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Original article

DOSIMETRIC EVALUATION OF SURFACE-GUIDED DEEP-INSPIRATION *VERSUS* FREE-BREATHING POSTOPERATIVE RADIOTHERAPY IN PATIENTS WITH LEFT-SIDED EARLY BREAST CANCER: EUROPEAN SCHOOL OF ONCOLOGY (ESO) CLINICAL TRAINING CENTER BREAST CANCER FELLOWSHIP EXPERIENCE

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Abstract

Introduction: Late toxicities related to radiotherapy in early breast cancer, especially cardiac toxicities are those that bring concerns in long-life survivors.

Material and methods: Patients who underwent breast-only postoperative irradiation utilizing the deep inspiration breath hold (DIBH) technique with the Optical Surface Monitoring System (OSMS) during the years 2024-2025 were randomly selected. All patients had two simulation CTs (free-breathing, FB, and DIBH). Three-dimensional radiotherapy treatment plans were created for both (FB and DIBH) CT scans. Dosimetric evaluations were made from the dose-volume histograms (DVH). Statistical evaluation was done with paired sample t-test (two-tailed) and statistical significance was determined at $p<0.05$.

Results: Eleven patients were included in the study. Target coverage (PTV95%) wasn't statistically significant between groups. The mean heart dose decreased significantly in DIBH plans by 57%, median difference 1.44 Gy. Heart D16Gy (%) and Heart D16Gy (cm3) were reduced by 91.5% and 89.1% in DIBH plans, respectively (p values 0.005 and 0.022). In comparison to FB plans, DIBH plans resulted in reductions of 87.7% in left anterior descending artery (LAD) Dmean and 68.2% in LAD Dmax ($p < 0.001$). The left ventricle Dmean and Dmax showed reduced values with DIBH plans by 68.2% and 68.9% ($p=0.003$ and <0.001), respectively. The ipsilateral lung volume was considerably greater in DIBH plans ($p < 0.005$), with a median difference of 1133 cm^3.

Conclusion: Our study has demonstrated a significant reduction in radiation doses delivered to the heart and its substructures in DIBH plans compared to FB plans, consistent with prior studies.

Key words: breast cancer, DIBH, late toxicities

Introduction

Breast cancer is the most common malignancy in women with 2,296,840 new cases diagnosed in 2022 and it accounted for approximately 15.4 % of all cancer deaths in women[1]. In Slovenia, breast cancer had an incidence of 1504 new cases per year (2017-2021), which accounted for 19.7% of all cancer cases, according to Slovenian cancer registry data[2]. It remains one of the most significant health concerns worldwide. Increased awareness and screening programs have resulted in the detection of the disease in early stages, characterized by smaller tumors and fewer positive lymph nodes at initial diagnosis. This ultimately led to improved prognosis and longer survival in patients with breast cancer. Advancements in treatment modalities resulted in increased life expectancy for breast cancer patients, yet treatment-related morbidity and mortality still pose significant challenges. The treatment of breast cancer is multidisciplinary, including radiotherapy as one of the most important strategies, especially after breast conserving surgery (BCS). Evidence from multiple trials shows that omission of postoperative radiotherapy after BCS is associated with an increased mortality risk (RR=1.086; 95% CI: 1.003-1.175) and reduction of overall survival [3].

Late toxicities related to radiotherapy in early breast cancer, especially cardiac toxicities are those that bring concerns in long-life survivors. There are different treatment techniques that are used to decrease cardiac irradiation for patients with left-sided breast cancer. Initial cut-off on cardiac doses was introduced by Gyenes *et al.* [4], who incorporated three-dimensional radiotherapy (3D-CRT) planning and showed the heart volume treated to 50% isodose to be 5.7% (compared to 25% in earlier trials). After adoption of 3D-CRT as minimum required for cardiac safety, researchers continued with more advanced techniques and implemented intensity-modulated radiation therapy (IMRT). This technique was especially important in more advanced stages where nodal irradiation was required [5,6,7]. Accelerated partial breast irradiation (IMRT or brachytherapy) significantly decreases the volume of heart receiving low to high doses in left-sided breast cancer [8, 9], but the selection criteria for this treatment are very strict. Prone position showed promising results in cardiac dose decrease in women with larger breasts (≥750 cm^3) [10].

The straightforward yet groundbreaking concept of irradiating during deep inspiration-when lung volume is increased, the heart is positioned lower in the chest cavity, and the space between the chest wall and heart is greater-has resulted in numerous technological advancements aimed at minimizing cardiac doses in patients with left-sided breast cancer. The two dominant deep inspiration breath hold technique (DIBH) methods are the spirometry-based active breathing coordinator (ABC) system (Elekta, Stockholm, Sweden) or ABC_DIBH and the video-based real-time position management (RPM) system (Varian Medical Systems, Palo Alto, CA) or vDIBH.

The Institute of Oncology in Ljubljana is providing DIBH in patients with left-sided breast cancer (and in some patients with right-sided breast cancer) using ABC system since 2016 and the OSMS real-time RPM system since 2019.

This study aimed to evaluate the dosimetric parameters of the planning target volume (PTV) and OARs-the heart, left descending coronary artery (LAD), left ventricle, and lungs - across two sets of CT scans (FB *vs.* DIBH).

Material and methods

This study employs a retrospective, observational design. Before starting the study, non-interventional protocol was created and approved by Institutional review board and committee with number ERIDSPRA-0055/2025.

Patients

After breast conserving surgery, patients treated with DIBH breast radiotherapy using OSMS in the period 2024-2025 were randomly selected. All patients previously had undergone two simulation CTs (FB and DIBH) with OSMS system, with identical setup using 3-mm slice thickness. Eleven patients with breast only (elective) radiotherapy, whose treatment plans were technically feasible for retrospective contouring were selected. All patients received 40.05 Gy delivered in 15 fractions of 2.67 Gy. Plans that included locoregional irradiation, simultaneous integrated boost, or plans that used IMRT/ VMAT planning were excluded from the study.

CT simulation, contouring and planning

CT simulation for all patients had been performed according to surface guided DIBH institutional protocols. CT datasets were used for retrospective contouring. On the FB series, organs at risk (OARs) were contoured, and target volumes were replicated from original plans according to institutional atlases. Three-dimensional conformal radiotherapy (3D-CRT) plans for FB were generated by a single planner using Varian Eclipse™. Previously contoured and delivered DIBH plans for the same patients were used for comparison.

Dosimetric evaluation was performed using dose–volume histograms for both FB and DIBH plans. PTV coverage was assessed using 95% of the PTVeval (PTV minus 5 mm under the skin). The parameters assessed for organs at risk included: mean dose and volume of 16 Gy (%) for the ipsilateral lung, mean dose and volume of 16 Gy (%) for the heart, mean and maximum doses for the left anterior descending artery (LAD), and mean and maximum doses for the left ventricle. LAD and left ventricle were not contoured as OARs in initial DIBH plans. They were retrospectively contoured by the investigator and were not taken in consideration as restrictions when 3D CRT plans were done for both (DIBH and FB) plans.

Results

Dosimetric evaluation for PTVeval, used as surrogate for target volume coverage is shown in Table 1.

Table 1. Dosimetric evaluation on PTVeval covered by 95% of prescribed dose expressed in %

PTVe 95%	Mean ± SD	p value
FB	97.69 ± 1.16	0.11
DIBH	98.4 ±- 0.77	

Dose-volume parameters for OARs are shown on the tables below. Heart and heart sub-structures are presented in Table 2, and dosimetric data from ipsilateral lung is shown in Table 3.

Table 2. Dosimetric evaluation of heart and heart substructures. Legend: Dx - dose received by x % of the target volume, Dmean - mean absorbed dose within a target volume, Vx - volume receiving x Gy, FB – free breathing, DIBH – deep inspiration breath hold

	FB	DIBH	Mean dif.	Reduction %	p value
Heart					
Dmean (Gy)	2.52 ± 1.5	1.08±0.5	1.44	57	0.005
V16 Gy (%)	4.06 ± 3.7	0.4 ± 1.0	3.6	91.5	0.005
V16 Gy (cm^3)	29.4 ± 33.2	3.5 ± 9.2	25.8	89.1	0.022
Volume (cm^3)	674.3 ± 163	661.3 ± 153.6			0.85
LAD					
Dmean (Gy)	15.4 ± 8.9	3.4 ± 4.6	11.9	87.7	0.001
Dmax (Gy)	31.3 ± 124	9,9 ± 9.6	21.3	68.2	<0.005
Left ventricle					
Dmean (Gy)	3.9 ± 2.6	1.2 ± 0.6	2.6	68.2	0.003
Dmax (Gy)	34.0 ± 8.6	10.6± 9.7	23.4	68.9	0.000085

Table 3. Dosimetric evaluation of lung. Legend: Dx - dose received by x % of the target volume, Dmean - mean absorbed dose within a target volume, Vx - volume receiving x Gy. FB – free breathing, DIBH – deep inspiration breath hold

	FB	DIBH	Mean dif.	p value
Lung				
Dmean (Gy)	6.7 ± 2.3	5.5 ± 1.6	1.22	0.17
V16 Gy (%)	15.6 ± 6.1	15.5 ± 4.1	3.07	0.18
LungV16Gy (cm^3)	203.3 ± 80.6	309.7 ± 123.3	-106	0.03
Volume(cm^3)	1287 ± 238.6	2421.9 ± 353.5	-1133	<0.005

Discussion

Our study showed a substantial decrease in the radiation doses administered to the heart in DIBH plans relative to FB plans, without reducing the dose provided to the PTV. These findings are similar to other published studies, despite the small sample size and the challenge to compare studies with differences in study methods.

DIBH is already established technique for lowering cardiac dose in postoperative radiotherapy in patients with left-sided breast cancer. Many centers across the world have rich experience with this technique and use different technologies. ESTRO-ASCOP guidelines[11] were released in 2023 explaining equipment, staff training and couching, image guidance and guidance in delivering DIBH radiotherapy according to site (breast cancer, thoracic and abdominal tumors) providing overview of available technical solutions and guidance for best practice in the implementation phase.

UK HeartSpare comparative study concluded that vDIBH and ABC_DIBH are comparable in terms of positional reproducibility and normal tissue sparing, but vDIBH is preferred by patients and radiographers, takes less time to deliver, and is cheaper than ABC_DIBH[12]. Both techniques can lower cardiac dose but neither of them can monitor treatment based on the breast position, so the idea for combined use of respiratory-gated DIBH and an optical surface scanning system (OSMS) was brought for more reliable dose delivery to the target. Optical tracking AlignRT (Vision RT Ltd., London UK) system uses stereo vision technology by viewing an object through three units, each containing two cameras, and reconstructs the 3D surface information of the object using a computer vision algorithm. This system can be used for patient positioning prior to treatment, real-time target monitoring, and respiratory tracking. Several investigators have studied the feasibility and accuracy of the AlignRT system for left-breast DIBH treatment and proved advantage compared to multiple on-board imaging modalities [13, 14]. Rong *et al.* [15] in their study showed that AlignRT 3D surface imaging provided better target position accuracy during DIBH treatment compared to RPM alone, as determined by the MV Cine imaging, while ensuring patient setup and monitoring inter- and intra- fractional motions.

There are multiple studies that show the benefit from using DIBH. SAVE-Heart study[16] is the largest prospective study enrolling 585 patients with left-sided invasive breast carcinoma with indicated adjuvant radiotherapy of the breast/thoracic wall with or without regional lymph nodes. DIBH have been applied using the automatically triggered surface guidance system Catalyst with audio–video feedback. The results were published in 2024 showing that mean and maximum doses to the heart and the left coronary artery were significantly reduced by 36%-42% ($p<0.001$), while the mean ipsilateral lung dose was reduced by 12%-14% ($p<0.001$). Estimated risk reduction for 10-year cardiovascular risk in these patients treated with DIBH was 5%.

In our study, as expected, target coverage was not statistically significant with both (FB and DIBH) plans covering ≥95% by a dose of 95%. The mean dose to the heart was significantly reduced ($p=0.005$) in plans during DIBH, with a reduction of 57% or average 1.44 Gy. In addition, the volume of the heart that received 16 Gy (restrictions as per institutional protocols) expressed in percentage and in cm^3 was also reduced by 91.5% and 89.1% in DIBH plans (p value 0.005 and 0.022, respectively). The results from other studies show decrease in mean heart dose between 24% in the study by Wolf *et al.* [17] to more than 50% in the prospective study by Gaál *et al.* [18].

The mean and maximum doses in LAD were reduced in plans during DIBH compared to FB, with reductions of 87.7% and 68.2%, respectively (p<0.001). In two prospective trials by Knöchelmann *et al.* [19] and Ferdinand *et al.* [20], the mean LAD dose was reduced by 32% and 30.1%, respectively. The highest reduction of 68% was noted in the small retrospective study by Eber *et al.* [21]. The evaluation of mean and maximal dose on left ventricle showed reduced values for DIBH plans by 68.2 and 68.9% (p=0.003 and <0.001), respectively. Heart volume was insignificantly different between the two groups (p=0.85). The reason why the difference of LAD doses in our study was higher than in other studies (Table 4) can be explained. As mentioned earlier, LAD and left ventricle were not initially contoured as organs at risk (OARs) in the DIBH plans. They were contoured retrospectively and were not considered as constraints when creating the 3D-CRT plans for both DIBH and FB. However, when these structures were additionally evaluated as OARs in the DIBH plans, it was found that 10 out of 11 plans had values within clinical protocol (LAD Dmean <8 Gy), compared to only 3 plans, out of 11 in the FB group. This suggests that the 3D-CRT plans in FB would have required additional work to achieve acceptable values for LAD and left ventricle, resulting in smaller differences between DIBH and FB groups.

Table 4. Studies with both conventional and/or hypofractionated dose prescriptions that used DIBH surface-guided radiotherapy (SGRT) for the patient setup

Study	Design	No. patients	LAD mean dose reduction	Heart mean dose reduction	Lung mean dose reduction
Schönecker *et al.*[16]	Prospective	585	58%	36-37%	12-14%
Wolf *et al.* [17]	Retrospective	130	71%	24%	12.5%
Knöchelmann *et al.* [19]	Retrospective	357	32%	47%	9%
Gaál *et al.* [18]	Prospective	88	>60%	>50%	
Sakyanun *et al.* [22]	Prospective	25	25.3-42.1%	37.2-45.2%	
Ferdinand *et al.* [20]	Prospective	31	30.1%	39.15%	9.9%
Eber *et al.* [21]	Retrospective	10	68%	54.2%	
Current study	Retrospective	11	57%	87%	

As shown in Table 3, the volume of the ipsilateral lung is significantly higher in DIBH plans (p<0.005) with a median difference of 1133 cm^3. In our study, we did not show significancy in the mean dose delivered to the lung although the median difference was 1.22 Gy in favor for DIBH plans. The lung volume (cm^3) that received 16 Gy was significantly higher (p=0.03) in DIBH group, but when converted in percentage this difference was insignificant (p=0.18). When analyzing data from SAVE Heart study[16], the mean lung dose in DIBH group had an absolute value of 0.7 in hypofractionated and 1.32 in normofracionated group and yielded statistically significant reduction of 12% and 14%, respectively. However, V_{20Gy}, V_{10Gy}, and V_{5Gy} means in the lung were significantly higher in DIBH plans compared to FB plans (p < 0.001).

Considering all of the above mentioned, the surface-guided DIBH technique is a valuable method in reducing cardiac dose and doses to other OARs (LAD and left ventricle) when irradiating patients with left-sided breast cancer. While it may not be relevant for all patients, the notion of "as low as possible" suggests that any reduction is significant, particularly if it does not compromise target coverage. All patients with left-sided breast cancer should, whenever feasible, be treated with DIBH rather than FB.

Conflict of interest statement. None declared.

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