Society of Medical Education & Research

2023, Volume 3, Issue 1, Page No: 104-115
ISSN: 3108-4834

Archive of International Journal of Cancer and Allied Science

Optimizing Cardiac-Sparing Radiotherapy: Final Analysis of the SAVE-HEART Study on Surface-Guided DIBH in Left-Sided Breast Cancer

Suresh Ramanathan Pillai[1]*, Ravi Shankar Menon[1]

[1]Cancer Research Center, Christian Medical College (CMC), Vellore, India.

***E-mail** ✉ s.pillai.cmc@outlook.com

Abstract

Radiotherapy (RT) is a key component in treating early-stage breast cancer (BC), but it may cause adverse effects on the heart and lungs. Deep inspiration breath hold (DIBH) has been shown to improve protection of these critical organs. In this prospective study, we investigated the use of surface-guided DIBH compared to standard free breathing (FB) in patients with left-sided BC, focusing on both individualized cardiovascular risk factors and the dosimetric characteristics of treatment plans. Between October 2016 and January 2021, a total of 585 patients with left-sided invasive breast carcinoma, eligible for adjuvant radiotherapy (RT) to the breast or thoracic wall with or without regional lymph nodes, were enrolled in the study. Patients were required to maintain a breath-hold of at least 20 seconds. Treatments were delivered either as hypofractionated (HF; 40.05 Gy in 15 fractions) or normofractionated (NF; 50.00 Gy in 25 fractions) regimens. Deep inspiration breath hold (DIBH) was implemented using the Catalyst surface-guided system, featuring audio–visual feedback. Both surface imaging data and computed tomography were acquired under DIBH and free breathing (FB) conditions. The primary objective of the study was to assess the reduction in cardiac dose achieved with DIBH compared to FB.

DIBH substantially enhanced treatment plan dosimetry. Compared with free breathing (FB), maximum and mean doses to the heart and left coronary artery were lowered by 36%–42% in both hypofractionated and normofractionated regimens ($P < 0.001$). The mean dose to the ipsilateral lung was also decreased by 12%–14% ($P < 0.001$). Additionally, DIBH led to a 5% relative reduction in the projected 10-year risk of cardiovascular disease, decreasing from 3.59% under FB to 3.41% ($P < 0.001$). This study is, to our knowledge, the most extensive prospective evaluation highlighting the enhanced cardiac and ipsilateral lung protection achieved with surface-guided DIBH versus conventional free breathing in left-sided breast cancer patients.

Keywords: Prospective studies, Adjuvant radiotherapy, Breast neoplasms, Radiation dosage, Heart disease risk factors, Coronary vessels

Introduction

Adjuvant radiotherapy (RT) remains a cornerstone in the treatment of early breast cancer (BC) following breast-conserving surgery, offering improvements in local tumor control, disease-free survival, and overall survival [1, 2]. Nevertheless, for patients with left-sided BC, RT can increase the long-term risk of cardiovascular disease (CVD) and pulmonary complications [3, 4]. Radiation-induced CVD arises from damage to both small and large vessels, including coronary arteries, which may lead to myocardial infarction or ischemic stroke [5–9]. Despite extensive research, defining a clear dose–response relationship has proven difficult. For example, Darby *et al.* [10] reported a linear 7.4% rise in major coronary events per Gray (Gy) of mean heart dose, yet recent studies have not established a safe radiation threshold for CVD [11–13]. Additionally, certain systemic treatments, such as anthracyclines or trastuzumab, may exacerbate cardiac toxicity when combined with RT [14].

Pulmonary toxicity is also a concern, with estimates suggesting an excess relative risk (ERR) of 0.11 per Gy of whole lung dose for secondary lung cancer [15].

Access this article online https://smerpub.com/

Received: 20 January 2023; **Accepted:** 16 April 2023

How to cite this article: Pillai SR, Menon RS. Optimizing Cardiac-Sparing Radiotherapy: Final Analysis of the SAVE-HEART Study on Surface-Guided DIBH in Left-Sided Breast Cancer. Arch Int J Cancer Allied Sci. 2023;3(1):104-15. https://doi.org/10.51847/ZPbOVVfhgC

Advances in radiation technology, along with growing awareness of long-term toxicities, have spurred the development of techniques that optimize dose distribution while sparing the heart, left anterior descending (LAD) artery, and lungs. Methods like intensity-modulated RT (IMRT) or helical tomotherapy can reduce mean heart and LAD doses but often increase low-dose exposure to surrounding tissues, whose long-term consequences remain uncertain [16–19]. In contrast, deep inspiration breath-hold (DIBH) physically increases the distance between the heart and chest wall, lowering doses to intrathoracic organs without compromising target coverage or causing additional low-dose scatter [20].

DIBH can be delivered using different approaches, which vary in complexity, monitoring, and patient feedback. Voluntary DIBH is the simplest, relying solely on treatment room light fields or lasers. Equipment-based methods include surface-guided or spirometry-guided systems, often providing visual feedback. These systems range from simple in-house setups to advanced commercial devices capable of integrating with treatment delivery for automated gating [21].

Surface-guided DIBH systems use optical scanning to monitor the patient's external surface in real time. Light patterns are projected and captured using charge-coupled device (CCD) cameras, while ceiling-mounted units reconstruct a three-dimensional (3D) model of the patient's surface. Respiratory motion is tracked, and a reference DIBH surface is recorded during CT simulation and treatment. Individual gating windows are established based on the patient's reproducible DIBH performance during training. Audio-visual feedback tools, such as video goggles or tablets, provide patients with continuous guidance [22, 23]. These systems allow precise positioning, intrafraction motion monitoring, and respiratory gating assessment, all without additional radiation exposure, and can be linked to treatment delivery for automatic gating.

The present prospective study was designed to compare surface-guided DIBH with conventional free breathing (FB) in patients with left-sided BC, evaluating both personalized cardiovascular risk profiles and treatment plan dosimetry.

Materials and Methods

This study examined a consecutive prospective cohort of breast cancer (BC) patients managed at our center from October 2016 through January 2021.

Key eligibility requirements encompassed histologically verified left-sided invasive breast cancer or ductal carcinoma in situ, treated via breast-conserving surgery or mastectomy, with a planned postoperative radiation therapy (RT) to the breast/chest wall, optionally including regional lymph nodes. Prior to enrollment, every patient completed a training session on deep inspiration breath-hold (DIBH) and had to demonstrate the ability to hold their breath for at least 20 seconds. All participants provided informed consent.

Conducting as a prospective single-institution trial, the work complied with the Declaration of Helsinki, gained approval from the LMU Medical Faculty Ethics Committee (dated 22 October 2013, project no. 496-12), and was listed in the German Clinical Trials Register (DRKS ID: DRKS00011213).

Patients had dual CT simulations under identical conditions (supine positioning with arms elevated) at 3-mm slices: one during free breathing (FB) and another in DIBH. The Sentinel laser system (C-RAD, Uppsala, Sweden) captured a baseline surface scan in FB and set a personalized gating window for DIBH. This window started at 4 mm around the patient's stable voluntary DIBH level but could be tightened to 2 mm if performance allowed [23, 24]. At the linear accelerator, the Catalyst optical surface scanner (C-RAD) handled positioning and DIBH monitoring during irradiation. Patients also received visual feedback through Epson Moverio BT-300 Smart Glasses (Epson Inc., Suwa, Japan) connected via Bluetooth.

Contouring of the heart and left anterior descending (LAD) artery followed the protocol outlined by Feng *et al*. [25]. The clinical target volume included the residual left breast or chest wall while sparing ribs, musculature, and skin. A 5-mm isotropic expansion formed the planning target volume (PTV) [26–29]. Regimens were either normofractionated (NF: 50.00 Gy at 2.00 Gy per fraction) or hypofractionated (HF: 40.05 Gy at 2.67 Gy per fraction), applied with 3D conformal field-in-field methods. To ensure comparable analysis, boost doses were omitted from dosimetry reviews. Planning utilized Oncentra 4.3 (Veenendaal, Nucletron, the Netherlands) with collapsed cone convolution dose computation on a 3 mm × 3 mm grid. Recorded parameters covered heart (Dmax, Dmean, V10Gy, V5Gy, V20Gy), PTV (Vtot), ipsilateral lung (Vtot, Dmean, V10Gy, V5Gy, V20Gy)

and LAD artery (Dmax, Dmean, D2). Plan differences (Δ′x′) between FB and DIBH were calculated. The main study goal focused on assessing cardiac dose sparing with DIBH.

To evaluate radiation-related risks, each patient completed a tailored questionnaire capturing cardiovascular risk factors. The 10-year probability of major coronary events (myocardial infarction or sudden cardiac death) was derived from the Prospective Cardiovascular Münster (PROCAM) score, factoring in lipids (HDL, LDL, triglycerides), age, gender, systolic blood pressure, smoking, family history, and diabetes [30]. Those with a baseline 10-year risk above 10% were offered individualized primary prevention guidance [31]. Excess relative risk (ERR) for radiation-associated cardiovascular disease within 10 years was derived from each patient's mean heart dose in both FB and DIBH plans. Assuming a linear 7.4% risk escalation per Gy of mean heart dose per Darby *et al*. [10], ERR was computed as mean heart dose (Gy) × 0.074 Gy−1. Excess absolute risk (EAR) followed as ERR multiplied by the PROCAM-derived baseline risk. Total cumulative 10-year risk then combined baseline risk with EAR: Cumulative risk = baseline + EAR.

Quantitative variables were summarized with means, ranges, standard deviations, and/or proportions. Dosimetric comparisons between methods employed paired t-tests, while variable relationships were explored via Pearson correlation. The threshold for significance was P = 0.05. All analyses used IBM SPSS Statistics version 28.0 (IBM Corp, Armonk, NY, United States).

Results and Discussion

The study involved 585 patients, with a median age of 57 years at diagnosis (ranging from 24 to 84 years). **Table 1** provides a detailed overview of baseline characteristics. Most tumors were invasive breast cancer (497 out of 585, 85%), with 89% being hormone receptor-positive, of which 9% were also HER2-positive. Additionally, 3% of tumors were solely HER2-positive, and 8% were triple-negative. Early-stage tumors (T1b-T2) represented 69% of cases (405/585), and 79% of patients (465/585) had no lymph node involvement (N0). The average body mass index was 24.2 kg/m², ranging from 15.6 to 44.4 kg/m². Furthermore, 13% of patients reported a family history of cardiovascular disease, 4% had diabetes, and 11% were smokers.

Table 1. The PROCAM scores and baseline characteristics

Characteristic	Value (N = 585)
Body mass index (kg/m²)	
Mean	24.20
Missing	17
Age (years) at diagnosis	
<40	53 (9%)
40–49	113 (19%)
50–59	182 (31%)
60–69	127 (22%)
70–79	95 (16%)
≥80	15 (3%)
Mean	56.89
Molecular biology	
Estrogen receptor positive	515 (88%)
Progesterone receptor positive	450 (77%)
Human epidermal growth factor receptor 2 positive	68 (12%)
Missing	3 (1%)
Histology	
Nonspecial type	426 (73%)
Lobular	59 (10%)

Ductal carcinoma in situ	66 (11%)
Nonspecial type + ductal carcinoma in situ	12 (2%)
Others	21 (4%)
Missing	1 (0%)
Tumor–node–metastasis (TNM) - N stage	
N0	465 (79%)
Nmi	29 (5%)
N1	62 (11%)
N2	19 (3%)
N3	10 (2%)
Tumor–node–metastasis (TNM) - T stage	
Tis	66 (11%)
T1	360 (62%)
T2	139 (24%)
T3	20 (3%)
Diabetes	
Yes	23 (4%)
No	542 (96%)
Missing	20 (3%)
Cardiovascular disease family history	
Positive	71 (13%)
Negative	490 (87%)
Missing	24 (4%)
Smoking habit	
Positive	62 (11%)
Negative	501 (89%)
Missing	22 (3%)
Low-density lipoprotein (mg/dL)	
<100	118 (27%)
100–149	237 (53%)
150–199	78 (17%)
≥200	12 (3%)
Missing	140 (24%)
Mean	121.02
Triglycerides (mg/dL)	
<50	13 (3%)
50–99	194 (43%)
100–149	138 (30%)
150–199	58 (13%)
200–249	30 (7%)
≥250	20 (4%)
Missing	132 (23%)
Mean	120.20
PROCAM score	

<1%	241 (46%)
1–10%	237 (45%)
>10%	45 (9%)
Missing	62 (11%)
Mean	3.08
High-density lipoprotein (mg/dL)	
<50	55 (12%)
50–99	375 (83%)
≥100	23 (5%)
Missing	132 (23%)
Mean	68.50

Unless otherwise specified, data are expressed as number and percentage (n [%]).

PROCAM stands for the Prospective Cardiovascular Münster study.

Using the PROCAM score to estimate 10-year cardiovascular disease (CVD) risk, nearly half of the patients (46%, 241/585) had a risk of less than 1%, whereas 9% (45/585) had a risk exceeding 10%. Across the entire study population, the average baseline risk was 3.08%, ranging from 0% up to 37.3% **(Figure 1)**.

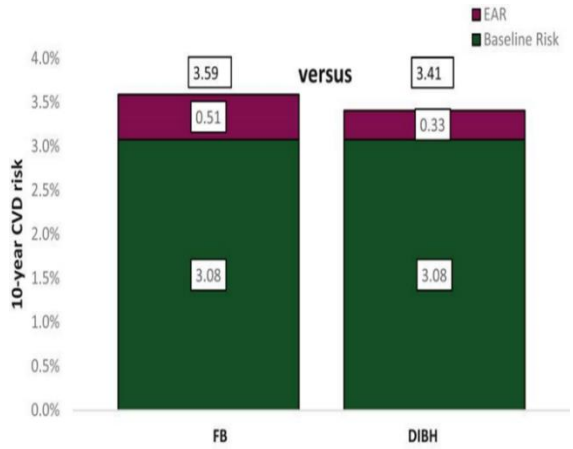

Figure 1. Shows the 10-year cumulative risk of cardiovascular disease (CVD) for radiotherapy plans delivered during free breathing (FB) versus deep inspiration breath-hold (DIBH).

In this cohort of 585 patients, 90% (526 cases) were treated with radiotherapy after breast-conserving surgery (of whom 16% also had elective nodal fields included), while the remaining 10% (59 cases) received post-mastectomy radiotherapy (76% with nodal irradiation). Fractionation was hypofractionated (HF) in 63% of patients (367 cases) and conventionally fractionated (normofractionated, NF) in 37% (218 cases). The planning target volume (PTV) was slightly larger (by 1%) with DIBH in hypofractionated schedules, but showed no meaningful difference in normofractionated ones ($P < 0.001$).

Use of DIBH led to substantial sparing of the heart in both fractionation groups: the average heart dose fell by 37% in HF plans (1.91 Gy to 1.21 Gy) and by 36% in NF plans (2.80 Gy to 1.78 Gy; $P < 0.001$ for both). Peak heart doses were similarly lowered, dropping 42% in HF (34.22 Gy to 19.85 Gy) and 41% in NF plans (42.45 Gy to 25.07 Gy; $P < 0.001$). The left anterior descending (LAD) coronary artery benefited even more markedly, with average dose, near-maximum dose (D2%), and peak dose reduced by around 58%, 55%, and 47%, respectively, across both regimens (all $P < 0.001$). A representative example is the near-maximum LAD dose in HF plans, which decreased from 21.86 Gy to 9.80 Gy ($P < 0.001$).

As expected with breath-hold technique, the total volume of the treated-side lung rose substantially—by 68% in HF and 69% in NF plans ($P < 0.001$). Despite this expansion, the average lung dose improved modestly, decreasing 12% in HF and 14% in NF plans ($P < 0.001$). However, intermediate- and low-dose lung volumes (V20Gy, V10Gy, V5Gy) were larger with DIBH than with free breathing ($P < 0.001$). Full dosimetric details appear in **Table 2 and Figure 2**.

The most robust relationship identified was between the degree of heart dose sparing and LAD dose sparing achieved with DIBH compared to FB (correlation coefficient $r = 0.764$, explaining 58% of variance). Strong associations were also seen between heart and LAD mean doses within FB plans ($r = 0.742$) and within DIBH plans ($r = 0.681$; **(Figure 3)**). In contrast, the increase in lung volume during breath-hold correlated

only weakly with the extent of heart dose reduction (r = 0.344).

Table 2. Lists key dose-volume parameters for the heart, LAD artery, ipsilateral lung, and PTV across hypofractionated and normofractionated treatment schedules.

Parameter	FB Mean ± SD	DIBH Mean ± SD	Δ Absolute	Δ Relative	95% CI	P value	FB Mean ± SD	DIBH Mean ± SD	Δ Absolute	Δ Relative	95% CI	P value
Heart												
Dmax (Gy)	34.22 ± 8.63	19.85 ± 11.76	14.37	42%	13.25 to 15.49	<0.001	42.45 ± 10.43	25.07 ± 14.16	17.38	41%	15.58 to 19.11	<0.001
Dmean (Gy)	1.91 ± 0.83	1.21 ± 0.43	0.70	37%	0.64 to 0.77	<0.001	2.80 ± 1.23	1.78 ± 0.62	1.02	36%	0.89 to 1.14	<0.001
V10 (cc)	13.20 ± 14.23	4.34 ± 43.17	8.86	67%	4.31 to 13.41	<0.001	37.35 ± 192.31	9.55 ± 63.96	27.8	74%	4.93 to 50.32	n.s.
V20 (cc)	8.34 ± 10.66	3.24 ± 43.05	5.12	61%	0.60 to 9.59	0.026	12.65 ± 18.61	7.56 ± 63.95	5.09	40%	−3.09 to 12.84	0.017
V5 (cc)	21.88 ± 19.34	7.68 ± 43.95	14.20	65%	9.52 to 18.88	<0.001	42.07 ± 44.05	19.24 ± 65.43	22.83	54%	14.39 to 30.65	<0.001
LAD artery												
Dmax (Gy)	26.16 ± 12.83	13.90 ± 10.69	12.26	47%	11.14 to 13.33	<0.001	33.48 ± 15.92	17.65 ± 13.38	15.83	47%	13.87 to 17.63	<0.001
Dmean (Gy)	9.34 ± 7.47	3.86 ± 3.60	5.48	59%	4.87 to 6.10	<0.001	13.00 ± 9.92	5.39 ± 4.71	7.61	58%	6.50 to 8.33	<0.001
D2	21.86 ± 13.54	9.80 ± 9.11	12.06	55%	10.92 to 13.17	<0.001	28.80 ± 16.81	13.06 ± 11.92	15.74	55%	13.68 to 17.58	<0.001
Ipsilateral lung												
Dmean (Gy)	5.92 ± 1.37	5.22 ± 1.13	0.70	12%	−0.62 to 0.79	<0.001	9.67 ± 2.76	8.29 ± 2.33	1.38	14%	1.18 to 1.58	<0.001
Vtot (cm^3)	1430.42 ± 320.33	2402.13 ± 424.31	−971.71	68%	−1001.82 to 941.59	<0.001	1406.52 ± 324.03	2381.17 ± 404.97	−974.65	69%	−1011.06 to 937.16	<0.001
V10 (cc)	239.41 ± 82.57	360.09 ± 108.09	−120.68	51%	−127.60 to 113.54	<0.001	369.36 ± 147.75	554.41 ± 186.44	−185.05	50%	−196.09 to 172.72	<0.001
V20 (cc)	160.52 ± 64.20	214.91 ± 75.54	−54.39	34%	−49.47 to 22.21	<0.001	253.30 ± 107.16	342.28 ± 125.68	−88.98	35%	−96.45 to 79.79	<0.001
V5 (cc)	359.44 ± 111.46	582.23 ± 158.30	−222.79	62%	−233.09 to 212.25	<0.001	543.20 ± 204.54	857.94 ± 256.98	−314.74	58%	−328.77 to 295.98	<0.001
Planning target volume												
Vtot (cc)	950.55 ± 416.78	964.64 ± 422.17	−14.09	1%	−17.68 to 10.48	<0.001	1082.93 ± 498.32	1090.78 ± 497.79	−7.85	1%	16.65 to 0.95	n.s.

D, dose; cc, cubic centimeter; LAD artery, left anterior descending; Gy, Gray; V(x), volume receiving x Gy of the dose; n.s., nonsignificant

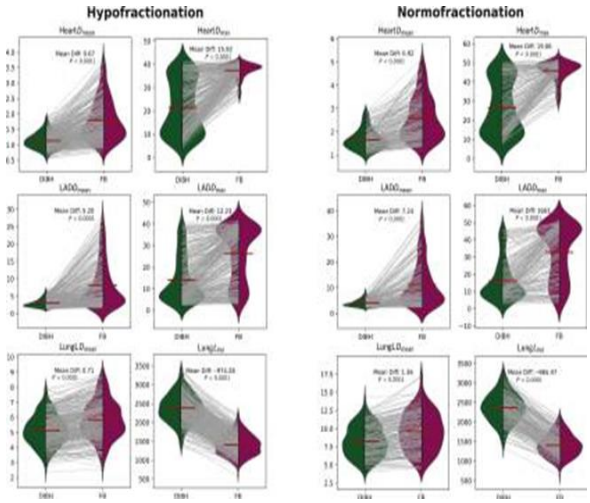

Figure 2. Comparison of dosimetric parameters between free breathing (FB) and deep inspiration breath hold (DIBH) for hypofractionated (HF, left panel) and normofractionated (NF, right panel) radiotherapy plans. Shown are the average radiation doses to the heart ($HeartD_{mean}$), left anterior descending (LAD) artery ($LADD_{mean}$), and ipsilateral lung ($LungLD_{mean}$), the maximum doses to the heart ($HeartD_{max}$) and LAD artery ($LADD_{max}$), and the total volume of the ipsilateral lung ($LungL_{Vol}$). Dose values are expressed in Gray (Gy), and lung volumes in cubic centimeters (cc).

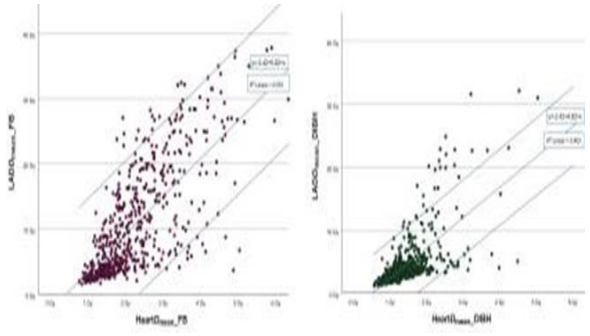

Figure 3. Scatterplot illustrating the relationship between the mean dose to the left anterior descending (LAD) artery and the heart mean dose (D_{mean}) under free breathing (FB) and deep inspiration breath hold (DIBH), with 95% confidence intervals (CI). The fitted linear equations were $f(x) = -2.42 + 5.82x$ for FB and $f(x) = -2.42 + 4.82x$ for DIBH. The corresponding coefficients of determination were $R^2 = 0.551$ for FB and $R^2 = 0.463$ for DIBH. CI, confidence interval; DIBH, deep inspiration breath hold; LAD artery, left anterior descending artery; FB, free breathing.

Following DIBH radiotherapy, the mean estimated radiation-induced 10-year cardiovascular disease (CVD) risk (ERR) was 0.11, ranging from 0.04 to 0.37. In comparison, FB plans yielded a higher mean ERR of 0.17 (range 0.06–0.67), representing a 35% reduction with DIBH (Δ: 0.06; 95% CI 0.057–0.068; $P < 0.001$). This reduction translated into a mean excess absolute risk (EAR) of 0.33% (0%–5.31%) for DIBH versus 0.51% (0%–10.18%) for FB, indicating a 35% decrease in 10-year CVD EAR (Δ: 0.18; 95% CI 0.14–0.23; $P < 0.001$). Accounting for baseline characteristics, the cumulative 10-year CVD risk averaged 3.41% (range 0%–42.65%) for DIBH, compared with 3.59% (range 0%–47.18%) for FB, equating to a 5% relative reduction (Δ: 0.18; 95% CI 0.14–0.23; $P < 0.001$). **Figure 1** provides an overview of these CVD risk estimations.

Multiple recent studies have demonstrated that deep inspiration breath hold (DIBH) can substantially lower the radiation dose received by thoracic organs at risk in patients with left-sided breast cancer (BC) [32–34]. In line with these findings, our large prospective study, which included nearly 600 patients, confirmed that DIBH significantly reduces the dose delivered to the heart, the left anterior descending (LAD) artery, and the ipsilateral lung compared with free breathing (FB) plans **(Table 2, Figure 2)**. The use of DIBH led to marked reductions in both mean and maximum doses to these structures ($P < 0.001$) across normal fractionation (NF) and hypofractionation (HF) treatment schedules.

To our knowledge, this study represents the largest prospective evaluation of dosimetric outcomes using a surface guided radiotherapy (SGRT) system for DIBH in BC. The procedure was performed with the Sentinel/Catalyst system. During CT simulation, the Sentinel laser-based system identifies the appropriate breath-hold level for each patient to ensure stability and reproducibility. During treatment at the linear accelerator, the Catalyst system projects optical light patterns on the patient's skin and captures the reflections with charge-coupled device cameras, enabling three-dimensional reconstruction of the external surface and monitoring of respiratory motion and DIBH. Real-time feedback is provided to patients through video goggles to guide breath-hold performance [23].

Earlier DIBH studies with 3D-conformal radiotherapy were limited by small sample sizes. Two retrospective series using the Catalyst HD SGRT system, conducted by Wolf *et al.* [35] and Knöchelmann *et al.* [36], reported significant reductions in mean doses to the heart, left lung

and LAD artery in 130 and 357 patients, respectively. Wolf *et al*. [35] observed dose decreases of 7%, 41%, and 71%, while Knöchelmann *et al*. [36] reported 47%, 32%, and 9% reductions, respectively. Both studies showed similar DIBH benefits for NF and HF plans, consistent with our findings.

Two additional prospective studies [37, 38] used a comparable SGRT approach (VisionRT, AlignRT, London, UK) in 88 and 25 patients, respectively, reporting substantial mean dose reductions for the heart and LAD artery. The reductions were similar to our results, ranging from 56% to 65% for the heart and 42% to 45% for the LAD artery ($P < 0.001$). In contrast, Ferdinand *et al*. [39] evaluated 31 patients using a spirometric method (Active Breathing Control; Elekta AB, Stockholm, Sweden) and found slightly smaller reductions: 39% for the heart ($P < 0.001$), 30% for the LAD artery ($P < 0.001$), and 10% for the ipsilateral lung ($P = 0.03$). While these results may suggest a smaller effect for spirometric techniques compared with SGRT DIBH, direct comparisons across studies are not appropriate for assessing efficacy.

Across studies, the reduction in mean LAD dose with DIBH varied widely, from 11% to 71%, with our cohort showing a 58% decrease. This variability may be partly due to challenges in contouring the thin LAD artery, which is often poorly visible on non-contrast CT scans. Furthermore, standardization of LAD dose constraints is lacking. Some studies [40] suggest a maximum LAD dose below 45.4 Gy to lower cardiac mortality, while others rely on the strong linear correlation between LAD and heart mean doses. Evans *et al*. [41] reported that each 1 Gy increase in mean heart dose corresponds to a 4.8 Gy increase in mean LAD dose. Our data corroborate this, showing increases of 5.82 Gy per 1 Gy for FB and 4.82 Gy per 1 Gy for DIBH, with a statistically significant correlation between heart and LAD mean doses (FB $R^2 = 0.551$; DIBH $R^2 = 0.463$; **(Figure 3)**). This relationship is anatomically explained by the LAD artery's course near the heart apex, adjacent to radiation fields. Given the link between LAD dose and coronary stenosis risk [42], we recommend contouring the LAD artery, particularly as standardized long-term data are limited.

Regarding lung dosimetry, the volumes receiving 20, 10, and 5 Gy were higher during DIBH due to the substantial increase in total lung volume (69%) during breath hold. These findings are expected, as dose–volume analyses do not account for reduced lung density in DIBH, potentially overestimating the dose. Accurate quantification would require complex tissue density analyses across the lung, which is not practical. Dose–mass histograms, rather than conventional dose–volume histograms, can address this issue [43].

Earlier small studies [35, 43] suggested that increases in ipsilateral lung volume could predict DIBH benefit via heart dose reduction. However, our prospective data did not confirm this correlation. Multiple attempts to define anatomical, radiological, or cardiovascular criteria for selecting DIBH over FB have not yielded definitive predictors [36, 39, 44–47]. We advocate offering DIBH to all eligible patients, regardless of baseline risk, to minimize long-term CVD in accordance with the ALARA principle. Proper patient education and breath-hold training several days before CT simulation are essential, as pre-training has been shown to lower heart doses [48].

Our cardiac risk modeling indicated a mean baseline 10-year CVD risk of 3.08%. The mean excess absolute risk (EAR) was 0.51% for FB plans versus 0.33% for DIBH plans, a 35% reduction. Despite this, the cumulative 10-year CVD risk changed modestly, from 3.59% (FB) to 3.41% (DIBH), a 5% difference. Although seemingly small, this percentage represents patients at risk for major coronary events over the next decade, highlighting the clinical relevance of minimizing cardiac exposure.

Some patients with BC may face higher 10-year CVD mortality than risk of tumor recurrence. For instance, a patient with a PROCAM score of 30 and T2 luminal A disease has a baseline 10-year recurrence risk of 10%. Without DIBH, radiation could raise the risk of serious cardiac events to 40%, while DIBH could reduce it to 35%, illustrating the potential impact of technique selection. In our cohort, 34 patients (7%) had baseline 10-year CVD risk >10%, emphasizing the importance of pre-treatment CVD risk assessment and long-term follow-up. Promoting lifestyle interventions—smoking cessation, physical activity, and healthy diet—can help reduce modifiable CVD risks [31].

We also observed a significant 1% increase in PTV during DIBH in HF plans ($P < 0.001$), likely due to chest wall shape changes during breath hold. Limitations of this study include the single-center design, limited follow-up, reliance on PROCAM for baseline CVD risk, and the use of mean heart dose for risk calculations, which differs from the estimations in Darby *et al*. [10].

Conclusion

To our knowledge, this study represents the largest prospective evaluation showing that surface-guided DIBH substantially decreases radiation exposure to the heart and lungs. Based on these results, we recommend using DIBH for all left-sided breast cancer patients undergoing radiotherapy whenever it is feasible.

Acknowledgments: None

Conflict of Interest: CB and SC received speaker honoraria and research grants from ELEKTA AB (Stockholm, Sweden). SC received speaker honoraria and research grants from C-RAD (Uppsala, Sweden). IM received honoraria for occasional attendance at advisory boards supported by Eli Lilly, Novartis, Pfizer, Seagen, Gilead, Astra Zeneca, Daiichi Sankyo, and Accuray. The other authors declare that they have no competing interests.

Financial Support: None

Ethics Statement: None

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