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# Dosimetric Comparison of IMRT, Hybrid IMRT and Hybrid VMAT for Early Stage Right-Sided Breast Cancer

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## Abstract

**Introduction:** This study aimed to evaluate the clinical impact of hybrid Intensity-Modulated Radiotherapy (IMRT) and hybrid Volumetric-Modulated Arc Therapy (VMAT) for early-stage breast cancer, including plan quality and Second Cancer Risk (SCR).

**Methods:** Three different plans were designed in full IMRT, hybrid IMRT, and hybrid VMAT for each of eight patients with early-stage breast cancer. Target quality, Organs at Risk (OARs) sparing, and SCR were compared among the three plans.

**Results:** Compared with the hybrid IMRT, full IMRT showed deterioration in terms of $D_{2\%}$ of Simultaneous Integrated Boost (SIB), $V_{10}$ of ipsilateral lung, and Excess Absolute Risk (EAR) to contralateral lung and esophagus. The Homogeneity Index (HI) of SIB, $V_5$ of ipsilateral lung and combined lung, the $D_{max}$ and $D_{mean}$ of the esophagus, the EAR to contralateral breast and lung, and the EAR to the esophagus with hybrid VMAT dramatically increased by 12.5%, 19.49%, 18.87%, 90.59%, 167.69%, 50.14%, 264.68%, and 160.95%, respectively (p=0.022; 0.040; 0.044; 0.041; 0.003; 0.020; 0.000; 0.003). The EAR to contralateral breast and contralateral lung by full IMRT was significantly decreased compared with the hybrid VMAT (26.97%, p=0.033; 50.01%, p=0.026).

**Conclusion:** The results confirmed that hybrid IMRT could achieve better target quality and OARs sparing than full IMRT and hybrid VMAT for early-stage right breast cancer. Hybrid IMRT was the best treatment option, while hybrid VMAT performed the worst among the three plans in terms of SCR to peripheral OARs.

**Keywords: Dosimetric; Second cancer risk; IMRT; Hybrid IMRT; Hybrid VMAT**

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## Abbreviations

IMRT: Intensity-Modulated Radiotherapy; VMAT: Volumetric-Modulated Arc Therapy; SCR: Second Cancer Risk; OARs: Organs at Risk; SIB: Simultaneous Integrated Boost; EAR: Excess Absolute Risk; HI: Homogeneity Index; RT: Radiotherapy; 3D-CRT: 3-Dimensional Conformal Radiation Therapy; MLCs: Multi-leaf collimators; DR: Dose Rate; CT: Computed Tomography; TPS: Eclipse Treatment Planning System; CTV: Clinical Target Volume; PTV: Planning Target Volume; MUs: Monitor Units; DVH: Dose-Volume Histogram; CI: Conformal Index

## Introduction

Usually diagnosed as early-stage female cancer, the 5-year specific survival rate of breast cancer is up to 98.9% [1]. Whole breast Radiotherapy (RT) and a boost to the tumor bed are considered as the adjuvant therapy after breast-conserving surgery for early-stage breast cancer [2,3]. Studies confirmed that patients benefited from RT and tumor bed boosting [3,4].

Various RT techniques, such as 3-Dimensional Conformal Radiation Therapy (3D-CRT), Intensity-Modulated Radiation Therapy (IMRT), and Volumetric-Modulated Arc Therapy (VMAT), have been adopted for treating breast cancer. Utilizing two opposed, wedged, and tangential fields, 3D-CRT treating the whole breast is carried out with Multi-Leaf Collimators (MLCs) to shield the adjacent normal tissue. 3D-CRT has the advantage of improving the local control, but the toxicities associated with radiation to the Organs at Risk (OARs) are a concern [5]. Dividing each treatment beam into smaller beam segments, IMRT delivers a non-uniform fluence to optimize the dose distribution [5]. VMAT can rotate the angle of gantry and radiate beams continuously, and modulate the Dose Rate (DR) and the shape of the MLCs simultaneously to achieve a highly conformal dose coverage [6]. IMRT and VMAT were reported to have incomparable advantages

in dose homogeneity and coverage compared with 3D-CRT [6,7]. However, IMRT might be more susceptible to setup error and shape changes of the breast in whole breast RT [8]. To reduce the effects of the geometrical uncertainties, Nakamura et al. [8] proposed a method of hybrid IMRT plan comprised of two opposed tangential open beams and two inverse-planned IMRT beams. And they proved the hybrid IMRT had excellent performance in target quality and offsetting the geometrical uncertainties for patients who underwent whole breast RT [8].

RT resulted in inevitably radiation damage and therapy-related Second Cancer Risk (SCR) for normal tissue, which was confirmed by studies [9,10]. With the improvement of the efficacy and overall survival of breast cancer patients, the SCR and radiation toxicity caused by RT has gradually become a research focus. Early studies showed that 3D-CRT possesses a lower SCR than IMRT and VMAT [11,12].

To pursue an excellent target dose coverage and OARs sparing, and also lower the SCR and radiation toxicity, selecting a reasonable RT modality is critical for treating breast cancer. To the best of our knowledge, the clinical impacts of hybrid VMAT for breast cancer have not been studied. This study aims to assess the plan quality and SCR among three treatment modalities (full IMRT, hybrid IMRT, and hybrid VMAT) for breast cancer.

## Materials and Methods

### Patients and materials

Eight females aged between 41 and 51 years old, with early-stage right-sided breast cancer after breast-conserving surgery, were randomly selected. None of the patients had contraindications for RT. This study was approved by the ethics committee of Chongqing University Cancer Hospital, and the informed consent was acquired from each enrolled patient.

All of the patients were positioned with a breast bracket and fixed foam plate on the affected side of the lower limbs. The Computed Tomography (CT) scans were acquired on a Philips Brilliance Big Bore CT (Philips, Holland) simulation in 5-mm-thick slices, in the supine position with the scan scope from the mandible to the thorax. In addition, all of the adjacent normal tissues, such as the heart, lung, esophagus, and contralateral breast, were completely covered.

### Definition of target volumes and OARs

Target volumes and OARs were delineated on the Eclipse treatment planning system (TPS, Varian Medical Systems, Version 13.6, Inc.). The Clinical Target Volume (CTV) and the boost region were delineated by the same radiation oncologist on each CT dataset. The CTV was the whole breast tissue identifiable on the CT scan assisted by wire markers, which were placed around the palpable breast tissue during the simulation. Then the CTV limited posteriorly by the intercostal front and retracted 5 mm from the skin. The boost region encompassed the surgical bed or seroma. The Planning Target Volume (PTV) was expanded 5 mm based on the CTV, excluding the heart. Then the PTV was retracted 5 mm from the skin and limited posteriorly by the intercostal front. The boost region was expanded by 5 mm in all directions to create the SIB (Simultaneous Integrated Boost) volume. The contoured OARs were the contralateral breast, heart, spinal cord, esophagus, and ipsilateral and contralateral lungs.

### RT plans

Figure 1 and 2 show the field's distributions and the dose distributions in CT images for the three RT techniques respectively. Three different RT plans (full IMRT, hybrid IMRT, and hybrid VMAT) were created for each case in the Eclipse TPS. Utilizing 6 MV photon beams generated by Varian IX linear accelerator, dose optimization and calculations were done in Eclipse TPS for all of the plans. The algorithms of dose-volume optimizer and progressive resolution optimizer were used for IMRT, and VMAT dose optimizations, respectively, and Anisotropic Analytical Algorithm was adopted for final dose calculations [13,14].

**Full IMRT:** The full IMRT plans contained two opposed tangential fields, and another four fields, which were at the angles of 10° or 20° to the two tangential fields in the direction of outside the body. The angles of the collimator and the position of jaws of all of the fields were adjusted before dose optimization to maximize the protection of the lungs. All of the fields were delivered with a dynamic sliding-window IMRT delivery technique and the fixed DR of 400 monitor units (MUs)/min.

**Hybrid IMRT:** The hybrid IMRT plans owned two opposed tangential open beams plus three IMRT beams. Two of the three IMRT beams were at the angles of 10° to the two tangential fields in the direction of outside the body, and the third IMRT beam had an angle of about 30° to 45° to the tangential field on the upper side avoiding exposure to the heart and contralateral breast. To maximize the protection of the lungs, the angles of the collimator of the three IMRT beams were adjusted, and the position of the jaws of the third IMRT beam was adjusted and fixed, adapting the shape of the SIB before dose optimization and calculation. The adopted delivery technique and DR were the same as that of the full IMRT plans. The open beams contributed 80% of the total dose, whereas the inversely optimized IMRT beams contributed to the remaining prescription dose.

**Hybrid VMAT:** The hybrid VMAT plans owned two opposed tangential open beams and a half arc beam. The gantry of the arc beam rotated from one tangential angle to the other tangential angle. The maximum DR of the arc beam was set to 600 MUs/min. The open beams contributed with 80% of the total dose, whereas the inversely optimized arc beams contributed to the remaining prescribed dose.

For the SIB and PTV-SIB of all of the plans, the prescribed doses were 50 Gy and 45 Gy in 25 fractions, respectively. The prescribed 95% isodose covered no less than 95% of the target volume [15], and the percentage volume of the target volume radiated over 110% of the prescribed dose was no more than 2%. The dose constraints for adjacent OARs of contralateral breast, heart, ipsilateral lung, contralateral lung, spinal cord, and esophagus were defined according to published literature [5].

### Treatment plan evaluation

The data collected from the Dose-Volume Histogram (DVH) of all of the plans were evaluated in the aspect of target coverage and OARs sparing. Figure 3 shows the representative DVHs for the three RT techniques.

SIB: the maximum dose ($D_{max}$), the mean dose ($D_{mean}$), and $V_{95\%}$ of SIB were assessed. The $D_{max}$ of SIB, also named $D_{2\%}$, is defined as the dose received by 2% of the target volume, and $V_{95\%}$ is defined as the percentage volume of the target volume receiving 95% of the prescribed dose. The Conformal Index (CI) and Homogeneity Index (HI) were also evaluated. The CI of SIB is defined as $CI=TV^2_{PTV}/(TV \times PIV)$ utilizing the Paddick conformity index, where the TVPTV was

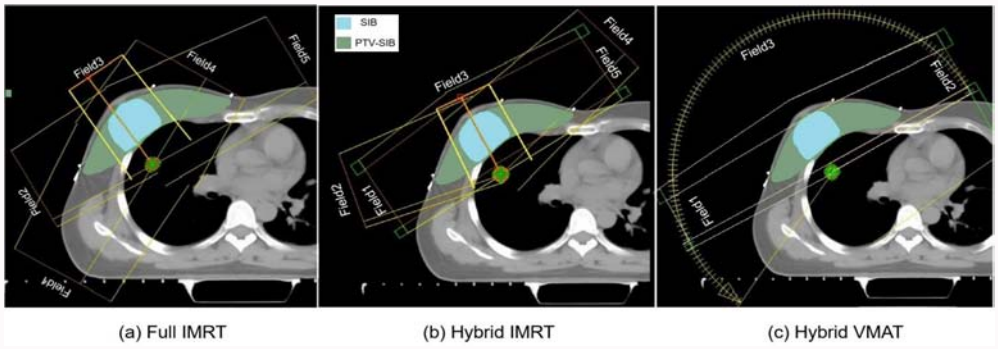


**Figure 1:** Fields distributions for (a) Full IMRT, (b) hybrid IMRT and (c) Hybrid VMAT.

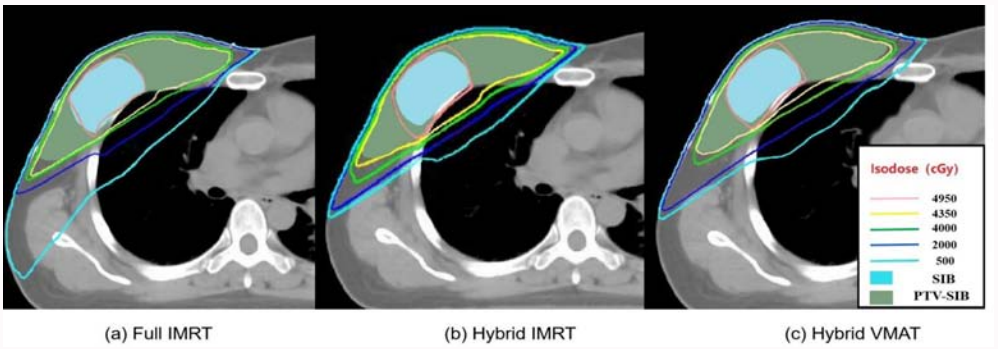


**Figure 2:** Dose distributions for (a) Full IMRT, (b) hybrid IMRT and (c) Hybrid VMAT.

the SIB volume receiving 95% of the prescription dose, the TV is the total volume of the SIB, and the PIV is the total volume covered by the prescribed 95% isodose. The HI of SIB was assessed using HI= $(D_{5\%}-D_{95\%})/D_{mean}$, where $D_{5\%}$ and $D_{95\%}$ are the minimum dose radiated to 5% and 95% of the SIB, respectively.

PTV-SIB: the $D_{2\%}$, the $D_{mean}$, $V_{95\%}$, and CI of PTV-SIB were assessed. These indicators were defined as described above.

OARs: The $D_{max}$ and $D_{mean}$ of contralateral breast, Heart, spinal cord and esophagus, and the $D_{mean}$ of contralateral lung were executed for dosimetric analysis. The $V_5$ (the percentage volume receiving 5 Gy), $V_{10}$ (the percentage volume receiving 10 Gy), $V_{20}$ (the percentage volume receiving 20 Gy), $V_{30}$ (the percentage volume receiving 30 Gy), and $D_{mean}$ of the ipsilateral lung and combined lung were also evaluated.

### SCR calculations

The SCR caused by RT of normal tissues can be assessed by Model Excess Absolute Risk (EAR), as proposed by Schneider [16,17]. The Equation (1) shown below can be utilized to calculate the SCR of an organ [18,19]:

$$EAR^{org} = \frac{1}{V_T}\sum_i V(D_i)\beta_{EAR} RED(D_i)\mu(x,a) \quad (1)$$

where $V_T$ is the total organ volume assessed for secondary carcinogenesis, V ($D_i$) represents the organ volume receiving the dose $D_i$, and the parameter $\beta_{EAR}$ is the slope of the dose-response curve in the low dose region. Equation (2), RED ($D_i$), represents the dose-response mechanistic model, which describes the fractionation effects and cell killing:

$$RED(D_i) = \frac{e^{-\alpha' Di}}{\alpha' R}\left(1-2R+R^2 e^{\alpha' Di} - (1-R)^2 e^{\frac{\alpha' R}{1-R}Di}\right) \quad (2)$$

where R is a parameter that represents the repopulation or repair ability of normal tissues between two dose fractions, and the parameter α' was calculated by Equation (3):

$$\alpha' = \alpha + \beta d = \alpha + \beta D_i / D_T d_T \quad (3)$$

where DT is the prescribed dose of 50 Gy to the SIB in this study, and dT represents the corresponding fractionation dose of 2 Gy. Given by Equation (4), μ(x, a) expresses the modifying function:

$$\mu(x,a) = e^{[\gamma e(x-30)+\gamma a 1n(a/70)]} \quad (4)$$

where $\gamma_e$ and $\gamma_a$ are both the age modifying parameters.

In this study, the EAR has been investigated to the organs of contralateral breast, contralateral lung, ipsilateral lung, and esophagus. The assumed value of α/β= 3 Gy for all of the organs needed to evaluate EAR, and all of the other parameters used in EAR calculation were selected from previous research [18]. The parameters are shown in Table 1 (Figure 3).

### Statistical analysis

To determine whether the pair parameters were different, a paired t-test was carried out using the Microsoft Excel. If the p-value is less than 0.05, the difference is considered to be statistically significant.

## Results

### Target coverage

The parameters of $D_{2\%}$, $D_{mean}$, $V_{95\%}$, CI, and HI were compared to

**Table 1:** The other parameters used in EAR.

| Site | $\beta_{EAR}$ | $\gamma_e$ | $\gamma_a$ | α | α/β | R |
|---|---|---|---|---|---|---|
| Contralateral breast | 9.2 | -0.04 | 1.7 | 0.04 | 3 | 0.2 |
| Contralateral lung | 7.5 | 0.002 | 4.2 | 0.04 | 3 | 0.8 |
| Ipsilateral lung | 7.5 | 0.002 | 4.2 | 0.04 | 3 | 0.8 |
| Esophagus | 0.58 | -0 | 1.9 | 0.03 | 3 | 0.8 |

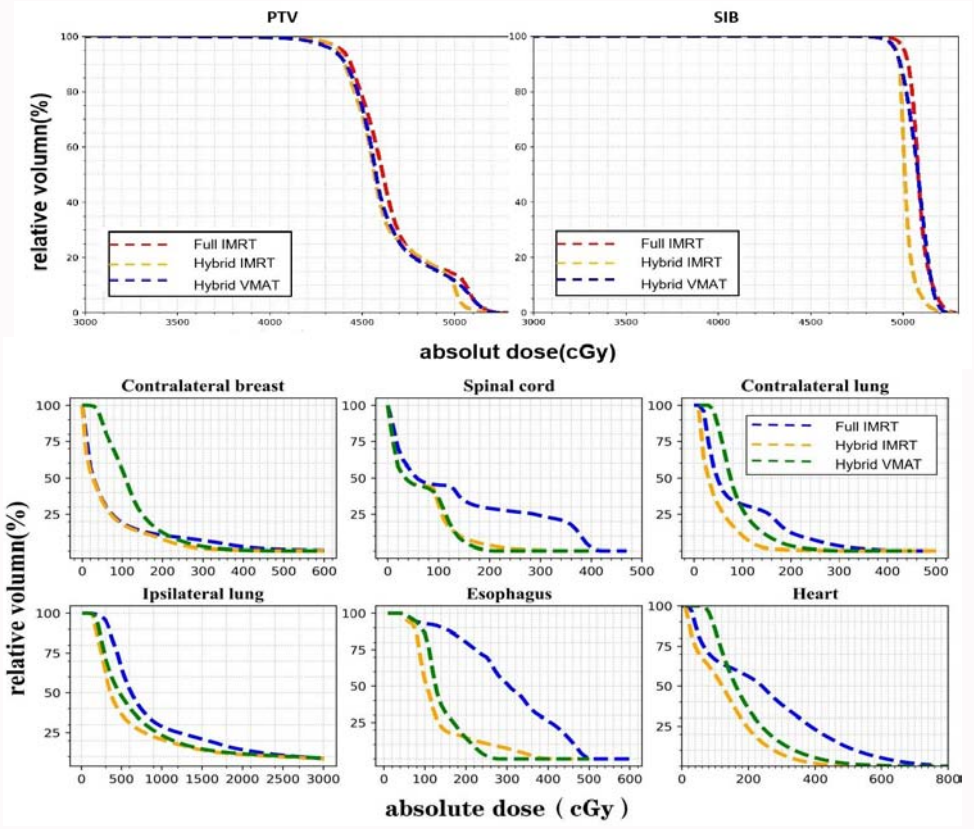


**Figure 3**: Representative DVHs for targets and OARs.

**Table 2:** The findings on SIB and PTV-SIB.

| | Parameters | full IMRT | hybrid IMRT | hybrid VMAT | P- Value | | |
|---|---|---|---|---|---|---|---|
| | | | | | full IMRT *vs.* hybrid IMRT | full IMRT *vs.* hybrid VMAT | hybrid IMRT *vs.* hybrid VMAT |
| SIB | $D_{2\%}$ (Gy) | 52.76 ± 0.59 | 52.35 ± 0.61 | 52.70 ± 0.48 | 0.044 | 0.745 | 0.046 |
| | $D_{mean}$ (Gy) | 51.20 ± 0.43 | 51.18 ± 0.59 | 51.41 ± 0.38 | 0.953 | 0.183 | 0.197 |
| | $V_{95\%}$ (%) | 99.88 ± 0.34 | 99.96 ± 0.11 | 100.00 ± 0.00 | 0.351 | 0.351 | 0.351 |
| | CI | 0.794 ± 0.058 | 0.820 ± 0.048 | 0.821 ± 0.046 | 0.153 | 0.07 | 0.908 |
| | HI | 0.051 ± 0.013 | 0.048 ± 0.012 | 0.054 ± 0.010 | 0.502 | 0.423 | 0.022 |
| PTV-SIB | $D_{2\%}$ (Gy) | 49.42 ± 0.66 | 49.32 ± 0.34 | 49.21 ± 0.36 | 0.655 | 0.318 | 0.355 |
| | $D_{mean}$ (Gy) | 45.74 ± 0.38 | 45.65 ± 0.16 | 45.60 ± 0.26 | 0.518 | 0.16 | 0.599 |
| | $V_{95\%}$ (%) | 98.98 ± 0.41 | 99.40 ± 0.50 | 99.07 ± 0.56 | 0.098 | 0.637 | 0.046 |
| | CI | 0.632 ± 0.073 | 0.656 ± 0.089 | 0.650 ± 0.09 | 0.459 | 0.588 | 0.628 |

evaluate the quality of target dose coverage. For the SIB, the hybrid IMRT obtained a lower $D_{2\%}$ than both full IMRT and hybrid VMAT ($p<0.05$) and achieved better HI than the hybrid VMAT ($p<0.05$). For the PTV-SIB, the $V_{95\%}$ of the hybrid IMRT (99.40 ± 0.50) was better than that of the hybrid VMAT (99.07 ± 0.56) ($p<0.05$). The findings on SIB and PTV-SIB are listed in Table 2.

### OARs

The delivered doses to the OARs are listed in Table 3. Compared with the hybrid IMRT, the $V_5$ of ipsilateral lung and combined lung with hybrid VMAT increased by 19.45% and 18.87%, respectively (p=0.040; 0.044), the $V_{10}$ of the ipsilateral lung with full IMRT increased 4.13 Gy (p=0.012), and the $D_{max}$ and $D_{mean}$ of the esophagus with hybrid VMAT dramatically increased by 90.59% and 167.69%, respectively (p=0.041; 0.003).

### SCR calculations

The EAR of the organs of contralateral breast, contralateral lung, ipsilateral lung, and esophagus with three treatment modalities are shown in Table 4. Compared with hybrid VMAT, the EAR to the contralateral breast with full IMRT and hybrid IMRT were decreased by 26.97% and 33.39%, respectively (p=0.033; 0.020), and the EAR to the contralateral lung with full IMRT and hybrid IMRT were reduced by 50.01% and 72.58%, respectively (p=0.026; 0.000). In comparison with the hybrid IMRT, the EAR to the esophagus with full IMRT and hybrid VMAT increased 80.21% and 160.95%, respectively (p=0.028; 0.003).

## Discussion

Since studies evaluating the hybrid IMRT and hybrid VMAT for

**Table 3:** The delivered doses to the OARs.

| Parameters full IMRT | | | hybrid IMRT | hybrid VMAT | P-Value | | |
|---|---|---|---|---|---|---|---|
| | | | | | full IMRT *vs.* hybrid IMRT | full IMRT *vs.* hybrid VMAT | hybrid IMRT *vs.* hybrid VMAT |
| Contralateral breast | $D_{max}$ (Gy) | 12.47 ± 9.58 | 12.34 ± 13.2 | 11.84 ± 12.86 | 0.933 | 0.651 | 0.113 |
| | $D_{mean}$ (Gy) | 0.82 ± 0.55 | 0.83 ± 0.51 | 1.00 ± 0.49 | 0.95 | 0.128 | 0.432 |
| Spinal cord | $D_{max}$ (Gy) | 2.88 ± 3.38 | 2.10 ± 1.86 | 2.54 ± 0.76 | 0.258 | 0.744 | 0.417 |
| | $D_{mean}$ (Gy) | 0.63 ± 0.53 | 0.58 ± 0.19 | 0.71 ± 0.24 | 0.801 | 0.615 | 0.137 |
| Ipsilateral lung | $V_{5Gy}$ (%) | 33.22 ± 23.14 | 35.96 ± 4.49 | 42.97 ± 9.41 | 0.732 | 0.18 | 0.04 |
| | $V_{10Gy}$ (%) | 24.89 ± 6.26 | 20.76 ± 3.29 | 19.76 ± 5.31 | 0.012 | 0.077 | 0.607 |
| | $V_{20Gy}$ (%) | 14.42 ± 3.41 | 13.38 ± 2.94 | 13.17 ± 3.02 | 0.181 | 0.072 | 0.267 |
| | $V_{30Gy}$ (%) | 10.02 ± 2.95 | 10.48 ± 2.79 | 10.39 ± 2.97 | 0.219 | 0.23 | 0.652 |
| Contralateral lung | $D_{mean}$ (Gy) | 18.72 ± 13.43 | 8.45 ± 1.27 | 9.01 ± 1.73 | 0.065 | 0.081 | 0.079 |
| | $D_{mean}$ (Gy) | 0.37 ± 0.42 | 0.33 ± 0.30 | 0.74 ± 0.34 | 0.826 | 0.157 | 0.078 |
| Combined lung | $V_{5Gy}$ (%) | 24.09 ± 7.87 | 20.19 ± 3.16 | 24.00 ± 5.26 | 0.124 | 0.96 | 0.044 |
| | $V_{10Gy}$ (%) | 15.06 ± 5.30 | 12.37 ± 2.83 | 11.97 ± 2.51 | 0.097 | 0.142 | 0.592 |
| | $V_{20Gy}$ (%) | 9.31 ± 1.85 | 8.03 ± 1.59 | 9.48 ± 3.54 | 0.211 | 0.908 | 0.232 |
| | $V_{30Gy}$ (%) | 6.42 ± 1.31 | 6.27 ± 1.41 | 7.45 ± 3.18 | 0.793 | 0.361 | 0.244 |
| Esophagus | $D_{mean}$ (Gy) | 4.54 ± 2.20 | 3.38 ± 2.60 | 5.08 ± 1.82 | 0.282 | 0.545 | 0.259 |
| | $D_{max}$ (Gy) | 3.39 ± 3.85 | 2.02 ± 1.67 | 3.85 ± 1.13 | 0.181 | 0.738 | 0.041 |
| | $D_{mean}$ (Gy) | 1.09 ± 0.97 | 0.65 ± 0.42 | 1.74 ± 0.40 | 0.07 | 0.161 | 0.003 |

**Table 4:** The EAR of the organs with three treatment modalities (means ± SD).

| EAR | full IMRT | hybrid IMRT | hybrid VMAT | *p*-Value | | |
|---|---|---|---|---|---|---|
| | | | | full IMRT *vs.* hybrid IMRT | full IMRT *vs.* hybrid VMAT | hybrid IMRT *vs.* hybrid VMAT |
| Contralateral breast | 5.139 ± 3.568 | 4.687 ± 3.353 | 7.037 ± 3.905 | 0.492 | 0.033 | 0.02 |
| Contralateral lung | 9.079 ± 7.911 | 4.980 ± 4.167 | 18.161 ± 5.143 | 0.03 | 0.026 | 0 |
| Ipsilateral lung | 99.864 ± 25.382 | 85.191 ± 32.877 | 106.410 ± 16.332 | 0.423 | 0.412 | 0.146 |
| Esophagus | 1.029 ± 0.752 | 0.571 ± 0.364 | 1.490 ± 0.321 | 0.028 | 0.217 | 0.003 |

early-stage breast cancer are rare, a comparison of the target dose coverage, OARs sparing, and SCR among full IMRT, hybrid IMRT, and hybrid VMAT for treating early-stage breast cancer is extremely relevant. This study aimed to estimate the three RT plans, and the expectation was to bring more clinical options to RT for early-stage right-sided breast cancer.

IMRT showed a significant advantage in target dose coverage, and surrounding OARs spring for left-sided breast cancer after breast-conserving surgery [5-7]. This could result in better tumor control rate and lower toxicity, and late effects compared with the conventional tangential pair treatment beams. However, IMRT had inherent geometrical uncertainties arising from the setup error and target motion, which offset the merits of IMRT for breast cancer [7,8,20]. Combining two opposed tangential open beams and IMRT beams, the hybrid IMRT plan might solve the geometrical uncertainties of IMRT. Nakamura et al. [8] compared the plan quality and robustness of the dose distributions against setup and motion uncertainties among four RT plans. They confirmed that hybrid IMRT performed better robustness against the uncertainties than full IMRT, and it offered excellent plan quality. Fogliata et al. [21] compared the dosimetric difference for the involved OARs among 3D-CRT plan with field in field technique, and two VMAT plans (VMAT_full and VMAT_tang, gantry rotation partial arc from about 295° to 173° without and with a sector of 0 MU, respectively) for breast cancer. They proved that full VMAT had an obvious weakness in radiating a higher mean dose to the nearby OARs compared with VMAT_tang. Considering the excellent characteristics of hybrid plans and the lack of studies on hybrid VMAT plan, here, we eagerly studied the clinical dosimetric characteristics and SCR of full IMRT, hybrid IMRT, and hybrid VMAT, and we found that hybrid IMRT was superior to full IMRT and hybrid VMAT in target quality, and OARs sparing for early-stage right-sided breast cancer. Adopting the VMAT_tang (partial arcs with a sector of 0 MU) method from Fogliata et al. [21] study, instead of two opposed tangential open beams plus a complete half arc in our study, the performance of hybrid VMAT in protecting peripheral OARs might be improved. However, different from irradiating the only target PTV as in Fogliata et al. [21] study, the hybrid VMAT in our study delivered a boost dose to the tumor bed, and achieved better CI and HI for both the tumor bed and the PTV. Thus, the hybrid VMAT with a complete half arc beam might be reasonable in this study. However, the half arc beam delivered only 20% of the total dose by continuous rotation 180°, and the dose to the surrounding OARs inevitably increased.

As a tumor with a better therapeutic effect and longer life expectancy than most other tumors, the radiation-related risk is the most serious sequela for breast cancer survivors, which has been confirmed by numerous epidemiological cohort studies [22]. The occurrence of secondary cancer is closely related to the tissues and

organs themselves. Studies have shown that fatal secondary cancer mainly occurs in the stomach, lungs, and colon, and the thyroid has a particularly low threshold of SCR (mean dose as low as 0.05 Gy in children and young adults) [22,23]. In addition, the occurrence of secondary cancer depends on the radiation dose. Secondary cancer tends to occur in volumes receiving a total dose or near volumes receiving dose from 2 Gy to 50 Gy radiation [22,24]. Several studies demonstrated that SCR dramatically increased when receiving a dose reaching a certain range in the kidney (from 1 Gy to 15 Gy), stomach and pancreas (from 1 Gy to 45 Gy), and bladder and rectum (from 1 Gy to 60 Gy) [22,25]. In our study, seeking the least toxic radiation modality for breast cancer, we compared the SCR of three modalities for the contralateral breast, contralateral lung, ipsilateral lung, and esophagus.

Recently, Schneider proposed a calculation model, namely, the EAR model, which can be adopted for SCR calculation and evaluation utilizing DVH data from the RT plan and related radiobiological parameters [16,19]. The EAR model has proved its feasibility to assess the SCR for patients with nasal natural killer T-cell lymphoma and breast cancer [19,21]. Fogliata et al. [21] applied the EAR model to compare the SCR among 3D-CRT, VMAT_full, and VMAT_tang for breast cancer. And they confirmed that VMAT_tang had advantages in reducing RT toxicity for the ipsilateral organs compared with 3D-CRT with field in field technique when they delivered the same SCR to the contralateral organs.

In this study, we also adopted the EAR model to calculate the SCR for right-sided breast cancer, and our results demonstrated that the hybrid IMRT performed best in target quality, OARs spring, and SCR to peripheral OARs. However, if the half arc had a sector of 0 MU in hybrid VMAT, the performance of hybrid VMAT in SCR to adjacent OARs probably approached or achieved the effect of hybrid IMRT. The percentage of radiated dose and the effective dose delivery angle for the arc beam in the VMAT_tang in Fogliata's study and the hybrid VMAT in our study was quite different. This could translate into a differentiated radiation dose and SCR to the nearby healthy tissue. Of course, the results of the EAR model in predicting SCR depend on the accuracy of commercial TPS system modeling and related biological parameters.

Hybrid IMRT combined the advantages of 3D-CRT and IMRT in treating early-stage right-sided breast cancer. Hybrid IMRT was shown to have significant advantages in target dose coverage, OARs sparing, and SCR to nearby normal tissues. Hybrid IMRT is worthy of clinical application and promotion.

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