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Cardiac doses with deep inspiration breath hold in breast cancer radiotherapy: direct comparison between WBI, PBI, and interstitial APBI

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Abstract

Background: The optimal radiotherapy technique for cardiac sparing in left-sided early breast cancer (EBC) is not clear. In this context, the aim of our dosimetric study was to compare cardiac and lung doses according to the type of radiotherapy — whole breast irradiation (WBI), external partial breast irradiation (PBI), and multicatheter interstitial brachytherapy-accelerated partial breast irradiation (MIB-APBI). The dosimetric results with the WBI and PBI were calculated with and without DIBH.

Materials and methods: Dosimetric study of 23 patients treated with WBI, PBI, with and without DIBH, or MIB-APBI. The prescribed dose was 40 Gy in 15 fractions for WBI and

PBI and 34 Gy in 10 fractions (bid) for MIB-APBI. Doses to the organs-at-risk (OAR) — heart, left anterior descending coronary artery (LAD), left ventricle (LV), and left lung — were recalculated to the equivalent dose in 2-Gy fractions (EQD2).

Results: The addition of DIBH significantly reduced EQD2 doses to all OARs (except for the left lung maximal dose) in WBI and PBI. MHD values were 0.72 Gy for DIBH-WBI, 1.01 Gy for MIB-APBI and 0.24 Gy for DIBH-PBI. There were no significant differences in cardiac doses between WBI with DIBH and PBI without DIBH. DIBH-PBI resulted in significantly lower mean doses to all OARs (except for maximum lung dose) compared to MIB-APBI. Conclusions: These results show that the use of DIBH significantly reduces cardiac doses in patients with left EBC. Partial irradiation techniques (PBI, MIB-APBI) significantly reduced cardiac doses due to the smaller clinical target volume. The best results were obtained with DIBH-PBI.

Key words: left breast irradiation; brachytherapy; cardiac doses

Introduction

Postoperative radiation therapy (RT) plays a key role in the treatment of early breast cancer (EBC), reducing the risk of local recurrence and cancer-specific mortality in patients treated with breast-conserving surgery (BSC) [1]. However, particularly in left breast cancer, there is an important risk of radiation-induced cardiac morbidity and mortality [2, 3], which increases linearly in a dose-dependent manner [4].

Numerous strategies have been developed to reduce radiation doses to the heart and its key structures — the left anterior descending (LAD) artery and the left ventricle (LV) — during radiotherapy for left breast cancer. Although whole breast irradiation (WBI) has long been the standard of care, patients with low-risk disease may be eligible to undergo partial breast irradiation (PBI), which reduces the target volume, thereby decreasing doses to these critical heart structures. A modified approach to PBI, known as accelerated partial breast irradiation (APBI), can also shorten treatment duration. Several different APBI techniques are available, including brachytherapy, intraoperative radiation therapy, and high-precision external beam radiotherapy. Of these techniques, the one supported by the largest body of evidence is multicatheter interstitial brachytherapy (MIB-APBI) [5]. Deep inspiration breath hold (DIBH) can further reduce the cardiac risks associated with radiotherapy [6]. In short, there are a wide range of treatment options, all of which provide excellent target coverage with good sparing of organs at risk (OAR) [7]. However, given that patients with low-risk EBC are likely to

survive for many years, it is crucial to minimize radiation doses to the heart and its key substructures. At present, however, the optimal approach to cardiac sparing is not entirely clear.

At our institution, we have treated eligible patients with MIB-APBI since 2012. In addition, we have been using DIBH for WBI in patients with left breast cancer since 2017. Although numerous studies have demonstrated the value of DIBH to reduce cardiac doses [8], there is a notable lack of studies directly comparing cardiac doses achieved with MIB-APBI to external beam radiotherapy techniques (such as WBI and PBI) combined with DIBH [9].

In this context, we performed a dosimetric study to compare three different techniques — WBI, external beam PBI, both delivered with and without DIBH, and MIB-APBI. Given the importance of cardiac sparing in patients with left-sided, EBC, the main aim of the study was to determine which of these techniques produces the lowest doses to the heart and its key structures.

Materials and methods

This was a prospective dosimetric study of 23 patients with low-risk, left-sided EBC. We directly compared dosimetric results obtained with the three most common radiotherapy techniques (WBI, PBI, and MIB-APBI) used to treat patients with EBC. The dosimetric results with the WBI and PBI were calculated with and without DIBH. The MIB-APBI plans were simulated only, without real brachytherapy procedures.

Consecutive patients who met criteria for PBI at our institution were considered for study inclusion. Inclusion criteria were as follows: age $\geq$ 55 years; diagnosis of invasive ductal carcinoma, or ductal carcinoma in situ $\leq$ 3 cm; stage pN0M0; unicentric, unifocal disease; clear resection margins (“no tumour in ink”); hormone sensitive; HER2 negative with unconfirmed BRCA positivity; any tumour grade; and no tumour invasion of blood vessels or lymph nodes. All patients provided written informed consent and the study was approved by the ethics committee at our institution (protocol code BCCG 1707).

The patient’s clinical and demographic characteristics are shown in Table 1. The tumour location (quadrant) for each patient is shown in Figure 1. The patient’s breath-hold capacity was assessed at baseline and after one-week of breath-hold training for DIBH. The aim was to hold a steady deep breath for $\geq$ 20 seconds. Patients who were able to meet this threshold were simulated on the computed tomography (CT) scanner (Siemens Somatom Sensation, Siemens AG, Germany) in the supine position with the arms elevated. Simulation was performed during a normal breathing cycle and then during DIBH using the Real Time

Position Management (RPM) audio-visual system (Varian Medical Systems, Inc., CA, USA). Target structures and OARs were contoured in both CT series (i.e., with and without DIBH).

For MIB-APBI, the estimated tumour bed (ETB) and clinical target volume (CTV) were defined according to GEC-ESTRO recommendations [10]. The CTV was delineated around the ETB to ensure a safety margin ≥ 20 mm in all directions, which was calculated by adding the free resection margin plus an additional safety margin ≥ 10 mm. The CTV was cropped to the chest wall (pectoral muscle or ribs) and 5 mm from the skin surface.

The CTV was identical for PBI and MIB-APBI plans. For WBI, the CTV comprised the entire breast in accordance with clinical recommendations [11]. The planning target volume (PTV) was created by adding a 7-mm margin in all directions around the CTV, which was then cropped onto the body surface. The PTV was defined only for WBI and PBI. No PTV was defined for MBI-APBI. The OARs, including the whole heart, the LV and the LAD, and left lung, were defined according to published recommendations and delineated manually [12]. The planning procedure was performed during 21 (+ 5 days) since the surgery.

Plan calculations were performed on the Eclipse planning system (Varian Medical Systems, Inc.; CA, USA). The prescribed dose for WBI and PBI was 40 Gy in 15 fractions with ≥ 95% prescribed dose coverage to ≥ 95% of the target volume. The medial and lateral tangential field-in-field (FIF) photon beam technique was used for all external beam treatment plans (Fig. 2).

In the patients who had a planning CT during the normal breathing cycle and during DIBH, MIB-APBI was simulated with plastic tubes and 15 mm spacing in a triangular setting according to the international Paris school recommendations [10] and our previously published experience [13, 14]. The prescribed dose for MIB-APBI was 34 Gy in 10 fractions (bid) with ≥ 90% prescribed dose coverage to ≥ 90% of the target volume. The target dose nonuniformity ratio was ≤ 0.25 (calculated as V100/V150). Additional treatment characteristics are shown in Table 2.

Dose volume histograms were used to evaluate the maximum and mean doses to the heart, LAD, LV, and left lung. All doses were calculated and corrected to biologically equivalent doses (BED) in 2 Gy fractionation (EQD2) according to the LQ model. The α/β ratio for the calculation of the OAR dose was 3.0.

Statistical analysis

Basic descriptive statistics were performed, including medians, means, and standard deviation (SD) for continuous data and absolute and relative frequencies for categorical data. The D'Agostino omnibus normality test was used to check the distribution of the continuous data. Paired two-sample t-test and regression analyses were used to evaluate the differences between the data sets. Linear regression and correlation analysis was performed to find a significant relationship between continuous variables. The cut-off for statistical significance was set at $p < 0.05$. All statistical analyses were performed using the NCSS statistical software program, v.8 (NCSS, Keysville, UT, USA).

Results

Table 3 shows the EQD2 values to the OARs according to the radiotherapy technique (WBI, PBI, with and without DIBH, and MIB-APBI). As that table shows, the addition of DIBH significantly reduced doses to all OARs, except for the left lung. The greatest absolute dose benefit for DIBH was observed in WBI plans, with a mean dose decrease of 61% (Hazard Ratio). However, the relative benefit was even greater for DIBH-PBI, with a mean dose reduction of 66%.

Table 4 presents comparison of EQD2 doses to the organs at risk for DIBH – WBI vs PBI without DIBH, vs MIB-APBI and DIBH-WBI vs MIB-APBI and DIBH-PBI. There were no differences in cardiac doses between DIBH-WBI and PBI without DIBH, although lung doses were lower with the latter technique. MIB-APBI resulted in significantly lower maximum heart dose, LAD maximum dose, LV maximum dose and lung doses compared to DIBH-WBI. DIBH-PBI yielded significantly lower mean EQD2 values for the MHD, LAD, LV, and mean lung dose than MIB-APBI despite the larger PTV.

In Table 5 the effects of breast volume on EQD2 for OARs according to the radiotherapy technique are summarized. Breast volume was significantly and positively correlated with body mass index (BMI) ($p < 0.0001$, $r = 0.77$). In general, breast volume did not significantly correlate with the radiation dose to the cardiac structures, regardless of the specific radiotherapy technique, with or without DIBH. However, in DIBH-PBI, larger breast volumes were associated with significantly higher mean doses to the whole heart and LV. The absolute doses were, however, not clinically significant, with a mean EQD2 doses to the heart and LV of 0.24 (± 0.16) Gy and 0.30 (± 0.11) Gy, respectively. In most cases, the lung Dmax was significantly lower in patients with larger breast volumes.

The CTV volume was positively correlated with the MHD in DIBH-PBI ($p = 0.001$). The significance disappeared in the comparison without DIBH ($p = 0.15$). The CTV did not correlate significantly with doses to OARs in WBI, regardless of whether DIBH was included or not, and also in MIB-APBI.

Discussion

In this study, we sought to determine the influence of DIBH on heart and lung doses in patients undergoing radiotherapy for left EBC and to compare dosimetric results according to the radiotherapy technique (WBI, PBI, and MIB-APBI). The addition of DIBH significantly reduced EQD2 doses to all OARs (except for the left lung maximal dose) in WBI and PBI (Tab. 3). The MHD values were 0.72 Gy for DIBH-WBI, 1.01 Gy for MIB-APBI and 0.24 Gy for DIBH-PBI. Importantly, DIBH-PBI resulted in significantly lower mean doses to all OARs (except for maximum lung dose) compared to MIB-APBI (Tab. 3). Of the three techniques, DIBH-PBI resulted in the lowest overall doses to the heart and its key structures (Tab. 4). Based on these findings, PBI with DIBH appears to be the technique of choice in this patient population.

Given the risks of cardiac morbidity in left-sided EBC, it is crucial to minimize radiation doses to the heart and its substructures. In fact, concerns about late radiation-induced adverse effects are now greater than ever given the improved survival rates after locoregional breast cancer [15]. In recent decades, technological advances have improved radiotherapy delivery, thus significantly reducing the risk of cardiac toxicity during radiotherapy, as evidenced by the decrease in MHD for standard WBI from 3.8 Gy in the year 2000 to only 2.6 Gy in 2017. Drost et al. [16] reviewed data from 84 studies published between 2014-2017, finding a substantial reduction in MHD values over that time period, from 4.6 Gy in 2014 to 2.6 Gy in 2017. In that same study, the MHD for left breast cancer was only 3.6 Gy, which was substantially lower than the 5.4 Gy reported in the systematic review by Taylor et al. [17] who reviewed studies published between 2003 and 2013. Similarly, the addition of breathing control significantly lowered MHD values when compared to treatment regimens that did not include breathing control (1.7 Gy vs. 4.5 Gy). In short, as those data clearly show, DIBH is an effective method of reducing doses to the heart and its substructures.

The MHD values obtained in our study for DIBH-WBI (0.72 Gy), DIBH-PBI (0.24 Gy) and MIB-APBI (1.01 Gy) were well below the 2.5 Gy threshold recommended by the German Society of Radiation Oncology (DEGRO) [18]. These values were lower than reported in previous studies [17], mainly due to the low-risk profile of our sample (all patients were eligible for PBI and did not require axillary or internal mammary node irradiation). Although advanced radiotherapy techniques, such as intensity-modulate radiotherapy (IMRT) and volumetric arc therapy (VMAT) combined with DIBH, could further reduce heart and lung doses in left EBC compared to 3D-CRT [19, 20], these techniques are associated with higher doses to the contralateral breast and lung, which is why they are not commonly used in this patient population.

In selected patients with low-risk EBC, external beam PBI is widely used to shorten the course of radiotherapy, thereby significantly reducing exposure to the lungs, heart, and breasts. In our study, we used the easily reproducible protocol described in the IMPORT-LOW trial for external beam PBI, which involves simple craniocaudal tangential field reduction and mild hypofractionation, which is standard in WBI [21]. This technique (40 Gy in 15 fractions), when combined with DIBH, resulted in the lowest cardiac and lung doses (EQD2) among the three techniques (Table 4). External beam DIBH-PBI was superior to MIB-APBI in terms of OAR doses, despite the larger PTV. It is important to note that the MIB-APBI treatment plan was only simulated and thus the implant geometry (and dose distribution) was more optimal than would normally be the clinical case, which further supports the advantage of DIBH-PBI.

Some studies have found that MIB-APBI results in lower cardiac doses than WBI. For example, Lettmaier et al. conducted a dosimetric study comparing MIB-APBI to conventional WBI (i.e., without DIBH) [22], finding that brachytherapy resulted in substantially lower radiation exposure for all OARs (including the heart and left lung). However, other studies have shown that WBI plus DIBH, appears to offer superior results compared to those achieved with brachytherapy, as evidenced in the study by Holliday et al. who compared single catheter APBI brachytherapy to DIBH-WBI in patients (n = 100) with left-sided EBC (n = 50 in each group) [23]. In that study, mean cardiac doses (MHD and LAD EQD2) were significantly lower with DIBH-WBI.

Knippen et al. recently compared MIB–APBI (30 patients) to DIBH-WBI (22 patients) [9]. They used normal fractionation, moderate hypofractionation, and ultrahypofractionation for free-breathing WBI and DIBH-WBI delivered with and without a simultaneous integrated boost. While both techniques resulted in very low doses to the OARs, the doses were slightly

lower with MIB-APBI (MHD EQD2, 0.81 vs 1.18, $p < 0.001$), leading the authors to conclude that MIB-APBI should be the technique of choice. However, that study did not determine radiation doses to the LV and LAD, two critical structures that play a key role in the risk of cardiovascular morbidity and that should, therefore, be considered in any comparative analysis. We found that MIB-APBI yielded a lower MHD compared to WBI without DIBH, but not in comparison with DIBH-WBI.

In our study, although both DIBH-PBI and MIB-APBI resulted in cardiac doses that were below the cut-off values recommended by DEGRO [24], the doses were substantially lower with DIBH-PBI, indicating better cardiac sparing. Moreover, the MHD, mean LAD dose, mean and maximal LV doses, and mean lung doses were all significantly lower with DIBH-PBI than with MIB-APBI (Table 4). In fact, the only parameter that was better with MIB-APBI was the maximal lung dose. Given these findings, it seems clear that the treatment of choice in patients with low-risk, left EBC should be external beam PBI with DIBH. Even though we have been using multicatheter brachytherapy to treat low-risk patients at our center for more than a decade, these findings—considered in the context of the available literature — have convinced us to switch from MIB-APBI to DIBH-PBI for this patient population.

Strengths and limitations

One limitation of this dosimetric study is the small sample size (n=23), although this number is largely in line with other reports. In addition, the MIB-APBI treatment plans were simulated and thus the implant geometry and dose distribution were likely superior to what would be found in routine clinical practice. The main strength of this study is that it directly compares cardiac does with MIB-APBI to external beam techniques with and without DIBH. Another important strength is that, in addition to calculating MHD values, we also determined doses to the LV and LAD, thus providing additional data to provide a more comprehensive picture of the impact of radiation doses to the heart and its key structures.

Conclusions

This comparative dosimetric study was performed to determine the optimal radiotherapy technique to treat patients with left-sided, early breast cancer. Of the three techniques examined (WBI, PBI, and MIB-APBI), the best results in terms of cardiac sparing were obtained with PBI combined with deep-inspiration breath hold.

To our knowledge, this is the first study to suggest that external beam PBI with DIBH is superior to MIB-APBI in selected patients with EBC. To further confirm these findings, additional dosimetric and clinical studies directly comparing these two methods are needed.

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Declaration of generative AI and AI-assited technologies in the writing process

No AI or AI-assisted technologies were used.

Conflict of interests

Authors declare no conflict of interests.

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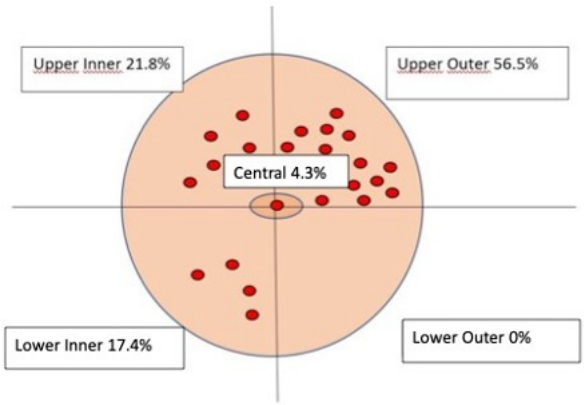

Figure 1. Tumour location by quadrant

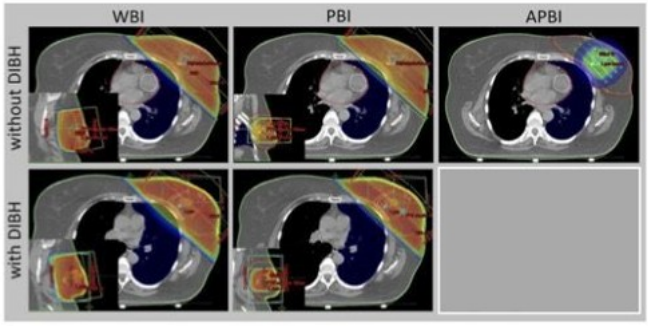

Figure 2. Computed tomography images showing the treatment plan contouring according to the radiotherapy technique: whole breast irradiation (WBI), external partial breast irradiation (PBI), and multicatheter interstitial brachytherapy-accelerated partial breast irradiation (MIB-APBI) with and without deep-inspiration breath hold (DIBH)

Table 1. Patient and tumour characteristics

Variable	**Mean ± SD (range)**
Age [years]	62.8 ± 7.6 (50–79)
BMI	27.9 ± 5.9 (18.7–44.1)
Breast volume [cm^3]	1110 ± 482 (380–2313)
Tumour diameter	10.4 ± 3.7 (3–15)
	n (%)
T stage	
pT1a	1 (4%)
pT1b	10 (44%)
pT1c	12 (52%)
N stage	
pNO	23 (100%)
M stage	

MO	23 (100%)
Grade	
Grade 1	7 (30%)
Grade 2	12 (52%)
Grade 3	4 (18%)
Histology	
Ductal	18 (78%
Lobular	4 (18%)
Mucinous	1 (4%)

SD — standard deviation; BMI — body mass index

Table 2. Radiotherapy parameters for whole breast irradiation (WBI), external partial breast irradiation (PBI), and multicatheter interstitial brachytherapy-accelerated partial breast irradiation (MIB-APBI)

Characteristic	**Mean or median ± SD (range)**
WBI	
CTV volume [cm^3]	110981 (380–2313)
PTV volume [cm^3]	1399 ± 531 (354–2703)
PBI	
CTV volume [cm^3]	70.7± 37.5 (11.1–151.8)
PTV volume [cm^3]	185.1 ± 77.9 (54–348.3)
MIB APBI	
CTV volume [cm^3]	70.7 ± 37.5 (11.1–151.8)
Median number of catheters	11 ± 4.4 (4–25)
Median number of planes	3 ± 0.9 (2–5)
V100 [cm^3]	93.4 ± 1.7 (90.6–98.1)
V150 [cm^3]	18.4 ± 7.6 (7.3–35.0)
Dose nonuniformity ratio	0.20 ± 0.08 (0.08–0.38)

SD — standard deviation; WBI = whole breast irradiation; PBI — partial breast irradiation; MIB APBI — multicatheter brachytherapy accelerated partial breast irradiation; CTV — clinical target volume; PTV — planning target volume

Table 3. Comparison of the equivalent dose in 2-Gy fractions (EQD2) doses to the organs-at-risk by technique [whole breast irradiation (WBI), external partial breast irradiation (PBI), both with and without deep-inspiration breath hold (DIBH), multicatheter interstitial brachytherapy-accelerated partial breast irradiation (MIB-APBI)]

	WBI		**PBI**		**MIB-APBI**
	No DIBH	**DIBH**	**No DIBH**	**DIBH**	
Heart mean dose	**2.04 (1.13)**	**0.72 (0.32)**	**0.67 (0.57)**	**0.24 (0.16)**	**1.01 (0.40)**
	p < 0.0001		p = 0.001		
Heart max dose	**45.87 (3.44)**	**26.52 (17.46)**	**21.56 (17.91)**	**4.82 (9.51)**	**5.99 (4.25)**
	p < 0.0001		p = 0.0004		
LAD mean dose	**18.02 (15.14)**	**3.63 (4.23)**	**5.15 (8.33**	**0.63 (0.58)**	**1.92 (1.14)**
	p < 0.0001		p = 0.014		
LAD max dose	**30.61 (17.51)**	**11.48 (12.75)**	**12.65 (13.55)**	**2.47 (5.45)**	**3.10 (2.18)**
	p < 0.0001		p = 0.0008		
LV mean dose	**3.94 (2.65)**	**1.02 (0.56)**	**1.07 (1.12)**	**0.30 (0.11)**	**1.55 (0.70)**

	p < 0.0001		p = 0.003		
LV max dose	**43.15 (7.06)**	**19.26 (17.13)**	**18.44 (17.91)**	**1.51 (1.62)**	**5.03 (3.78)**
	p < 0.0001		p = 0.0001		
Lung mean dose	**5.07 (1.61)**	**3.83 (1.39)**	**1.97 (0.88)**	**1.03 (0.56)**	1.30 (0.39)
	p < 0.0001		p < 0.0001		
Lung max dose	48.02 (1.75)	44.87 (9.42)	40.11 (3.48)	37.72 (5.07)	20.90 (14.85)
	p = 0.12		p = 0.16		

Gy — Gray; LAD — left anterior descending artery; LV — left ventricle

Table 4. The equivalent dose in 2-Gy fractions (EQD2) doses to the organs-at-risk: direct comparison of radiotherapy techniques [deep-inspiration breath hold whole breast irradiation (DIBH-WBI) vs. partial breast irradiation (PBI) without DIBH, DIBH-WBI vs. MIB-APBI; DIBH PBI vs. multicatheter interstitial brachytherapy accelerated partial breast irradiation (MIB-APBI)].

	Selected comparisons					
	DIBH WBI	**no DIBH-PBI**	**DIBH WBI**	**MIB-APBI**	**DIBH-PBI**	**MIB-APBI**
	EQD2 dose (SD) in Gy					
Heart mean dose	0.72 (0.32)	0.67 (0.57)	**0.72 (0.32)**	**1.01 (0.40)**	**0.24 (0.16)**	**1.01 (0.40)**
	p = 0.38		p = 0.006		p < 0.0001	

Heart max dose	26.52 (17.46)	21.56 (17.91)	**26.52 (17.46)**	**5.99 (4.25)**	4.82 (9.51)	5.99 (4.25)
	p = 0.99		p < 0.0001		p = 0.58	
LAD mean dose	3.63 (4.23)	5.15 (8.33)	3.63 (4.23)	1.92 (1.14)	**0.63 (0.58)**	**1.92 (1.14)**
	p = 0.38		p = 0.053		p < 0.0001	
LAD max dose	11.48 (12.75)	12.65 (13.55)	**11.48 (12.75)**	**3.10 (2.18)**	2.47 (5.45)	3.10 (2.18)
	p = 0.71		p = 0.002		p = 0.60	
LV mean dose	1.02 (0.56)	1.07 (1.12)	**1.02 (0.56)**	**1.55 (0.70)**	**0.30 (0.11)**	**1.55 (0.70)**
	p = 0.84		p = 0.004		p < 0.0001	
LV max dose	19.26 (17.13)	18.44 (17.91)	**19.26 (17.13)**	**5.03 (3.78)**	**1.51 (1.62)**	**5.03 (3.78)**
	p = 0.85		p = 0.0007		p = 0.0002	
Lung mean dose	**3.83 (1.39)**	**1.97 (0.88)**	**3.83 (1.39)**	**1.30 (0.39)**	**1.03 (0.56)**	**1.30 (0.39)**
	p < 0.0001		p < 0.0001		p = 0.02	
Lung max dose	**44.87 (9.42)**	**40.11 (3.48)**	**44.87 (9.42)**	**20.90 (14.85)**	**37.72 (5.07)**	**20.90 (14.85)**
	p = 0.027		p < 0.0001		p < 0.0001	

Gy — Gray; SD — standard deviation; LAD — left anterior descending artery; LV — left ventricle; p — p-value

Table 5. Influence of breast volume on the radiation dose to the organs-at-risk

	Breast volume				
	WBI		**PBI**		**APBI**
	noDIBH	**DIBH**	**noDIBH**	**DIBH**	
Heart mean dose	p = 0.87 r = 0.03	p = 0.58 r = 0.12	p = 0.70 r = –0.09	**p = 0.007** **r = 0.55**	p = 0.79 r = –0.06
Heart max dose	p = 0.45 r = –0.17	p = 0.77 r = 0.07	p = 0.45 r = –0.17	p = 0.16 r = 0.31	p = 0.53 r = –0.14
LAD mean dose	p = 0.49 r = –0.15	p = 0.41 r = –0.18	p = 0.61 r = –0.11	p = 0.55 r = –0.13	p = 0.11 r = –0.34
LAD max dose	p = 0.05 r = –0.41	p = 0.28 r = –0.23	p = 0.37 r = –0.20	p = 0.50 r = –0.15	p = 0.15 r = –0.31
LV mean dose	p = 0.70 r = 0.09	p = 0.57 r = 0.13	p = 0.75 r = –0.07	**p = 0.049** **r = 0.41**	p = 0.90 r = –0.03
LV max dose	p = 0.77 r = 0.06	p = 0.99 r = –0.002	p = 0.56 r = –0.13	p = 0.85 r = –0.04	p = 0.54 r = –0.14
Lung mean dose	p = 0.26 r = –0.24	p = 0.35 r = 0.21	p = 0.08 r = –0.37	p = 0.63 r = 0.11	p = 0.25 r = 0.25
Lung max dose	**p = 0.007** **r = –0.55**	p = 0.45 r = 0.16	**p = 0.002** **r = –0.62**	p = 0.08 r = –0.37	p = 0.08 r = –0.38

MBI — body mass index; WBI — whole breast irradiation; PBI — partial breast irradiation; MIB APBI — multicatheter interstitial brachytherapy accelerated partial breast irradiation; DIBH — deep inspiration breath hold; LAD — left anterior descending artery; LV — left ventricle; p — p-value; r — correlation coefficient (+ positive correlation; –negative correlation)