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# Quantifying benefit of deep inspiration breath hold technique in reducing cardiac avoidance area (CAA) and liver doses for right-sided breast cancer

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## Abstract

**Introduction:** The present study aimed to observe the difference in dosimetry between Deep inspiration breath hold (DIBH) and Free breathing (FB) in patients who received right-sided breast radiotherapy with Intensity-Modulated Radiotherapy (IMRT), focusing on the cardiac avoidance area (CAA) and liver doses.

**Materials and methods:** This retrospective study analyzed twenty-one right-sided breast cancer patients from 2018 to 2023 at our centre. Tangential multiple-field IMRT plans were generated using two scan datasets with identical field arrangements. Dose-volume histograms (DVH) were analyzed to compare dose to target volume and organs at risk. The mean and standard deviation represent continuous variables. Pairwise, Wilcoxon signed rank tests with two tails were used to compare the groups. The Statistical Package for the Social Sciences (SPSS) version 21 was used for all statistical calculations.

**Results:** The study found that PTV coverage was similar for both FB and DIBH. Most patients are stage II (52.4%) with invasive ductal carcinoma histology. Over half had undergone mastectomy. The primary endpoint of CAA exposure and liver doses was significantly lower in DIBH than in FB. The maximum dose to the CAA was 5.23 (0.00-11.09) with DIBH compared to 6.35 (2.89-14.32) with FB (p=0.05). The mean dose of the liver was 2.27 (0.45-6.38) with DIBH compared to 3.91 (0.95-10.36) with FB (p =0.001); similar trends were observed across other liver volumes. The mean dose to the right lung was 6.38 (1.88-12.94) with DIBH compared to 6.92 (1.66-16.09) with FB (p=0.018); similar trends were observed across other lung volumes. The mean dose to right coronary artery and contralateral breast was less with DIBH, but not statistically significant.

**Conclusion:** DIBH for right-sided breast irradiation effectively reduces CAA and liver exposure while maintaining target volume coverage. However, larger studies are needed to determine clinical benefits.

**Keywords:** Breast cancer, DIBH, Liver dosimetry, Cardiac avoidance area

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## Introduction

Breast cancer is the most common cancer diagnosed globally (1). Among women, it is the fifth leading cause of cancer-related death worldwide (2). A multidisciplinary approach is applied to the treatment of breast cancer, which includes surgical oncology, medical oncology, radiation oncology and pain and palliative care. Radiation Oncology forms a cornerstone in breast cancer management. It reduces both loco-regional recurrence and breast cancer mortality (3). As the chances of survival increase, the toxicities of radiation therapy may become more significant than the risks associated with the disease and become the critical factor in determining survival (4). Technical advancements in radiotherapy, such as intensity-modulated radiotherapy (IMRT), have improved dose distribution, sparing surrounding healthy tissues. Yet, even with IMRT, the proximity of the CAA, liver and other organs at risk (OARs) to the treatment area poses a challenge. The Deep Inspiration Breath Hold (DIBH) technique has emerged as a promising approach to mitigate this issue. DIBH has been proven to decrease the amount of radiation that reaches the heart and coronary arteries in patients with left-side breast cancer (LSBC) (5). Several dosimetric studies unequivocally endorse the use of this approach in patients with LSBC, with the expectation that it will lead to tangible therapeutic advantages (6). DIBH has become a standard of care in LSBC patients.

The potential benefit of DIBH in right-sided breast cancer (RSBC) has not been thoroughly explored, particularly concerning liver and cardiac or cardiac substructure dosimetry. Even though there is less risk to the heart during the treatment of RSBC, all possible methods to reduce the heart dose should be employed. A novel cardiac avoidance area (CAA) concept has emerged (7). This region corresponds to the base of the heart and has high radiosensitivity. CAA is located predominantly on the right side and should be explored for RSBC patients. The study aims to quantify the reduction in radiation dose to the CAA and liver achieved by employing DIBH during IMRT for right breast cancer patients. This is the first study that addresses the dosimetric advantage of CAA.

## Materials and methods

This study retrospectively analyzed twenty-one patients treated with adjuvant radiotherapy for RSBC between April 2018 and December 2023 at Manipal Hospital, Delhi, India. Inclusion criteria was non-metastatic right sided breast cancer patients, post-surgery (either mastectomy or lumpectomy) who received adjuvant radiotherapy (including regional nodal irradiation). Patients with age > 75 years or those unable to cooperate for DIBH were excluded. Patients were simulated in the supine position, with arms overhead. Planning CT was done using a 3mm slice thickness from chin to umbilicus. Two scans were taken, one with FB and the other with DIBH. The scans were imported to the Varian Eclipse treatment planning system version 15.6 (Varian Medical System, Palo Alto, CA). Target volumes and OARs were contouring per standard guidelines (8). The CAA that we established is based on the research done by McWilliam et al. (7). The CAA constitutes the following structures located at the base of the heart- the proximal portion of left and right coronary arteries, the right atrium and the aortic valve root. Structures were contoured separately and combined as a composite CAA. Both AM and VKP verified all contours. All patients received tangential multiple-field IMRT. IMRT plans were generated for all patients using two scan datasets with identical field arrangements: 1)FB and 2) DIBH. Photons of energy 6 MV were used. Prescription dose for post mastectomy radiotherapy was 40.05 Gray (Gy) in 15 fractions over 3 weeks whereas post BCS patients received 40.05Gyin 15 fractions over 3 weeks followed by boost (10-12.5 Gy in 5 fractions over 5 days)Plans were calculated using Eclipse version 15.6. To ensure uniformity, the same physicist was asked to plan on both CT data sets (FB and DIBH scans) for each patient. Predefine coverage acceptance criteria for PTV was V95 ≥ 95% and maximum dose (Dmax) < 107%. Dose-volume histograms were compared across both datasets. The primary objectives were dosimetric measurements of the dose to CAA, including mean and maximum (max) dose and liver, including mean dosage and volumes of ≥10 Gy (V10Gy) and ≥20 Gy (V20Gy) and ≥30 Gy (V30Gy). The study also compared the mean dose of the ipsilateral lung, the percentage of right lung volume receiving ≥5 Gy, ≥20 Gy and ≥30 Gy, the mean dose of the heart, the mean dose to the right coronary artery and the dose to the contralateral

breast. The mean represents continuous variables. Pairwise, Wilcoxon signed rank tests with two tails were used to compare the groups. The Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA) was used for all statistical calculations. Any change deemed statistically significant had a p-value of less than 0.05.

## Results

PTV coverage was comparable for both FB and DIBH. Mean V95 was 97% for both FB and DIBH. Table 1 shows the patient characteristics. The mean age of the patient was 48 years (range 34 to 69 years). The average Body Mass Index (BMI) was 27.26 kg/m$^2$. Most patients were stage II (52.4%), followed by stage III (38%). All patients had invasive ductal carcinoma histology. On immunohistochemistry, 47.6% of patients were hormone receptor-positive, followed by triple-negative breast cancer (TNBC). A total of 52.4% underwent mastectomy, and 90% received chemotherapy. Table 2 summarises the dosimetric comparison between FB and DIBH.

**Table 1.** Patient characteristics.

| | Number of patients (%) |
|---|---|
| **Age in years Mean (Range)** | 48.9 (34-69) |
| **BMI in kg/m$^2$ Median (range)** | 27.26 (21.2-35.7) |
| **Stage** | |
| **I** | 2 (9.6%) |
| **II** | 11 (52.4%) |
| **III** | 8 (38%) |
| **Histology** | |
| **IDC** | 21 (100%) |
| **ILC** | 0 |
| **Other** | 0 |
| **Receptor status** | |
| **ER/PR positive** | 10 (47.6%) |
| **Triple positive** | 3 (14.3%) |
| **Her2Neu positive** | 1 (4.8%) |
| **TNBC** | 7 (33.3%) |
| **Chemotherapy:** | |
| **Yes** | 19 (90.4%) |
| **No** | 2 (9.6%) |
| **Surgery** | |
| **Lumpectomy** | 10 (47.6%) |
| **Mastectomy** | 11 (52.4%) |

**Table 2.** The dosimetric endpoint of each target volume and organs at risk shown by Wilcoxon signed-rank test.

| Dosimetric endpoints | FB | DIBH | P value |
|---|---|---|---|
| PTV V95% | 97.88 (95.49-99.79) | 97.72 (95.2-99.29) | 0.650 |
| Cardiac Avoidance area (CAA), in Gy | 1.52 (0.65-3.58) | 1.48 (0.62-3.07) | 0.140 |
| Dmean | 6.35 (2.89-14.32) | 5.23 (0.00-11.09) | 0.050 |
| Dmax | | | |
| Liver mean dose , in Gy | 3.91 (0.95-10.36) | 2.27 (0.45-6.38) | 0.001 |
| Liver V30Gy | 2.62 (0.00-16.64) | 1.21 (0.00-7.98) | 0.001 |
| Liver V20Gy | 5.01 (0.58-16.64) | 3.50 (0.00-16.64) | 0.001 |
| Liver V10Gy | 11.73 (0.64-36.23) | 6.02 (0.00-24.16) | 0.001 |
| Right Lung mean dose, in Gy | 6.92 (1.66-16.09) | 6.38 (1.88-12.94) | 0.018 |
| Right Lung V30Gy | 5.33 (0.00-16.64) | 2.40 (0-16.08) | 0.016 |
| Right Lung V20Gy | 11.97 (1.91-35.36) | 5.92 (0.00-27.17) | 0.007 |
| Right Lung V5Gy | 37.03 (20.37-59.80) | 32.49 (0.01-57.72) | 0.274 |
| Heart mean dose, in Gy | 0.81 (0.32-2.62) | 1.11 (5.30-0.35) | 0.543 |
| Right coronary artery mean dose, in Gy | 2.87 (1.26-7.65) | 2.55 (0.49-5.58) | 0.099 |
| Opposite breast mean dose, in Gy | 0.41 (0.08-2.07) | 0.51 (0.10-2.82) | 0.794 |

### CAA

The primary endpoint, CAA exposure, was significantly lower with DIBH compared to FB. The maximum CAA dose was 5.23 Gy (0.0–11.09) under DIBH versus 6.35 Gy (2.89–14.32) with FB (p = 0.05). The mean CAA dose was slightly lower with DIBH at 1.48 Gy (0.62–3.07) compared to 1.52 Gy (0.65–3.58)

with FB, though this difference was not statistically significant (p = 0.14).

**Liver**

Liver exposure was also significantly reduced with DIBH. The mean liver dose decreased from 3.91 Gy (0.95–10.36) with FB to 2.27 Gy (0.45–6.38) with DIBH (p < 0.001). Similarly, the percentage of liver volume receiving ≥30 Gy was reduced from 2.62% (0.00–16.64) with FB to 1.21% (0.0–7.98) with DIBH (p < 0.001). The liver volume receiving ≥20 Gy decreased from 5.01% (0.58–16.64) with FB to 3.50% (0.00–16.64) with DIBH (p < 0.001), and the volume receiving ≥10 Gy decreased from 11.73% (0.64–36.23) with FB to 6.02% (0.0–24.16) with DIBH (p < 0.001).

**Right Lung**

The mean right lung dose was 6.38 Gy (1.88–12.94) with DIBH compared to 6.92 Gy (1.66–16.09) with FB (p = 0.018). The percentage of lung volume receiving ≥30 Gy was significantly reduced with DIBH (2.40%, range 0.00–16.08) compared to FB (5.33%, range 0.00–16.64) (p = 0.016). Similarly, lung V20Gy was reduced from 11.97% (1.91–35.36) with FB to 5.92% (0.0–27.17) with DIBH (p = 0.007). No significant difference was observed for lung V5Gy (37.03% vs. 32.49%, p = 0.274).

**Heart and Right Coronary Artery**

The mean heart dose was slightly higher with DIBH at 1.11 Gy (0.35–5.30) compared to 0.81 Gy (0.32–2.62) with FB, though this was not statistically significant (p = 0.543). The mean dose to the right coronary artery was lower with DIBH (2.55 Gy, range 0.49–5.58) than with FB (2.87 Gy, range 1.26–7.65), but again not statistically significant (p = 0.099).

**Contralateral Breast**

The mean contralateral breast dose was comparable between techniques: 0.51 Gy (0.10–2.82) with DIBH versus 0.41 Gy (0.08–2.07) with FB (p = 0.794).

Figure 1 (A and B) demonstrates 95% colour wash in the coronal and axial plane for DIBH versus FB in patients treated for the right chest wall. Figure 1 (C and D) demonstrates 95% colour wash in the coronal and axial plane for DIBH versus FB in a patient treated for right breast. Figure 2 A demonstrates 50% colour wash in the axial plane for DIBH, respectively, while Figure 2 B demonstrates 50% colour wash in the coronal and axial plane for FB in patients treated for right chest wall. Figure 3 shows the V30 Gray (Gy) liver dose for DIBH and FB.

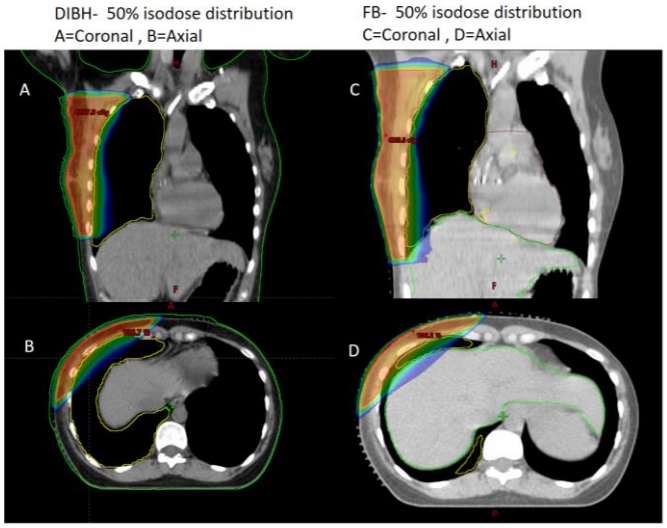


**Figure 1.** A and B demonstrate 95% colour wash in the coronal and axial plane for DIBH, respectively, while C and D demonstrate 95% colour wash in the coronal and axial plane for FB in patients treated for the right chest wall.

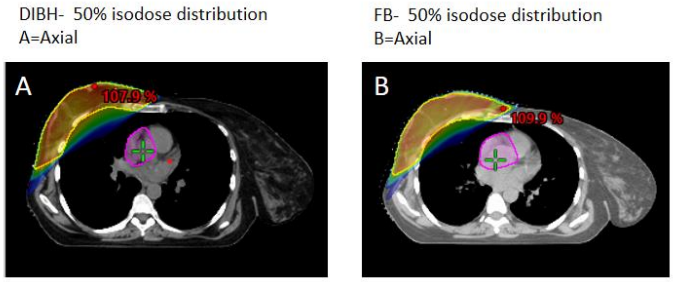


**Figure 2.** A demonstrate 50% colour wash in the axial plane for DIBH, respectively, while B demonstrates 50% in the coronal and axial plane for FB in patients treated for right chest wall.

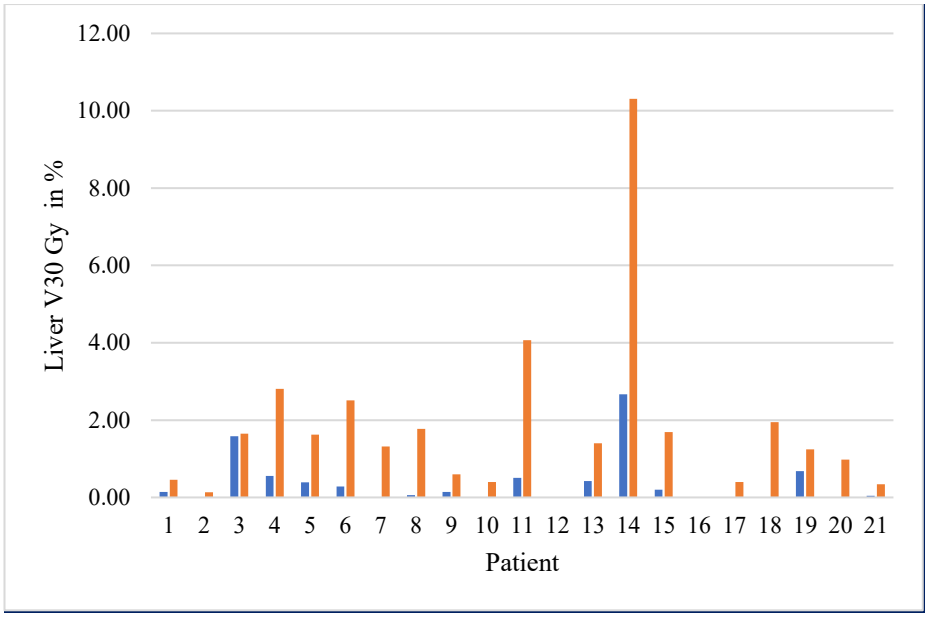


**Figure 3.** Demonstrates V30 Gy of the liver in percentage for DIBH and FB.

## Discussion

The present study is the first to evaluate and demonstrate a significant reduction in dose to the cardiac avoidance area (CAA) in patients with right-sided breast cancer (RSBC) undergoing IMRT with DIBH. In addition, our findings highlight the dosimetric advantages of DIBH for the liver in this patient group. These results have important implications, as DIBH may help minimize radiation-induced morbidities by reducing exposure to both cardiac and hepatic structures.

Since the initial demonstration of DIBH efficacy in lowering organ-at-risk (OAR) doses for left-sided breast cancer (LSBC) (11), the technique has become standard of care in LSBC management (9). However, fewer studies have investigated its role in RSBC.

Esser et al. (2016) were the first to explore DIBH in RSBC, showing reductions in cardiac and pulmonary doses in a small cohort of 14 patients treated with three-dimensional conformal radiotherapy (3D-CRT), though liver doses were not assessed (10). Conway et al. (11) and Haji et al. (12) also demonstrated reduced cardiac, lung, and liver doses using 3D-CRT with DIBH. Importantly, these studies did not report on CAA doses. Lia et al. (13) extended this work by incorporating surface-guided radiotherapy (SGRT)-based DIBH with IMRT, reporting dosimetric advantages for heart, liver, right coronary artery, and right lung, though CAA was again not evaluated.

By contrast, the current study used IMRT tangential fields and, uniquely, included the CAA as a structure of interest. To our knowledge, this is the first dosimetric analysis in RSBC patients to demonstrate CAA sparing with DIBH. Notably, Loap et al. (18) found no meaningful cardiac dose reduction with DIBH in RSBC when volumetric modulated arc therapy (VMAT) was employed, likely reflecting differences in planning technique. This underscores the importance of distinguishing among 3D-CRT, IMRT, and VMAT when interpreting prior findings.

While the dosimetric benefits of DIBH are evident, their clinical significance must be critically appraised. For example, in our study, the maximum CAA dose was significantly lower in the DIBH group, suggesting a potential reduction in long-term cardiac risk. Although mean heart and CAA doses were not statistically different between DIBH and free-breathing (FB), the consistent trend toward lower values supports the cardioprotective role of DIBH. Even modest reductions in heart exposure are clinically relevant, as prior research shows that each 1 Gy increase in mean heart dose raises the relative risk of coronary events by 7.4% (4).

For the liver, although baseline FB doses (mean ~3.9 Gy) were already well below accepted tolerance thresholds (30 Gy for partial liver irradiation) (20),

additional sparing with DIBH may still be beneficial in selected patients. This is particularly relevant for those who develop synchronous or metachronous liver tumors or who have received hepatotoxic chemotherapy, where minimizing hepatic exposure may reduce the risk of radiation-induced liver disease (RILD) (19,21,22).

Similarly, the reduction in ipsilateral lung dose (mean dose and V20Gy/V30Gy) observed with DIBH is consistent with prior RSBC studies (11,12). Even small improvements in lung dose metrics may lower the risk of radiation pneumonitis or long-term pulmonary dysfunction.

Overall, while our study is purely dosimetric and does not evaluate clinical outcomes, the observed dose reductions cross thresholds that are biologically and clinically meaningful.

Incidental radiation exposure to the heart can result in a spectrum of toxicities collectively termed radiation-induced heart disease (RIHD), including coronary artery disease, cardiomyopathy, and valvular dysfunction (14). Recent studies, such as that by McWilliam et al. (7), have emphasized the radiosensitivity of the CAA, where maximum dose strongly correlates with survival outcomes. The RAPID-RT program, currently underway in the UK, further highlights the clinical interest in CAA dosimetry (15). Our study contributes novel evidence by extending this concept to RSBC, showing that DIBH can significantly reduce CAA dose with IMRT tangents.

Thus, while RSBC patients are traditionally considered at lower risk for cardiac exposure than LSBC patients, our results suggest that careful incorporation of DIBH and modern planning techniques may provide meaningful long-term cardioprotection.

### Limitations of the study

The implementation and application of DIBH treatment pose several challenges. First, having an experienced clinic team with a quality assurance program for proper implementation is crucial. Procedures and guidelines for CT simulation and treatment delivery must be established, including patient training, breathing patterns, and imaging techniques. Quality assurance is also necessary for equipment related to breath holding and gated beam delivery. Patient cooperation and compliance are challenging, as not all cancer patients can hold their breath long enough and perform DIBH reproducibly. 4D gated treatment delivery may be a viable option for these patients, but its accuracy, reproducibility, and impact on treatment efficiency still need evaluation (23). Technical challenges include the longer imaging and treatment time required when using DIBH. Although the patient numbers in our study may be small, they still provide valuable insight into the potential dosimetric benefits of critical OARs. Finally, our study is single centre, retrospective study with small sample size and has reported the outcomes for DIBH only. Further studies are needed to evaluate the benefits of other 4D techniques, such as gating.

## Conclusion

Using IMRT with the DIBH technique is a valuable tool in reducing radiation exposure to surrounding healthy tissues, including the novel cardiac radiosensitive structure, CAA. In addition, it reduces radiation dose to liver, lung, and heart during radiation therapy for right breast cancer patients. Further research is needed to determine the long-term benefits of this technique, including its impact on disease-free survival and overall survival.

### Author contribution

Conceptualisation: **VKP** and **AM**

Data curation: **VKP** and **AM**

Methodology/formal analysis/validation: **VKP** and **AM** and **AMJ**

Project administration: **VKP** and **AM**

Writing original draft: **VKP** and **AM**

Writing review & editing: **VKP** and **AM** and **AMJ**

### Conflicts of interest

There are no conflicts of interest.

### Funding

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