Cardiac dosage comparison among whole breast irradiation and partial breast irradiation techniques

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Background: This planning comparison study aimed to compare the dosimetry of the organs at risk (OARs), especially the heart and the left anterior descending artery (LAD), among the interstitial brachytherapy (ISBT), the partial breast external beam radiotherapy (PB-EBRT) and the whole breast external beam radiotherapy (WB-EBRT) in left-sided early breast cancer patients.

Methods: Patients with early stage left-sided breast cancer receiving ISBT under prescription of 26–28 Gy/4 fractions were included. For each patient, the digital phantom PB-EBRT and WB-EBRT plan were created using the same computed tomography (CT) images and contours in the ISBT plans, under the prescriptions of 38.5 Gy/10 fractions and 50 Gy/25 fractions respectively. Dosimetric parameters of lung, heart and LAD including mean dose, maximum dose, dose to certain volumes and volumes to certain dose were collected and compared after converting into equivalent dose in 2 Gy fractions (EQD_2). ANOVA was used for statistical analysis.

Results: Twelve patients were included in this study. All parameters in the whole breast irradiation (WBI) were significantly higher than both accelerated partial breast irradiation (APBI). Comparing between both APBI, there was no significant difference in the mean heart dose of the ISBT and the PB-EBRT (1.05 *vs.* 0.47 Gy, P>0.05). The D_{max} of the LAD was 3.08, 1.80 Gy in ISBT and PB-EBRT, respectively (P>0.05). There were no significant differences between both APBI in lung dosimetry, except for D_{max} (14.86 *vs.* 36.87 Gy, P<0.05) and $D_{2\ cc}$ (10.56 *vs.* 23.02 Gy, P<0.05).

Conclusions: Compared to WBI, both APBI showed a significant reduction in radiation dose for the heart, LAD and lung. The dosimetry of the heart, LAD and lung was equivalent low in both APBI. Further investigations of clinical outcomes of OARs in APBI were needed.

Keywords: Accelerated partial breast irradiation (APBI); interstitial brachytherapy (ISBT); dosimetry; breast cancer

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Introduction

The adjuvant whole breast irradiation (WBI) after breast conservative surgery (BCS) is now the standard care for early-stage breast cancer patients (1). From the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) study, adjuvant WBI for early-stage breast cancer patients receiving BCS would have significantly higher loco-regional control survival and overall survival (2). However, long term follow-up indicated that the incidence of major coronary events increased linearly with the mean dose to the heart by 7.4% per Gray (3). In the recent update results of the

Danish part of the above study, the linear increase in the excess odds ratio of major coronary events was 19% per Gray in the tangential photon techniques patients, and for the patients treated with electron techniques, there was no significant association between mean heart dose and the risk of major coronary events (4). In recent years, accelerated partial breast irradiation (APBI) has obtained more and more attention due to early diagnosis of breast cancer and the significant reduction of total treatment time (5). Studies have shown that the most common site of tumor recurrence is the region around the tumor bed after surgery in early breast cancer (6,7), therefore relatively large fraction size irradiation over the lumpectomy cavity in a shorter time should have a considerably good local control rate (8). In conventional WBI, it will take around 5–6 weeks for a complete treatment course, whereas APBI can shorten the treatment course to 4–5 days. It is essentially beneficial for the radiation oncologists and the patients especially in the COVID-19 pandemic nowadays (9).

There are several modalities of APBI and the most common techniques are the interstitial brachytherapy (ISBT) and the partial breast external beam radiotherapy (PB-EBRT) (10-12). Compared to the whole breast external beam radiotherapy (WB-EBRT), the APBI can lower the dose of the normal tissue and the organs at risk (OARs) received (e.g., contralateral breast, lung and heart) (13). Recently, cardiovascular toxicity of radiotherapy has been emphasized, therefore decreasing the heart dose should be taken into account especially in the long-lived and left-sided breast cancer patients (14).

However, there are few studies comparing the dosimetry among different techniques of APBI and WBI (15). Furthermore, fewer studies focus on cardiovascular toxicity and dosimetry and the results still remain equivocal (16). The purpose of this study was to compare the dosimetry of the heart, the left anterior descending artery (LAD) and the lung among the ISBT, the PB-EBRT and WB-EBRT. We present the following article in accordance with the STROBE reporting checklist (available at https://tro.amegroups.com/article/view/10.21037/tro-21-27/rc).

Methods

Ethics

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Kaohsiung Veterans General Hospital Institutional Review Board (VGHKS21-CT7-01) and individual consent for this retrospective analysis was waived.

Patient eligibility

We included patients with early stage left breast cancer receiving ISBT from January, 2015 to June, 2021. All patients were treated with multi-catheter interstitial brachytherapy (MIBT) with APBI protocol by high-dose-rate (HDR) Ir-192 stepping source. The selection criteria for ISBT were based on the American Society for Radiation Oncology (ASTRO) APBI guideline consensus statement (11,12). According to these criteria, this study included patients ≥45-year-old, tumor greatest diameter ≤2 cm (pT1 disease), surgical margins ≥2 mm, negative of lymphovascular invasion, positive of estrogen receptor (ER) and negative of nodal metastasis or distant metastasis.

Clinical target volume (CTV) definition and contouring

The computed tomography (CT) scans with 1.25 or 2.5 mm slice thickness were acquired for each patient from lower neck to upper abdomen including bilateral breasts and lungs after the implantation of catheters. The lumpectomy cavity was first delineated, then a margin was added for clinical suspicious tumor spread and pathological tumor-free margin in all three dimensions. In the ISBT plan, the planning target volume (PTV) was considered as CTV because the position relationship between the catheters and the lumpectomy cavity was fixed and there was no setup error in this treatment modality. A digital phantom PB-EBRT plan and a digital phantom WB-EBRT plan was created for each patient based on the same CT images. In the PB-EBRT plan, the PTV was defined as a 10 mm margin applied to CTV (11). In the WB-EBRT plan, the whole breast was contoured as CTV and a margin of 5 mm was added as PTV (17). OARs included ipsilateral and contralateral breasts, lungs, skin, ribs, heart and LAD. The delineation of the cardiovascular system was based on the 2020 Danish Multidisciplinary Cancer Groups (DMCG) National guidelines of delineation of whole heart and substructures in thoracic radiation therapy (18). NSABP B-39/RTOG 04-13 guidelines were used for target and normal tissue constraints (19).

ISBT plan

Total dose of 26–28 Gy in 4 fractions was prescribed. If feasible, two fractions a day were performed for all patients.

Oncentra Brachy v4.5.3 (Nucletron, Veenendaal, The Netherlands) planning system was used for contouring, catheters reconstruction and treatment plan. Dosage optimization was done by the planning system first then confirmation by manual adjustment of the radiation oncologists to reduce the hot spot and the non-uniformity of the dose prescription. Treatment plans were accepted if requirements for target and normal tissue were met as at least 90% of PTV coverage under prescribed dose; dose-nonuniformity ratio (DNR) = $V_{150}/V_{100} \leq 70\%$.

Digital phantom PB-EBRT plan

For PB-EBRT, we used the same CT images from ISBT CT simulation. All contours on Oncentra Brachy were transferred to Pinnacle[3] v14.0.0 (PHILIPS, Fitchburg, WI, USA). The digital phantom PB-EBRT plan was created for each patient. The CTV and OARs were the same as in the ISBT plan, whereas the PTV in the digital phantom PB-EBRT plan was defined as a 10 mm margin applied to CTV in all directions in consideration of daily setup errors and organ motions, and 4 mm from body surface was excluded from the PTV. The prescribed dose of 38.5 Gy in 10 fractions was set. Volumetric modulated arc therapy (VMAT) with two partial arcs with optimal gantry and collimator rotations were employed to achieve minimal ipsilateral lung and heart irradiation. Each plan was accepted if all the following constraints for coverage, homogeneity and OARs were fulfilled: PTV coverage (D_{100}) ≥95%, $D_{105} \leq 5\%$, ipsilateral lung V_{30} <15%, contralateral lung V_5 <15% and heart V_5 <40% (19).

Digital phantom WB-EBRT plan

For WB-EBRT, we used the same CT images from ISBT CT simulation. All contours on Oncentra Brachy were transferred to Pinnacle[3] and the whole breast was contoured on Pinnacle[3]. The digital phantom WB-EBRT plan was created for each patient. The OARs were the same as in the ISBT plan, whereas the CTV was defined as whole breast and the PTV was defined as a 5 mm margin applied to CTV in all directions in consideration of daily setup errors and organ motions, and 4 mm from body surface was excluded from the PTV. The prescribed dose in the digital phantom WB-EBRT plan was given as 50 Gy in 25 fractions. VMAT with two partial arcs with optimal gantry and collimator rotations were employed to achieve minimal ipsilateral lung and heart irradiation. Each plan was accepted if all the following constraints for coverage, homogeneity and OARs were fulfilled: PTV coverage (D_{100}) ≥90%, $D_{105} \leq 5\%$, ipsilateral lung V_{20} <30% and mean heart dose <10 Gy (20).

Dosimetric assessment and statistical analysis

Dose-volume histograms (DVH) were acquired for analyzing the heart dose for each patient in the ISBT plan, the digital phantom PB-EBRT plan and the digital phantom WB-EBRT plan. Parameters of the maximum dose (D_{max}), mean dose (D_{mean}), dose to certain absolute volumes $D_{Volume/cc}$ ($D_{2\ cc}$, $D_{10\ cc}$ and $D_{25\ cc}$) and volumes receiving 5, 10 and 20 Gy ($V_{5\ Gy}$, $V_{10\ Gy}$ and $V_{20\ Gy}$) were calculated. As for LAD, which is generally regarded as a serial organ, dose-volume parameters were not applicable, thus the D_{max} and D_{mean} were used for parameter analysis. The parameters of lung were also collected, including D_{max}, D_{mean}, $D_{2\ cc}$, $D_{10\ cc}$, $D_{25\ cc}$, $V_{5\ Gy}$, $V_{10\ Gy}$ and $V_{20\ Gy}$.

The dose of the ISBT plan may not be radiobiological comparable to the digital phantom PB-EBRT plan and the digital phantom WB-EBRT plan due to different fraction sizes. Therefore, the dose parameters were calculated to biological equivalents using the linear quadratic equation, and an alpha/beta of 3 Gy was used for late effects to the heart and lung (21).

The mean and standard deviation (SD) for each dosimetric parameter was calculated. The significance of the difference among the above three treatment plans was assessed using ANOVA. The null hypothesis was assumed that there were no significant statistical differences among three groups of treatment plans. If there were significant differences noted among three groups of treatment plans, post-hoc analysis was further applied for comparison between each two groups. All statistical analyses were performed using SPSS Statistics v25. We considered $P<0.05$ to be statistically significant.

Results

In our institution, 25 breast cancer patients received ISBT treatment, and 12 patients (48%) had left-sided lesions. The mean age of the 12 left-sided breast cancer patients was 57.8±8.3 (mean ± SD) years old and all patients included were female. According to the 8th edition of American Joint Committee on Cancer (AJCC) cancer staging system, 1 patient was ductal carcinoma in situ (DCIS) disease and 11 patients were stage IA [pT1N$_{(sn)}$0M0] disease (22). Among these 12 patients, 1 (8.3%) was located at upper

Table 1 Patients characteristics (n=12)

Variables	Number (%)	Mean ± SD
Age	–	57.8±8.3
Gender		
Female	12 (100.0)	–
Male	0	–
AJCC 8th stage group		
DCIS	1 (8.3)	–
IA (pT1N$_{(sn)}$0M0)	11 (91.7)	–
Quadrant		
Upper inner	1 (8.3)	–
Upper outer	4 (33.3)	–
Lower inner	3 (25.0)	–
Lower outer	4 (33.3)	–
ISBT doses		
28 Gy/4 fractions	11 (91.7)	–
26 Gy/4 fractions	1 (8.3)	–
Digital phantom PB-EBRT doses		
38.5 Gy/10 fractions	12 (100.0)	–
Digital phantom WB-EBRT doses		
50 Gy/25 fractions	12 (100.0)	–

All the data are original from the study approved by Kaohsiung Veterans General Hospital Institutional Review Board (VGHKS21-CT7-01). AJCC, American Joint Committee on Cancer; DCIS, ductal carcinoma in situ; ISBT, interstitial brachytherapy; PB-EBRT, partial breast external beam radiotherapy; WB-EBRT, whole breast external beam radiotherapy; SD, standard deviation.

inner quadrant, 4 (33.3%) were at upper outer quadrant, 3 (25%) were at lower inner quadrant and 4 (33.3%) were at lower outer quadrant. The mean number of catheters inserted was 12.75 (range, 9–20), and the mean plane of catheters was 2.67 (range, 2–4). Eleven patients received a total 28 Gy in 4 fractions, and one patient received 26 Gy in 4 fractions. For the digital phantom PB-EBRT plan, all 12 patients received 38.5 Gy in 10 fractions. For the digital phantom WB-EBRT plan, all 12 patients received 50 Gy in 25 fractions. The characteristics of the patients are summarized in *Table 1*. The axial view base on CT simulation of the isodose distribution in the same patient of ISBT, PB-EBRT and EB-EBRT were presented in *Figure 1*.

After converting to equivalent dose in 2 Gy fractions (EQD_2), the dosimetry of heart for the ISBT plan, digital phantom PB-EBRT plan and digital phantom WB-EBRT plan were presented in *Table 2*. The mean heart dose in the ISBT plan, the digital phantom PB-EBRT plan and the digital phantom WB-EBRT plan was 1.05, 0.47, 3.24 Gy respectively (P<0.05). A box-plot of the mean heart dose in different types of treatment modalities was presented in *Figure 2*. Both APBI techniques were significantly lower than the WBI technique (P<0.05), and there was no significant difference between two techniques of APBI (P=0.64). There was also a significant difference in D_{max}, $D_{2\ cc}$, $D_{10\ cc}$, and $D_{25\ cc}$ among three techniques of radiotherapy (*Table 2*). Compared to the digital phantom WB-EBRT plan, the dosimetry in both APBI plans was all significantly lower in post-hoc analysis, whereas no significant difference was noted between two groups of APBI (*Table 2*). For the volume irradiated by the specific dose (5, 10 and 20 Gy), there was also a significant difference in $V_{5\ Gy}$, $V_{10\ Gy}$ and $V_{20\ Gy}$ among three methods of irradiation, and the parameters in the digital phantom WB-EBRT plan were all significantly higher than the two methods of APBI. There was no significant difference between two methods of APBI (*Table 2*).

As for the dose of LAD, there was a significant difference in the mean dose among the ISBT plan, the digital phantom PB-EBRT plan and the digital phantom WBEBT plan, and the post-hoc analysis showed that both APBI plans were significantly lower than the digital phantom WB-EBRT plan, meanwhile the ISBT plan was significantly higher than the digital phantom PB-EBRT plan (*Table 3*). The mean LAD dose in the ISBT plan, the digital phantom PB-EBRT plan and the digital phantom WB-EBRT plan was 1.68, 0.49, 3.34 Gy respectively. Although there was a significant difference in D_{max} among three techniques of irradiation, there was no significant difference between the ISBT plan and the digital phantom PB-EBRT plan with P=0.703. The value of D_{max} in the ISBT plan, digital phantom PB-EBRT plan and digital phantom WB-EBRT plan was 3.08, 1.80 and 12.13 Gy, respectively (*Table 3*).

Comparing the lung dosimetry among the ISBT plan, the digital phantom PB-EBRT plan and the digital phantom WB-EBRT plan, all parameters were significantly different among three techniques. In post-hoc analysis, both the ISBT plan and the digital phantom PB-EBRT plan were all significantly lower than the digital phantom WB-EBRT plan (*Table 4*). There was no significant difference in the D_{mean}, $D_{10\ cc}$, $D_{25\ cc}$ between the ISBT plan and the digital phantom PB-EBRT plan (*Table 4*). However, the D_{max} and

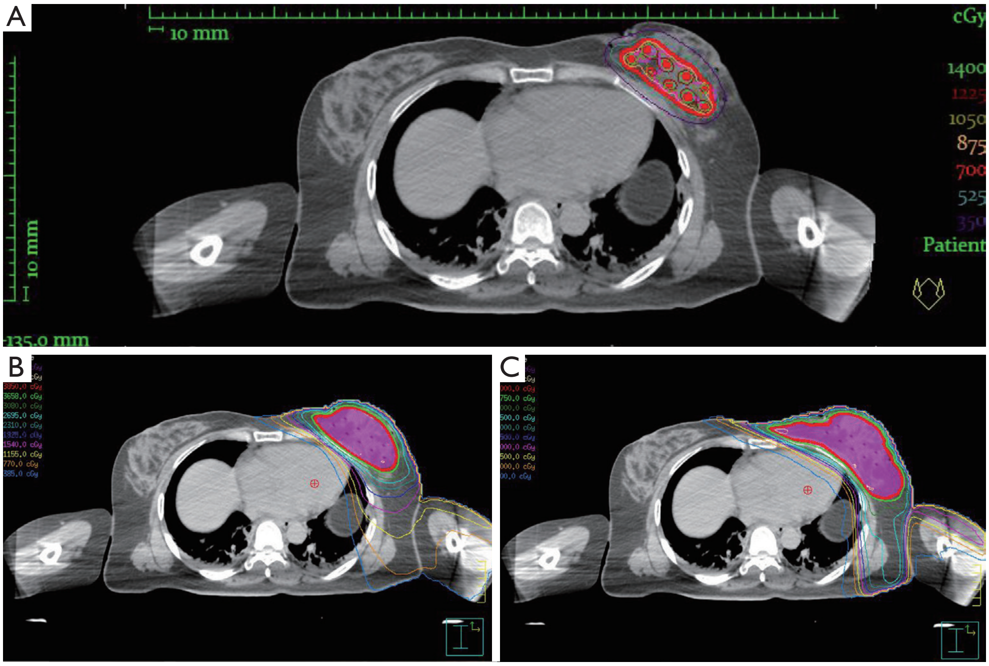

Figure 1 Axial view base on CT simulation of the isodose distribution. (A) ISBT; (B) PB-EBRT; (C) WB-EBRT. The figure is original. CT, computed tomography; ISBT, interstitial brachytherapy; PB-EBRT, partial breast external beam radiotherapy; WB-EBRT, whole breast external beam radiotherapy.

Table 2 Dosimetry of heart among ISBT, digital phantom PB-EBRT and digital phantom WB-EBRT

Dosimetric parameter	ISBT [1] (Gy, mean ± SD)	Digital phantom PB-EBRT [2] (Gy, mean ± SD)	Digital phantom WB-EBRT [3] (Gy, mean ± SD)	P	P (post-hoc)		
					1 *vs.* 2	1 *vs.* 3	2 *vs.* 3
D_{mean}	1.05±0.30	0.47±0.23	3.24±0.93	<0.001	0.064	<0.001	<0.001
D_{max}	9.38±4.14	20.46±21.67	47.47±5.87	<0.001	0.136	<0.001	<0.001
$D_{2\ cc}$	6.74±2.60	10.97±13.19	33.15±8.29	<0.001	0.530	<0.001	<0.001
$D_{10\ cc}$	4.85±1.79	4.21±4.29	18.99±9.25	<0.001	0.967	<0.001	<0.001
$D_{25\ cc}$	3.62±1.24	1.64±1.20	10.99±7.46	<0.001	0.552	0.001	<0.001
$V_{5\ Gy}$	1.85±1.71 (%)	1.08±1.40 (%)	9.44±4.89 (%)	<0.001	0.833	<0.001	<0.001
$V_{10\ Gy}$	0.08±0.11 (%)	0.57±0.79 (%)	4.30±2.98 (%)	<0.001	0.800	<0.001	<0.001
$V_{20\ Gy}$	0 (%)	0.21±0.37 (%)	1.94±1.69 (%)	<0.001	0.876	0.001	<0.001

All parameters were converted to EQD_2. All the data are original from the study approved by Kaohsiung Veterans General Hospital Institutional Review Board (VGHKS21-CT7-01). ISBT, interstitial brachytherapy; PB-EBRT, partial breast external beam radiotherapy; WB-EBRT, whole breast external beam radiotherapy; EQD_2, equivalent dose in 2 Gy fractions; SD, standard deviation.

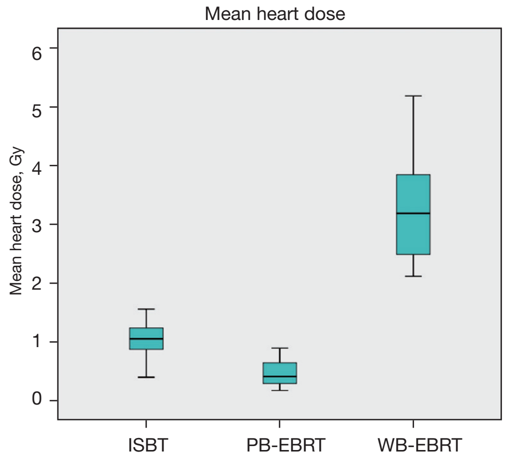

Figure 2 Box-plot of the mean heart dose in different types of treatment modalities. The figure is original. ISBT, interstitial brachytherapy; PB-EBRT, partial breast external beam radiotherapy; WB-EBRT, whole breast external beam radiotherapy.

$D_{2\ cc}$ in the ISBT plan were significantly lower than those in the digital phantom PB-EBRT plan (*Table 4*). For the volume irradiated by the specific dose, there was significant difference in $V_{5\ Gy}$, $V_{10\ Gy}$ and $V_{20\ Gy}$ among three techniques, and both APBI groups were all lower than the digital phantom WB-EBRT group, but no significant difference was noted between the ISBT plan and the digital phantom PB-EBRT plan (*Table 4*).

Discussion

In conventional WBI, the standard prescribed dose was suggested 45–50.4 Gy in 25–28 fractions to the whole breast. For left-sided breast cancer patients under this prescription, the mean heart dose could range from 1.29–1.94 to 8.5–8.9 Gy (23,24). The high variability may due to different consistency of manual contouring of the heart structure, the experience and the technique of the treatment and even the anatomy difference in every patient. Several studies had indicated that the risk of myocardial infarction has a linear dose response to the mean heart dose (3,4,23-28). Patients receiving a mean dose of 20 Gy to the heart had a 3.4-fold higher myocardial infarction rate than unirradiated patients, and the cumulative risk of myocardial infarction increased over time from the year when breast cancer was diagnosed (24). Meanwhile, there was also a trend that the excess rate ratio of myocardial infarction was higher for younger women (20,24). This is essentially important because of the early detection of breast cancer and the prolonged survival after surgery and radiotherapy. Reducing the mean heart dose is expected to contribute to lower the cardiovascular events of long-term breast cancer survivors.

APBI has been proven that the long-term ipsilateral breast-tumor recurrence (IBTR) rate was non-inferior to that of WBI in selected patients based on phase 3 randomized trials (8,29). However, long-term follow up of the heart and lung toxicity has not been interpreted yet. Before regular application of APBI treatment, it will be helpful to understand the differences of heart and LAD dosimetry between WBI and APBI. In our study, the mean heart dose was 3.24, 1.05 and 0.47 Gy in the WB-EBRT plan, the ISBT plan and the PB-EBRT plan, respectively. The mean heart doses in both APBI techniques were all significantly lower than that in the WBI technique ($P<0.05$, *Table 2*). The mean heart doses in both APBI plans were all lower than the DEGRO recommendation, which suggested the mean heart dose <2.5 Gy (30). For dosimetry comparison, we used the same CT images in the ISBT plan and both digital phantom plans, therefore the dosimetry of the heart in the digital phantom PB-EBRT plan and the digital phantom WB-EBRT plan could be underestimated, because the breast tissue was pulled away from its normal position due to the implantation of the catheters. The distance between the actual tumor bed and the heart was farther compared to preoperative CT images. It was our understanding that the external beam technique could shape the lower isodose lines more apart from the heart due to higher conformal capability. On the other hand, brachytherapy with dose delivery via multi-catheter had less capacity for heart sparing in order not to compromise PTV coverage.

Besides, there were few studies mentioning the dose distribution impact on the LAD. Stenosis of the coronary artery may lead to consequential coronary artery disease (CAD) and the LAD is one of the most important arteries. Nilsson *et al.* demonstrated that the distribution and extent of coronary stenosis in the heart was correlated to the radiation dose delivered and its location in the heart (31). In our study, the D_{max} of the LAD was 3.08 and 1.80 Gy in the ISBT plan and the digital phantom PB-EBRT plan respectively with no significant difference and the D_{max} was 12.13 Gy in the digital phantom WB-EBRT plan. In a left-sided breast cancer patient receiving irradiation, the LAD and the left ventricle usually lie in the high dose region due to the anatomic location of the heart. The LAD is situated at the surface of the left heart, which is nearest the chest

Table 3 Dosimetry of LAD among ISBT, digital phantom PB-EBRT and digital phantom WB-EBRT

Dosimetric parameter	ISBT [1] (Gy, mean ± SD)	Digital phantom PB-EBRT [2] (Gy, mean ± SD)	Digital phantom WB-EBRT [3] (Gy, mean ± SD)	P	P (post-hoc)		
					1 *vs.* 2	1 *vs.* 3	2 *vs.* 3
D_{mean}	1.68±1.00	0.49±0.30	3.34±0.68	<0.001	0.001	<0.001	<0.001
D_{max}	3.08±2.01	1.80±2.34	12.13±5.63	<0.001	0.703	<0.001	<0.001

All parameters were converted to EQD_2. All the data are original from the study approved by Kaohsiung Veterans General Hospital Institutional Review Board (VGHKS21-CT7-01). ISBT, interstitial brachytherapy; PB-EBRT, partial breast external beam radiotherapy; WB-EBRT, whole breast external beam radiotherapy; EQD_2, equivalent dose in 2 Gy fractions; LAD, left anterior descending artery; SD, standard deviation.

Table 4 Dosimetry of lung among ISBT, digital phantom PB-EBRT and digital phantom WB-EBRT

Dosimetric parameter	ISBT [1] (Gy, mean ± SD)	Digital phantom PB-EBRT [2] (Gy, mean ± SD)	Digital phantom WB-EBRT [3] (Gy, mean ± SD)	P	P (post-hoc)		
					1 *vs.* 2	1 *vs.* 3	2 *vs.* 3
D_{mean}	1.06±0.33	1.11±0.51	5.76±1.72	<0.001	0.993	<0.001	<0.001
D_{max}	14.86±7.06	36.87±13.84	50.02±2.32	<0.001	<0.001	<0.001	0.005
$D_{2\ cc}$	10.56±5.31	23.02±13.06	43.34±5.29	<0.001	0.005	<0.001	<0.001
$D_{10\ cc}$	7.37±3.90	14.84±11.85	36.30±8.79	<0.001	0.132	<0.001	<0.001
$D_{25\ cc}$	5.29±2.87	9.49±9.06	29.10±11.20	<0.001	0.488	<0.001	<0.001
$V_{5\ Gy}$	3.56±2.81 (%)	5.83±3.52 (%)	25.54±9.22 (%)	<0.001	0.647	<0.001	<0.001
$V_{10\ Gy}$	0.63±0.85 (%)	2.59±2.27 (%)	14.80±6.92 (%)	<0.001	0.532	<0.001	<0.001
$V_{20\ Gy}$	0.03±0.09 (%)	0.77±1.29 (%)	7.85±4.22 (%)	<0.001	0.779	<0.001	<0.001

All parameters were converted to EQD_2. All the data are original from the study approved by Kaohsiung Veterans General Hospital Institutional Review Board (VGHKS21-CT7-01). ISBT, interstitial brachytherapy; PB-EBRT, partial breast external beam radiotherapy; WB-EBRT, whole breast external beam radiotherapy; EQD_2, equivalent dose in 2 Gy fractions; SD, standard deviation.

wall, therefore the LAD would receive higher dose despite slope dose gradient.

In a study by Chan *et al.*, the authors performed the dosimetry comparison between multi-catheter APBI and WB-EBRT (15). The maximum dose of LAD was 6.0 and 45.9 Gy respectively (P<0.05). The dose in the ISBT plan was significantly lower than the WB-EBRT plan. To our knowledge, there was no study comparing the radiation dose to the LAD in different APBI methods. In our study, we found that no matter which technique of APBI was used, both could greatly reduce the radiation dose to the LAD, suggesting possibly decreasing the risks of CAD.

In WBI, all parameters of lung dosimetry were significantly higher than both APBI techniques, and the D_{max}, D_{mean} and $V_{20\ Gy}$ could reach 50.02, 5.76 and 7.85% respectively. We noticed that in the lung dosimetry compared between the ISBT plan and the digital phantom PB-EBRT plan, the dose in the ISBT plan was significantly lower than in the digital phantom PB-EBRT plan in the doses to small volumes (D_{max} and $D_{2\ cc}$), and no significant difference when the volumes increased. According to the characteristic of partial breast irradiation, the ipsilateral lung volume receiving radiation exposure was confined in a certain region. As a consequence, when the volume increased, the ratio of the dose taken into account would then decrease. In addition, in order to spare the heart receiving additional exposure dose and by the limitation of the physics of radiation, the lung would receive an additional low dose in compensation in the digital phantom PB-EBRT plan.

One of the remarkable studies performed by Major *et al.* conducted a dosimetric comparison using MIBT and intensity modulated radiotherapy (IMRT) for APBI with focus on dosimetry to normal tissues and OARs (32). This was the first study using an advanced external beam radiotherapy technique, IMRT, for partial breast irradiation. In their study, the results were identical with our study, while the mean heart dose was 4.5 and 2 Gy in MIBT and IMRT respectively (P<0.05) and the ipsilateral lung was spared better with MIBT. The author concluded that the MIBT could generally spare the normal tissues and critical structures (except for heart) better compared to IMRT.

Further studies were recommended to take into account the location in the breast quadrant of the tumor bed and the anatomy of the OARs to decide whether modalities of treatment were suitable. Medially-located tumors may receive higher mean heart dose and LAD dose compared to laterally-located tumors. The relative position of the heart and LAD and even the cardiac size was also needed to be evaluated before treatment. Another difference should be taken into account was the different breast volumes between Asian and Caucasian women. Asian women generally have smaller breast volumes compared to Caucasian women. Due to smaller breast volume, the tumor bed of the breast was closer to the chest wall, hence resulting in higher dose to the heart and LAD.

There are some limitations in this study. First, this is a retrospective study in a single center, and the study population was small. Second, the CT images used for the digital phantom plan were the same as the ISBT plan, therefore the body contour and the patient position were not identical to the real-world clinical practice. Third, the catheters indwelling in the breast may draw the breast tissue away from the chest wall from its normal condition and the catheters in the breast may slightly change the tissue inhomogeneity of breast. Forth, in this study the alpha/beta of the heart was set as 3 Gy due to late response tissue. However, the variability in the alpha/beta may lead to a different result in biological equivalent dose. In larger fraction size of ISBT, the alpha/beta of 3 Gy may not be suitable, therefore the biological equivalent dose may be underestimated. These limitations could lead to underestimate the dosimetry of the digital phantom plans.

Conclusions

The results of this study provided several useful information of dosimetric comparison of OARs for left-sided breast cancer patients receiving APBI. Based on our findings, the mean heart dose of the ISBT and the PB-EBRT were all significantly lower than the WB-EBRT. Meanwhile, the mean dose to the ipsilateral lung was equivalent low in both APBI techniques. Further investigations were needed whether the dosimetric outcome was correlated with the clinical outcome of OARs treated by ABPI.

Acknowledgments

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Footnote

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