.62	<0.001	<0.001
CI	0.40±0.12	0.001	0.48±0.12	<0.001	0.57±0.12	<0.001	<0.001
HI	0.20±0.02	<0.001	0.13±0.01	<0.001	0.17±0.02	0.001	<0.001

There were significant differences in dose distribution and conformity index CI of target volume between the three kinds of plans (p<0.01). The conformity of FIF-IMRT was higher than that of TF-3DCRT, and the conformity of FFIO-IMRT was higher than that of the former two groups (as shown in Figures 1, 2 and 3).

3.2. Dose Comparison of Organs at Risky

The data in Table 2 showed that there were significant differences between D_{mean}, D_1, V_{10} and V_{20} in the ipsilateral lung (p<0.01, and the values of D_{mean}, V_{10} and V_{20} were FIF-IMRT<TF-3DCRT<FFIO-IMRT. There was no significant difference in V_{30} (p>0.05).

The data in Table 3 showed that there were significant differences between the contralateral lung dose D_{mean}, breast dose D_1, spinal cord dose D_{mean}, heart dose D_{mean} and esophageal dose D_{mean} in the three kinds of plans (p<0.05). The mean dose comparison of contralateral lung, spinal cord, heart and esophagus was FIF-IMRT<TF-3D CRT<FFIO-IMRT, and contralateral breast dose was TF-3DCRT<FIF-IMRT<FFIO-IMRT, as shown in Figure 4.

The DVH plot in Figure 4 shows that the FIF-IMRT program achieves a steeper dose gradient, which effectively reduces the maximum dose in the target volume. At the same time, the maximum dose of radiation to the lung, heart, spinal cord, esophagus and other dangerous organs on the healthy side was much lower than that of FFIO-IMRT.

Table 2. *Dose comparison of the ipsilateral lung on three kinds of plans.*

Ipsilateral Lung	TF-3DCRT		FIF-IMRT		FFIO-IMRT		p
	$\bar{x}$ ±s	p_1	$\bar{x}$ ±s	p_2	$\bar{x}$ ±s	p_3	
D_{mean}	811.00±180.25	<0.001	734.76±205.07	<0.001	1184.80±95.89	<0.001	<0.001
D_1	5369.33±293.60	<0.001	5047.07±287.82	<0.001	4636.90±246.67	<0.001	<0.001
V_{10}	18.86±4.55	<0.001	17.08±4.78	<0.001	32.75±2.73	<0.001	<0.001
V_{20}	14.68±3.11	0.003	12.79±4.19	0.001	19.10±1.85	0.002	<0.001
V_{30}	11.47±4.06	0.117	11.15±3.84	0.204	12.80±1.45	0.314	0.307
V_{40}	9.27±3.47	0.031	8.56±3.03	0.109	6.55±1.22	0.064	0.007
V_{50}	3.77±2.47	0.005	2.03±1.57	0.005	0.68±0.77	0.003	<0.001

Table 3. *Dose comparison of other OARs.*

Other OARs	TF-3DCRT		FIF-IMRT		FFIO-IMRT		p
	$\bar{x}$ ±s	p_1	$\bar{x}$ ±s	p_2	$\bar{x}$ ±s	p_3	
Contralateral Lung D_{mean}	6.77±1.95	<0.001	5.96±1.96	<0.001	321.74±108.84	<0.001	<0.001
Contralateral Breast D_1	274.75±64.37	<0.001	313.13±62.14	0.003	431.29±68.68	0.001	<0.001
Spinal Cord D_{mean}	14.73±5.62	<0.001	12.83±5.37	<0.001	449.21±174.01	<0.001	<0.001
Heart D_{mean}	76.88±58.38	<0.001	54.25±52.20	<0.001	1022.11±272.74	<0.001	<0.001
Esophagus D_{mean}	29.09±10.50	0.040	27.89±9.58	<0.001	680.11±257.80	<0.001	<0.001

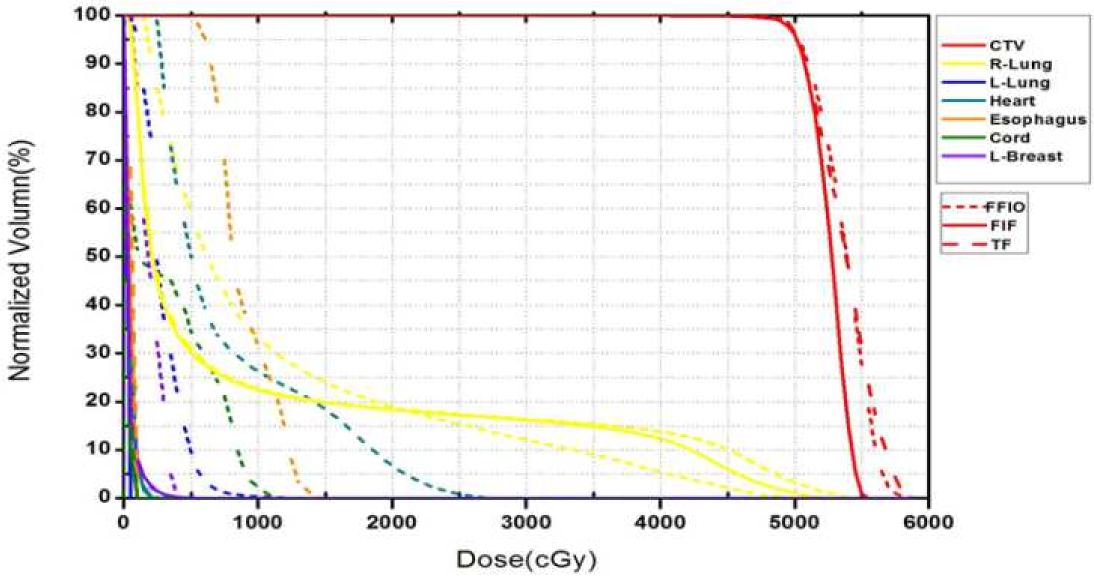

Figure 4. *DVH comparison of three kinds of treatment plans for one patient.*

3.3. Efficiency Comparison of RT Plan Implementation

The comparison parameter for the execution efficiency of the three kinds of plans is the total number of machine Monitor Units, and the result is shown in table 4, where FFIO-IMRT plan significantly increases the number of Monitor Units.

Table 4. *The efficiency of three kinds of plans.*

Monitor Units	TF-3DCRT		FIF-IMRT		FFIO-IMRT		p
	$\bar{x}$ ±s	p_1	$\bar{x}$ ±s	p_2	$\bar{x}$ ±s	p_3	
MUs	244.9±8.3	<0.001	285.9±20.3	<0.001	534.0±56.2	<0.001	<0.001

4. Discussion

Li Quanhai's article [10] briefly annalyzes the indication for breast cancer radiation therapy. The high incidence of breast cancer in women and its long-term survival rate make the risk of heart disease caused by radiation effects in radiotherapy and the recurrence of secondary primary tumors become an important issue to be considered. The clinical importance of heart disease caused by postoperative radiotherpy for breast cancer has been paid more and more attention in recent years [11]. This risk depends on the amount of radiation dose received during radiotherapy. Traditionally, tangent field irradiation therapy is still the most widely used and even more advanced technology in the main radiotherapy technology for breast cancer. Dosimetry studies using traditional techniques and advanced multifield irradiation techniques have been reported in many literatures [12-16]. The general conclusion drawn from these reports is that advanced radiotherapy techniques can improve dose uniformity in tumor target volumes and reduce high-dose areas in the heart and lungs, but more normal tissues are exposed to low-dose radiation. The radiation dose of normal tissues in breast cancer is greatly affected by the anatomical relationship between target volume and normal organs. The research of Taylor et al. [19] showed that the dose inhomogeneity in the target volume of breast was related to the fibrosis of breast tissue, which had a direct impact on the cosmetic effect after treatment. Improving the uniformity of the target volume dose and reducing the range of high-dose areas were of great significance to improving the quality of life of patients. In this study, three different dose distribution maps of the same patient are shown in Figures 1, 2 and 3. In order to make the coverage rate of TF-3DCRT to target volume not less than 95%, it is unavoidable to expose normal tissues such as axilla and brachial plexus outside target volume to a large range of high-dose radiation, while FIF-IMRT plan avoids dose in axilla and brachial plexus by increasing the angle of small field and properly deflecting the rack angle of small field. The high dose caused by overlap in normal tissues can also improve the uniformity of dose distribution in target volume. Although the conformity of dose distribution of FFIO-IMRT plan is higher than that of the former two, it inevitably causes large doses of radiation to normal tissues such as ipsilateral/contralateral lung, heart and spinal cord while increasing target coverage and conformity. Compared with TF-3DCRT and FFIO-IMRT plans, the above data show that FIF-IMRT has obvious advantages in reducing the maximum dose in the target volume, improving the uniformity of dose distribution in the target volume, reducing the average dose of irradiation to the ipsilateral lung, and reducing the volume V_{10} and V_{20} of low-dose irradiation. In the FIF-IMRT plan, the mean dose for contralateral lungs, heart, spinal cord, esophagus and other organs at risk was slightly lower than TF-3DCRT plan, and far lower than FFIO-IMRT plan. Of course, the latest technologies such as spiral TomoDirect radiotherapy (HT, including TomoDirect) and volumetric modulation arc therapy (VMAT) have the potential to increase the dose, but studies show that HT and VMAT will increase the low-dose area, while TomoDirect technology may lead to the increase in the treatment time is a factor that cannot be ignored [12, 13, 15, 17, 18].

The maximum dose of contralateral breast in the FIF-IMRT plan was slightly higher than that in the TF-3DCRT plan, while the FFIO-IMRT plan had a higher dose of contralateral breast than the first two. Comparing the total monitor units of the three kinds of plans, it can be seen that the monitor units of the FIF-IMRT plan is higher than the TF-3DCRT plan, and the FFIO-IMRT plan is much higher than the first two groups. Combined with the positive correlation between the two group data, it can be seen that the increase of monitor units leads to the increase of the maximum dose of contralateral breast. In the case of multi-beam IMRT, it is necessary to understand that this may lead to an increased risk of secondary cancer [19]. In other word, FIF-IMRT plan aims to increase the number of smaller fields and monitor units on the basis of TF-3DCRT plan in a targeted and directional manner, Although the conformity index was slightly lower than the FFIO-IMRT plan, multiple dosimetry parameters such as the dose limitation of the ipsilateral/contralateral lung, heart, spinal cord, esophagus and the dose uniformity in the target volume were integrated to judge. It can improve the efficiency of clinical treatment more effectively.

5. Conclusion

In conclusion, all three radiotherapy techniques can achieve better target volume coverage. However, FIF-IMRT technique has been comprehensively evaluated in conformal degree of target volume, uniform dose distribution, protection of normal tissues and organs at risk and other aspects. Among various clinical radiotherapy technologies after breast conserving surgery, FIF-IMRT will still be a conventional radiotherapy technique with high cost-performance. There will be greater potential for development in radiotherapy of postoperative of breast conserving.

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