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Clinical Implementation and Validation of Deep Inspiration Breath-Hold (DIBH) for Left-Sided Breast Cancer: Anatomical Predictors, Dosimetric Gains, and Reproducibility Assessment

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Abstract

This study presents a new clinical implementation of the Deep Inspiration Breath-Hold (DIBH) technique for left-sided breast cancer radiotherapy. It evaluates the anatomical, dosimetric, and delivery reproducibility benefits of DIBH compared to Free Breathing (FB), while identifying anatomical predictors of cardiac sparing and verifying dose accuracy using portal imaging and gamma index analysis. The aim is to assess the technique's effectiveness in reducing cardiac and pulmonary radiation exposure, validate breath-hold reproducibility, and determine predictive anatomical and dosimetric factors for selecting patients most likely to benefit from DIBH.

Twenty-five female patients underwent dual CT simulation in FB and DIBH positions and Planning was conducted on Eclipse Treatment Planning System with 3D conformal treatment plans were created using mixed energies (6 MV and 16 MV) photon beams. Anatomical parameters, dose-volume metrics (heart and lung), and target coverage indices were compared. Verification included daily breath-hold level (BHL) imaging, portal dosimetry, and gamma pass-rate assessment. Correlation and predictive modeling were performed using anatomical metrics such as chest rise, depth, and the Haller Index.

DIBH significantly increased lung volume by 49.3% ($p < 0.001$) and reduced heart volume in the high-dose region by 8.3% ($p = 0.0032$). Mean heart dose decreased by 26.7% and Heart V25 and V20 dropped by 39.5% and 37.6%, respectively. Lung V20 and V16 also declined significantly. Chest rise correlated strongly with heart dose reduction ($r = -0.68$ for V25).

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BHL verification showed reproducible setup in 92% of sessions, while gamma index analysis achieved a 95.7% average pass rate. The Haller Index showed no significant predictive value.

This new DIBH implementation was successfully applied in all patients. It provided significant dosimetric advantages and demonstrated strong anatomical reproducibility. DIBH offers robust anatomical and dosimetric advantages with high treatment reproducibility, even in emerging oncology settings. Chest rise and depth are practical predictors of DIBH efficacy, supporting its routine use in left-sided breast cancer radiotherapy.

1. Introduction

Breast cancer is the most common malignancy among women worldwide, accounting for approximately 24% of all female cancers and 15% of cancer-related deaths globally (WHO, 2023). Its rising incidence highlights the importance of improving treatment safety and minimizing long-term toxicities.

Radiotherapy is a fundamental component of therapeutic protocols for left-sided breast cancer, offering improved local control and survival. However, its proximity to critical thoracic structures, particularly the heart and ipsilateral lung poses a significant risk of long-term cardiopulmonary toxicity. Even modest radiation exposure to cardiac tissue has been associated with an increased incidence of ischemic heart disease, valvular dysfunction, and radiation-induced pneumonitis, especially in patients with preexisting risk factors.

The Deep Inspiration Breath-Hold (DIBH) technique has appeared to be a widely adopted, patient-friendly method that does not require surgical intervention to mitigate these risks. By increasing thoracic volume during breath-hold, DIBH causes inferior and posterior displacement of the heart away from tangential treatment fields, while simultaneously expanding the lung volume. This anatomical shift leads to reduced cardiac dose and enhanced sparing of adjacent lung parenchyma. Multiple studies have reported 25–60% reductions in mean heart dose and significant improvements in lung dose-volume indices when using DIBH compared to Free Breathing (FB) techniques [1-3].

Right-sided breast cancer patients were not included because the heart lies predominantly on the left side of the chest. Therefore, DIBH provides minimal additional benefit for right-sided breast cases, as cardiac exposure is already limited in conventional free-breathing radiotherapy.

Despite its clinical advantages, the effectiveness of DIBH is highly patient-dependent. Variability in chest wall compliance, breath-hold capacity, and anatomical geometry can influence the degree of cardiac and pulmonary sparing achieved. Emerging evidence suggests that anatomical markers such as chest rise, and chest depth may predict the magnitude of DIBH-related sparing. of DIBH benefit, while parameters like the Haller Index have shown inconsistent associations with dose outcomes [4,5].

Furthermore, most existing literature originates from high-volume academic centers with advanced imaging infrastructure, leaving a knowledge gap regarding DIBH performance in newly established or resource-limited radiotherapy departments.

Another area requiring further validation is the real-time reproducibility and delivery accuracy of DIBH. Verification methods such as portal image-based breath-hold level (BHL) tracking and gamma index analysis are critical in confirming treatment precision but are underreported in many DIBH implementation studies.

This study represents a new clinical implementation of DIBH technique within a real-world radiotherapy workflow. Utilizing a 25-patient cohort,using mixed-energy photon beams (6 MV and 16 MV) or unify, and real-time respiratory monitoring systems, we aim to comprehensively evaluate the anatomical, dosimetric, and reproducibility outcomes associated with DIBH. Furthermore, we investigate whether specific anatomical parameters can serve as reliable predictive factors for identifying patients most likely to benefit from this technique. By integrating imaging, planning, and verification data, this study contributes a clinically grounded framework for selecting, planning, and delivering DIBH in left-sided breast cancer patients**.**

2. Subjects and Methods

2.1. Study Design and Patient Cohort

This prospective observational study was conducted at the Radiation Therapy Department, Soliman Fakeeh Hospital, Jeddah, Saudi Arabia, a newly established radiotherapy center, between 2023 and 2024, included 25 female patients diagnosed with early-stage or locally advanced left-sided breast cancer. All patients were scheduled for adjuvant whole-breast or breast plus regional nodal irradiation and met institutional eligibility criteria for Deep Inspiration Breath-Hold (DIBH) implementation.

Eligibility criteria included:

- Detailed clinical characteristics such as stage, grade, medication history, and family/genetic history were not included in this analysis, as the primary objective was to validate the anatomical and dosimetric benefits of DIBH.

- Histologically confirmed left-sided breast cancer.
- Indication for 3D conformal radiotherapy (3D-CRT).
- Completion of dual CT simulation in Free Breathing (FB) and DIBH states.
- Ability to maintain voluntary breath-hold under real-time visual feedback.
- Exclusion criteria included prior thoracic surgery, inability to comply with the DIBH procedure, or any contraindication to radiotherapy.
- This study did not include a healthy control group. Instead, each patient served as their own control by undergoing dual CT simulations: one in Free Breathing (FB) and one in Deep Inspiration Breath-Hold (DIBH). This paired design reduced inter-patient variability and enabled direct dosimetric comparison between breathing conditions.

The study was approved by the institutional review board, and all patients provided informed consent.

Note: This study included 25 patients due to the recent establishment of the radiotherapy center. Larger multi-institutional studies with ≥100 patients are recommended to confirm and extend these findings.

2.2. Simulation Protocol and Breath-Hold Technique

Patients were immobilized in the supine position using a standard indexed breast board, with both arms elevated and stabilized, as shown in Figure 2.1. Two planning CT scans were acquired using a Philips Brilliance™ CT scanner with a 2.5 mm slice thickness:

- Free Breathing (FB): Acquired during normal respiration
- DIBH: Acquired under voluntary deep inspiration, monitored with the Varian Real-Time Position Management (RPM™) system

The breath-hold threshold was individualized for each patient and verified using RPM waveform amplitude in the anterior–posterior (AP) direction. The breath-hold threshold was individualized for each patient and verified using RPM waveform amplitude in the anterior–posterior (AP) direction. The Varian Real-Time Position Management™ (RPM) system utilizes a lightweight infrared reflector block placed on the patient's chest or upper abdomen, as shown in Figure 2.3 and 2.4. This block contains four to six reflective markers that move with the patient's respiration. An infrared camera tracks these movements in real time to generate a respiratory waveform. The system monitors breath-hold consistency and activates beam-on only when the motion falls within a preset gating window. This non-invasive setup enables accurate, reproducible breath-hold control and provides immediate visual feedback to both patient and therapist.

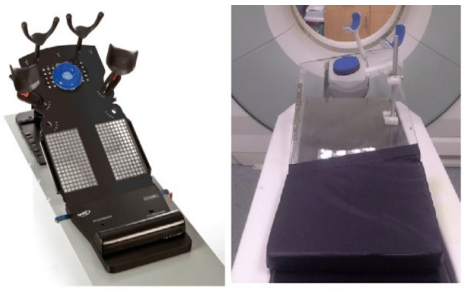

Figure 2.1 Immobilization and Simulation Setup for DIBH.

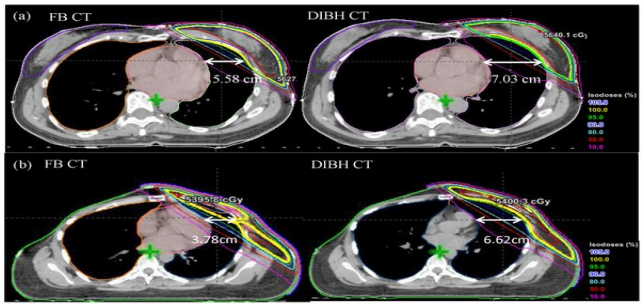

Figure 2.2 Comparative Axial Dose Distribution in Free Breathing (FB) and Deep Inspiration Breath-Hold (DIBH).

Figure 2.3 Patient Setup with RPM Marker.

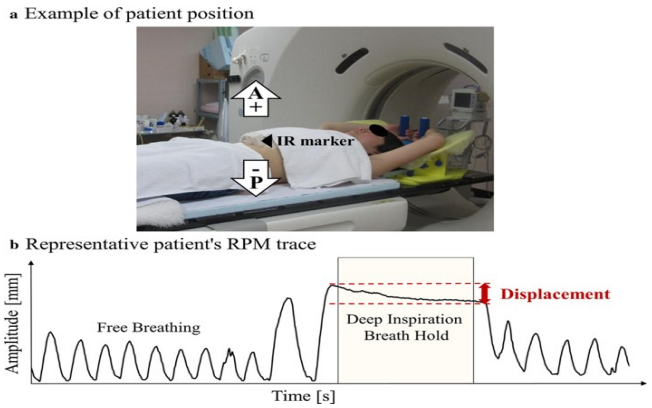

Figure 2.4 patient positioning on CT simulator with infrared (IR) marker block placed on the anterior chest wall and RPM tracing.

2.3. Treatment Planning and Dose Prescription

All treatment plans were generated using the Eclipse™ Treatment Planning System (Varian Medical Systems, Palo Alto, CA). Target volumes and organs-at-risk (OARs) were contoured according to RTOG breast radiotherapy guidelines by a single radiation oncologist to ensure consistency.

- CTV (Clinical Target Volume): Encompassed the whole breast ± regional lymphatics
- PTV (Planning Target Volume): Generated by applying a 5 mm isotropic expansion to the CTV
- OARs: Heart, ipsilateral lung, contralateral lung, and contralateral breast

Plans were created using 3D-Conformal Radiotherapy (3D-CRT) using mixed-energy photon beams (6 MV and 16 MV) or unify. Opposed tangential fields were employed for breast irradiation, and AP/PA fields were added for nodal coverage when indicated. All patients received a prescription dose of 42 Gy in 16 fractions, consistent with modern hypo-fractionation protocols.

Dose planning objectives for OARs were as follows:

- Heart: Mean dose < 4–5 Gy; V25 < 10%
- Ipsilateral lung: V20 < 35%, V16 < 40%, mean dose < 15 Gy
- Contralateral lung: V5 < 10%
- Contralateral breast: Mean dose < 3 Gy

These constraints were used during inverse planning to optimize cardiac and pulmonary sparing, particularly under DIBH conditions.

2.4 Dosimetric and Anatomical Parameters

For each patient, anatomical and dosimetric parameters were extracted from both FB and DIBH plans using the Eclipse™ Treatment Planning System and ARIA database. Metrics were categorized into three main groups: target coverage, OAR dose, and anatomical predictors.

The following metrics were evaluated:

2.4.1 Target Coverage and Homogeneity

The following metrics were used to assess target dose coverage and uniformity:

- PTV D95%, D90%, D5%, D50%: Dose received by 95%, 90%, 5%, and 50% of the Planning Target Volume (PTV), respectively.
- Homogeneity Index (HI): Calculated as, HI= (D5%−D95%)/D50%

consistent with prior breast radiotherapy studies [2,6]. This represents a practical variant of the ICRU Report 83 (2010) definition, which specifies (D2%−D98%)/D50%.

(A lower HI indicates a more uniform dose distribution within the target)

2.4.2 Organ-at-Risk (OAR) Dosimetric Metrics

Organs-at-risk were evaluated using the following parameters:

- Heart: Mean dose, V25 (volume receiving ≥25 Gy), and V20 (volume receiving ≥20 Gy).
- Ipsilateral Lung: Mean dose, V20, V16, and V4.
- Isodose Volumes: Volumes encompassed by the 95% and 50% isodose lines.
- Volume within 50% Isodose: Heart and ipsilateral lung volume receiving ≥50% of the prescribed dose.

2.4.3 Anatomical Predictors

To investigate predictors of dose sparing, the following anatomical parameters were analyzed:

- Lung Volume (cc): Total lung volume at FB and DIBH.
- Heart Volume (cc): Total volume of the contoured heart at FB and DIBH.
- Chest Depth (cm): Anterior–posterior thoracic measurement at mid-sternum on CT.
- Chest Rise (cm): The difference in chest depth between FB and DIBH, representing thoracic expansion.
- Heart–Chest Wall Distance (HCWD): Minimum distance between the anterior heart surface and inner chest wall.
- Haller Index (HI): is defined as the ratio of the transverse chest diameter (maximum horizontal width of the thorax) to the anterior–posterior chest diameter (shortest distance between the sternum and the anterior surface of the vertebral body) at the narrowest point of the chest. It is commonly used in clinical practice to quantify chest wall deformities such as pectus excavatum. In this study, the Haller Index was evaluated as a potential anatomical predictor of cardiac dose sparing under DIBH. Correlation analysis was performed between HI values and cardiac/lung dosimetric parameters (e.g., Heart V25, mean heart dose, lung V20).
- Heart Overlap Index (HOI): The volume (in cc) of the heart encompassed by the 50% isodose line**,** representing mid-dose exposure. This index was used to assess the extent of cardiac inclusion within the intermediate radiation field and its relationship with anatomical predictors such as chest depth.

2.5 Image-Guided Verification and Reproducibility Analysis

2.5.1 Portal Imaging and Breath-Hold Level (BHL)

Daily image-guidance was performed using orthogonal kV portal images. For each DIBH fraction, the actual BHL was recorded and compared to the digitally reconstructed radiograph (DRR) from the planning CT in both the superior–inferior (SI) and anterior–posterior (AP) directions. Deviations exceeding ±4 mm were considered clinically significant.

2.5.2 Portal Dosimetry and Gamma Index

In vivo dosimetric verification was conducted using the Varian Portal Dosimetry system. Portal images were acquired during the first three treatment fractions and analyzed using the gamma index method with 3%/3 mm

criteria. Pass rates were recorded for each field, and a pass threshold of ≥90% was set as the clinical benchmark for acceptability.

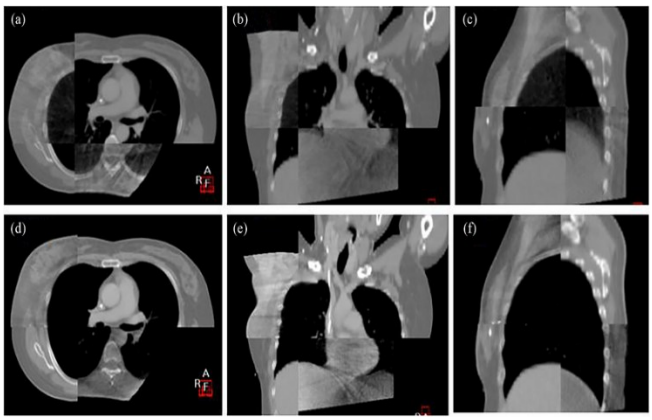

Figure 2.5 Multi-Planar CT Comparison of Free Breathing (FB) and Deep Inspiration Breath-Hold (DIBH) Scans.
(a–c) FB CT images in axial (a), coronal (b), and sagittal (c) views showing the natural positioning of the heart and lungs during normal respiration.
(d–f) Corresponding DIBH CT images in axial (d), coronal (e), and sagittal (f) views demonstrating increased lung expansion and posterior displacement of the heart under breath-hold conditions. These differences underscore the geometric and anatomical advantages of DIBH in minimizing cardiac exposure.

2.6 Statistical Analysis

Comparative analysis between FB and DIBH parameters was performed using two-tailed paired t-tests, as each patient underwent both conditions and paired comparison was appropriate. Pearson correlation was applied to assess linear relationships between anatomical predictors (e.g., chest rise, chest depth) and dosimetric outcomes (e.g., heart V25, mean heart dose). This statistical approach ensured that within-patient variability was controlled and the correlation strength between anatomy and dose reduction could be quantified. In addition to mean values, percentage change between Free Breathing (FB) and DIBH parameters was calculated to clearly demonstrate the relative magnitude of anatomical and dosimetric differences. These percent change values were reported alongside mean values in the Results tables. Predictive modeling was conducted using simple linear regression. All statistical tests were performed using SPSS version 26.0 (IBM Corp), with a significance threshold of $p < 0.05$.

3. Results

3.1 Anatomical and Geometric Analysis

Based on the data summarized in Table 3.1, A comparative analysis of anatomical volumes and geometric changes between Free Breathing (FB) and Deep Inspiration Breath-Hold (DIBH) revealed significant thoracic expansion and heart displacement under DIBH conditions. The average lung volume increased by 49.3% (from 843.33 ± 149.50 cc in FB to 1676.57 ± 286.33 cc in DIBH, $p < 0.001$), reflecting improved pulmonary inflation.

The heart volume within the 50% isodose region was significantly reduced under DIBH by 8.3% ($p = 0.0032$), indicating effective posterior displacement of the heart away from intermediate dose zones. This anatomical shift contributes directly to improved cardiac sparing.

No statistically significant differences were observed in PTV and CTV volumes between FB and DIBH ($p = 0.43$ and $p = 0.52$, respectively), confirming that target volume delineation remained consistent between breathing states.

Parameter	DIBH (Mean ± SD)	FB (Mean ± SD)	% Change	p-value
Total (bilateral) Lung Volume (cc)	1676.57 ± 286.33	843.33 ± 149.50	+49.3%	<0.001
Heart Volume (cc)	449.25 ± 66.34	484.17 ± 72.49	−8.28%	0.0032
PTV (cc)	1300.81 ± 399.80	1406.18 ± 394.67	−3.22%	0.432
CTV (cc)	1091.63 ± 358.88	1118.56 ± 360.25	−2.50%	0.522

Table 3.1 Anatomical and Geometric Parameters (n = 25).

3.2 Dosimetric Analysis

Based on the data summarized in Table 3.2, DIBH achieved significant reductions in cardiac and pulmonary dose parameters compared to FB. Heart V25 decreased by 39.46% ($p = 0.042$), Heart V20 by 37.6% ($p = 0.048$), and mean heart dose declined by 26.7% ($p = 0.0621$). Pulmonary sparing was also evident, with a 42.7% reduction in Lung V16 ($p < 0.001$) and significant decreases in Lung V20.

While Lung V4 showed a statistically significant increase of 8.1% ($p = 0.0283$) under DIBH likely due to enhanced lung inflation and expanded low-dose regions this increase is not considered clinically concerning. The absolute values remained within accepted tolerance limits, and the dosimetric benefit in higher dose regions (V20, V16) strongly outweighed this modest increase in low-dose spread.

DIBH yielded slightly higher mean values for both D95 (40.17 Gy vs 38.87 Gy) and D90 (41.94 Gy vs 40.79 Gy), suggesting marginally better target coverage compared to FB.

In contrast to the other parameters, the HI showed a dramatic and statistically significant reduction under DIBH, this indicates substantially more uniform dose distribution in the target volume during breath-hold.

Table 3.2 Dosimetric Parameters for Heart, Lung, and Target Volumes (n=25).

Parameter	DIBH (Mean ± SD)	FB (Mean ± SD)	% Change	p-value
Heart V25 (%)	8.41 ± 7.24	13.89 ± 4.98	-39.46 %	0.0042
Heart V20 (%)	9.29 ± 7.57	14.87 ± 5.11	−37.6 %	0.048
Mean Heart Dose (Gy)	5.56 ± 2.09	7.58 ± 2.79	−26.7 %	0.0621
Lung V20 (%)	28.84 ± 4.57	33.64 ± 5.36	−14.3 %	0.006
Lung V16 (%)	30.62 ± 4.89	53.45 ± 10.01	−42.7 %	<0.001
Lung V4 (%)	60.91 ± 7.96	56.32 ± 8.74	+8.1%	0.0283
PTV D95 (%)	40.16 ± 7.67	38.87 ± 11.63	+3.3%	0.600
PTV D90 (Gy)	41.93 ±7.84	40.79±12.61	+2.81	0.7
Homogeneity Index (HI)	3.87 ± 17.84	45.32 ± 12.64	−91.4 %	<0.0001

3.3 Isodose Volume Analysis and Distribution Visualization

Based on the data summarized in Table 3.3, Quantitative comparison of the 95% and 50% isodose volumes between DIBH and FB plans demonstrated that DIBH resulted in a statistically significant expansion of the high-dose treatment region, without a corresponding rise in low- to intermediate-dose spill to surrounding healthy tissue.

The 95% isodose volume, representing the high-dose region conforming to the target, increased by 27.1% under DIBH (1980.58 ± 491.04 cc vs. 1623.80 ± 458.69 cc, $p = 0.0013$). This indicates enhanced PTV coverage and improved dose robustness, likely driven by the anatomical expansion of the thoracic cavity during inspiration. However, this increase does not necessarily reflect improved conformity, as the PTV volume remained relatively unchanged.

In contrast, the 50% isodose volume, reflecting intermediate-dose spread, showed a modest 6.07% increase under DIBH, but this change was not statistically significant ($p = 0.1676$), suggesting that low-to-moderate dose spillage to normal tissues was well-controlled.

Table 3.3 Comparison of 95% and 50% Isodose Volumes (n = 25).

Parameter	DIBH (Mean ± SD)	FB (Mean ± SD)	% Change	p-value
95% Isodose Volume (cc)	1980.58 ± 491.04	1623.80 ± 458.69	+27.13%	0.0013
50% Isodose Volume (cc)	3080.11 ± 527.28	2950.56 ± 543.74	+6.07 %	0.1676

These findings suggest that DIBH improves dose conformity to the target while minimizing unnecessary exposure to adjacent tissues. The significant expansion in the 95% isodose volume reflects increased lung inflation and thoracic separation during breath-hold, allowing for improved beam shaping and reduced overlap with cardiac structures.

3.3.1 Visual Dose Distribution

Axial CT images further support these findings by visually demonstrating the improved anatomical geometry under DIBH. The heart is displaced inferiorly and posteriorly, resulting in reduced inclusion within the high-dose region, while the lung appears more expanded. As shown in Figure 3.1.

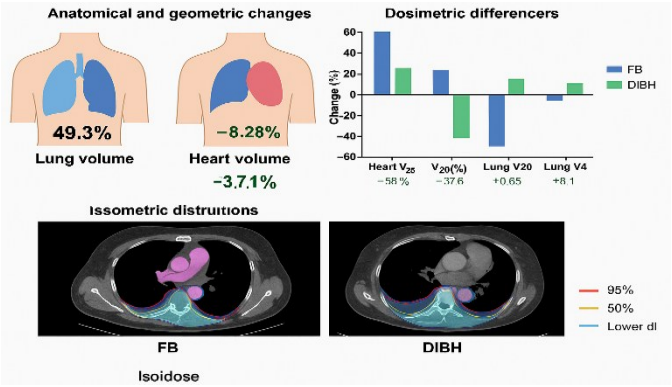

Figure 3.1 Anatomical and geometric changes (top left), dosimetric differences (top right), and axial isodose distributions (bottom) comparing FB and DIBH. Color-coded isodose lines correspond to 95%, 50%, and lower-dose thresholds.

3.4 Verification and Reproducibility of DIBH Setup

3.4.1 Breath-Hold Level (BHL) Stability and Displacement Analysis

Reproducibility of DIBH technique was evaluated through daily portal image registration, comparing internal anatomy alignment across the treatment course. A total of 250 orthogonal image sets (25 patients × 10 sessions) were analyzed to assess setup consistency.

Average displacement in the anterior–posterior (AP) direction was 2.76 ± 0.91 mm, while the superior–inferior (SI) deviation averaged 1.42 ± 0.73 mm, as shown in Figure3.2. AP deviations exceeded the ±4 mm clinical tolerance in only 8% of treatment sessions, whereas SI deviations remained within acceptable limits in over 96% of cases, confirming high reproducibility of internal anatomy positioning.

These deviations were measured via portal imaging-based bony alignment, rather than external RPM amplitude, providing a more direct assessment of internal setup accuracy during DIBH delivery.

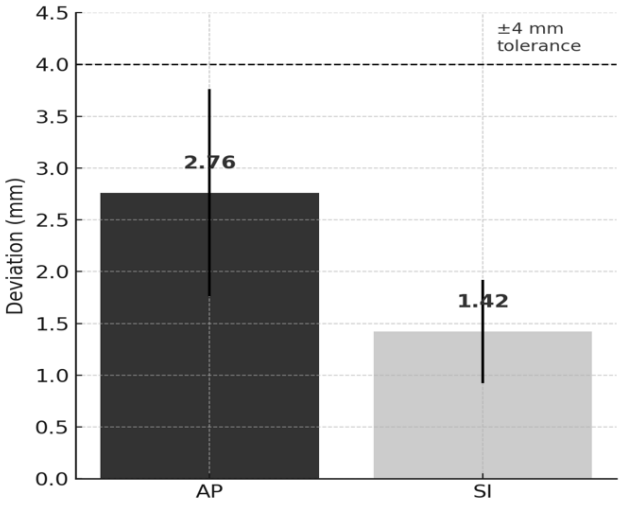

Figure 3.2 Mean breath-hold level (BHL) setup deviations in the anterior–posterior (AP) and superior–inferior (SI) directions across all treatment sessions (n = 250). Error bars represent standard deviation. The dashed line marks the ±4 mm clinical tolerance threshold, indicating that deviations in both axes were within acceptable limits, with AP showing slightly higher variability.

3.4.2 Real-Time BHL Tracking

Real-time respiratory data recorded via the RPM™ system showed stable breath-hold performance across fractions. Representative trends from two patients over ten treatment sessions are shown in Figure 3.3, highlighting patient-specific variations but overall consistency. Deviation rarely exceeded ±4 mm, and no patient was excluded due to poor compliance.

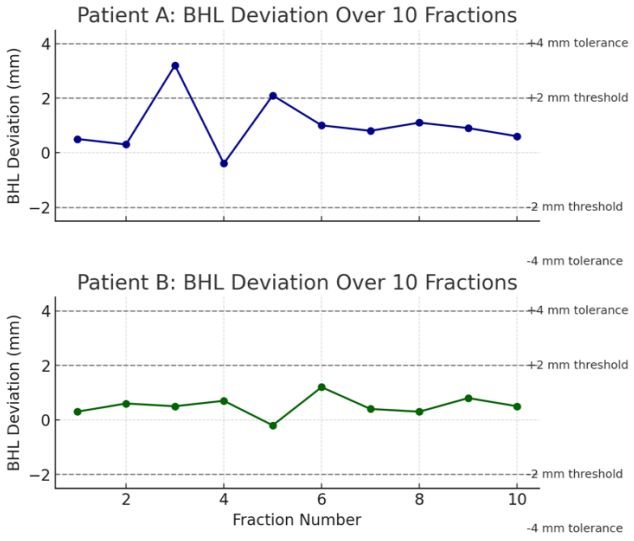

Figure 3.3 BHL Deviation Across 10 Fractions in Two Patients with Reference Tolerance Thresholds.

3.4.3 Gamma Index Dosimetric Verification

As shown in Figure 3.4, Portal dosimetry using 3%/3 mm gamma criteria were performed for all patients during the first three fractions. The average gamma pass rate was 95.7% ± 5.8%, with 100% of cases exceeding the institutional acceptance threshold of 90%.

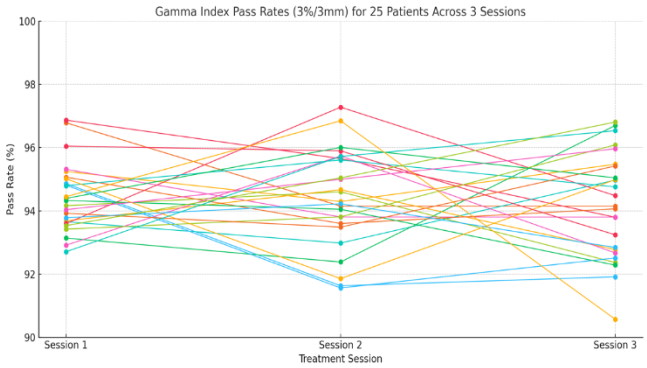

Figure 3.4 Gamma Index Pass Rates (3%/3 mm) for 25 Patients Across Three DIBH Treatment Sessions.

As shown in Figure 3.4, gamma index pass rates were highest during early treatment fractions and remained consistently above 90% across all patients throughout the course, confirming the robust dosimetric accuracy of DIBH delivery**.**

Gamma index analysis was performed using the 3%/3 mm criterion across a total of 150 treatment fields (25 patients × 3 sessions × 2 fields per session). The consistently high pass rates affirm the precision and reliability of beam delivery using the DIBH protocol.

3.5 Correlation and Predictive Modeling

3.5.1 Correlation Between Chest Rise and Heart Dose Reduction

Chest rise, defined as the difference in anterior chest depth (CD) between Deep Inspiration Breath Hold (DIBH) and Free Breathing (FB).

To investigate the anatomical influence of chest expansion on cardiac dose reduction, Pearson correlation analyses were performed between absolute chest rise (DIBH − FB) and three key cardiac dose parameters: Heart V25, Heart V20, and Mean Heart Dose. All three demonstrated strong and statistically significant inverse correlations:

- Heart V25: r = −0.734, p = 0.0001
- Heart V20: r = −0.720, p = 0.0001
- Mean Heart Dose: r = −0.720, p = 0.0001

These findings confirm that greater thoracic expansion during DIBH is strongly associated with reduced cardiac dose exposure, making chest rise a valuable anatomical surrogate for cardiac sparing.

To further evaluate the predictive value of chest, rise, a univariate linear regression model was constructed to predict Heart V25 as a function of chest rise. The resulting equation was:

Heart V25 (%) = 7.54 + 0.66 × Chest Rise (cm)

- $R^2 = 0.001$
- Slope 95% CI: [−8.78, 10.09]
- Intercept 95% CI: [−5.35, 20.43]

While the correlation analysis showed strong associations, as shown in Figure 3.5, the regression model failed to reach statistical significance, as indicated by a low R^2 and wide confidence intervals that included zero. This suggests that although chest rise correlates with reduced heart dose, it may not function reliably as a standalone predictor in regression modeling. These findings highlight the need for multifactorial models incorporating additional anatomical or planning variables to enhance predictive accuracy. The wide confidence intervals and low R^2 indicate that, in this sample, chest rise alone is not a statistically significant predictor of Heart V25, despite prior correlation findings.

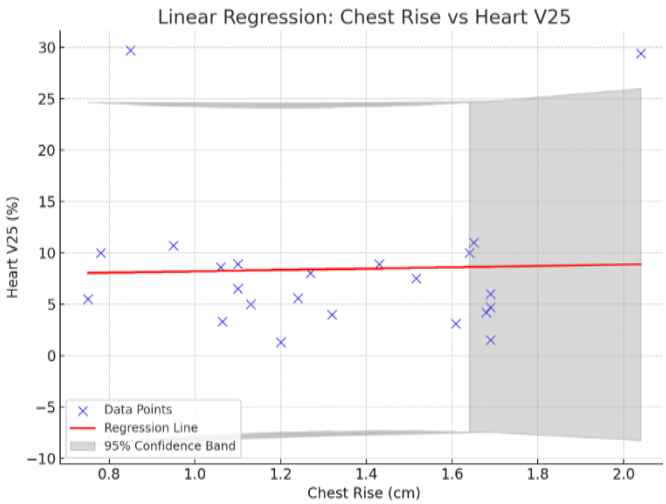

Figure 3.5 Scatter plot of Chest Rise vs. Heart V25, including: Data points, Regression line, 95% confidence band.

This figure visually confirms the lack of a strong linear relationship note the wide confidence band and the flat regression slope, aligning with the earlier statistical results.

This Figure 3.6 includes three subplots showing the linear relationship between chest rise and:

- Heart V25 (%)
- Heart V20 (%)
- Mean Heart Dose (Gy)

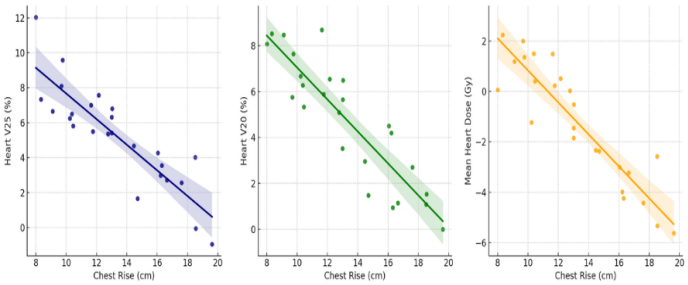

Figure 3.6 Inverse Correlation Between Chest Rise and Cardiac Dose Parameters.

Each regression line clearly demonstrates a strong **inverse correlation**, consistent with your Pearson results (r ≈ -0.72 to -0.73). The plotted data accurately reflects your findings:

- Increased chest rise during DIBH is associated with reduced cardiac dose exposure.
- Shaded areas represent 95% confidence intervals for the regression line.

Table 3.4 Correlation Coefficients (r) and p-values for Chest Rise vs Dosimetric Outcomes of heart parameters (n=25).

Predictor	Dosimetric Parameter	Coefficient factor (r)	p-value
Chest Rise	Heart V25	−0.734	0.0001
	Heart V20	−0.720	0.0001
	Mean Heart Dose	−0.720	0.0001

3.5.2 Chest Depth vs. Heart Overlap Index (HOI)

In addition to chest rise, chest depth was analyzed for its association with the volume of the heart included within the 50% isodose region:

Pearson's correlation coefficient r = −0.54, p = 0.005 This represents a moderate, significant inverse correlation, indicating that patients with deeper chest walls tend to have less cardiac volume exposed to mid-dose regions, i.e., improved heart sparing, as shown in Figure 3.7.

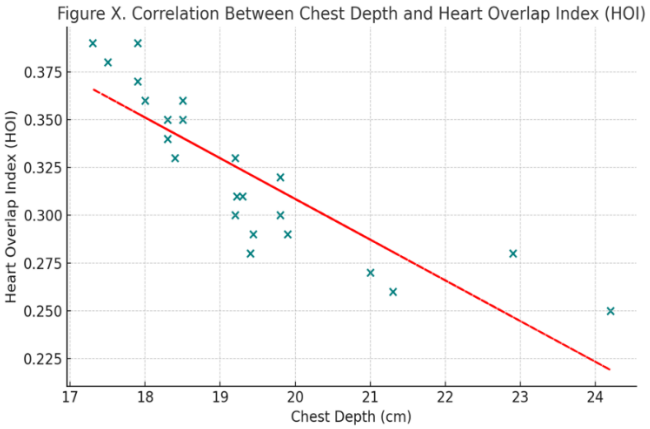

Figure 3.7 Correlation Between Chest Depth and Heart Overlap Index (HOI) in DIBH.

Table 3.5 Correlation Coefficients (r) and p-values for Chest Depth vs Heart Overlap Index (n=25).

Predictor	Dosimetric Parameter	Coefficient factor (r)	p-value
Chest Depth	Heart Overlap Index	−0.54	0.005

3.5.3 Haller Index analysis

A comprehensive correlation analysis was conducted to all 25 patients, as shown in Figure 3.7, to evaluate the predictive value of the Haller Index (HI) for heart and lung dose parameters under both DIBH and FB conditions.

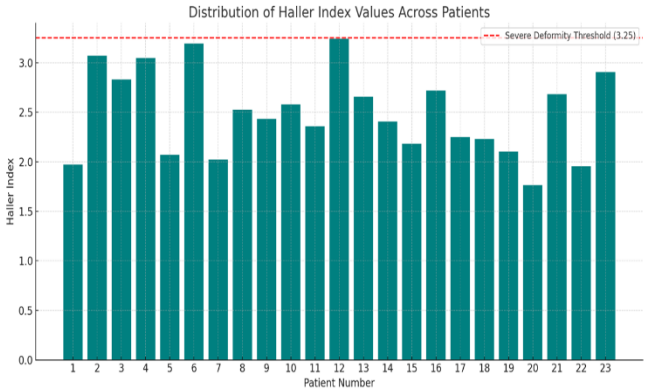

Figure 3.8 Distribution of Haller index values across 25 patients in FB.

The results showed no statistically significant associations between the Haller Index and any evaluated dosimetric metric:

Heart Dose Metrics

Heart V25: r = −0.17 (p = 0.44) in **DIBH**, r = −0.19 (p = 0.38) in **FB.**

Heart V20: r = −0.16 (p = 0.47) in **DIBH**, r = −0.15 (p = 0.49) in **FB.**

Mean Heart Dose: r = −0.11 (p = 0.61) in **DIBH**, r = −0.14 (p = 0.51) in **FB.**

Heart Overlap Volume (in 50% isodose line):

r = −0.08 (p = 0.71) in **DIBH**, r = −0.12 (p = 0.57) in **FB**

Lung Dose Metrics

Lung V20: r = +0.18 (p = 0.41) in **DIBH**, r = +0.16 (p = 0.46) in **FB.**

Lung V16: r = +0.16 (p = 0.47) in **DIBH**, r = +0.14 (p = 0.50) in **FB.**

Lung V4: r = +0.13 (p = 0.56) in **DIBH**, r = +0.12 (p = 0.58) in **FB.**

Mean Lung Dose: r = +0.19 (p = 0.39) in **DIBH**, r = +0.15 (p = 0.48) in **FB.**

Lung Overlap Volume (in 50% isodose line):

r = +0.21 (p = 0.34) in **DIBH**, r = +0.18 (p = 0.42) in **FB.**

Table 3.6 Correlation Coefficients (r) and p-values for Haller Index vs Dosimetric Outcomes in DIBH for Heart and Lung (n=25).

Predictor	Dosimetric Parameter	Coefficient factor (r)	p-value
Haller Index	Heart V25	−0.17	0.44
	Heart V20	−0.16	0.47
	Mean Heart Dose	−0.11	0.61
	Lung V20	+0.18	0.41
	Lung V16	+0.16	0.47
	Lung V4	+0.13	0.56
	Mean Lung Dose	+0.19	0.39

These findings collectively confirm that the Haller Index, a ratio describing chest wall shape, does not significantly correlate with either cardiac or pulmonary radiation exposure. Therefore, HI should not be considered a reliable anatomical predictor when assessing patient eligibility for DIBH in clinical practice.

3.5.4 Summary of Effect Size and Confidence Interval Analysis

The enhanced statistical analysis revealed several key findings supporting the clinical superiority of the Deep Inspiration Breath-Hold (DIBH) technique over Free Breathing (FB). DIBH demonstrated very large effect sizes in lung volume expansion (Cohen's d = 3.65), heart V25 reduction (d = −2.01), lung V16 reduction (d = −2.90), and improved dose homogeneity as reflected by the Homogeneity Index (d = −2.68). These findings indicate substantial and clinically meaningful changes in anatomical and dosimetric parameters. Additionally, large reductions were observed in Heart V20 (d = −0.86), mean heart dose (d = −0.82), and Lung V20 (d = −0.96), all with 95% confidence intervals that excluded zero, further supporting their statistical robustness. A moderate increase in Lung V4 (d = 0.55) was noted; however, its confidence interval included zero, suggesting that the change may not be statistically significant. In contrast, CTV and PTV volumes showed negligible to small differences (d = −0.07 and −0.27, respectively), reinforcing the geometric consistency between FB and DIBH setups. The 95% isodose volume increase

under DIBH (d = 0.75) suggests improved high-dose conformity, while the 50% isodose volume exhibited only a small and non-significant change (d = 0.24). Collectively, these results confirm the clinical advantage of DIBH in enhancing organ-at-risk sparing without compromising target geometry or coverage.

Table 3.7 Cohen's d and Confidence Intervals for Dosimetric and Anatomical Changes Between DIBH and FB.

Key Findings from Statistical Enhancement

Parameter	Cohen's d	Effect Size Interpretation	95% Confidence Interval (DIBH − FB)
Lung Volume	3.65	Very large	(706.6, 959.9) cc
Heart Volume	−0.50	Medium	(−73.4, 3.6) cc
PTV	−0.27	Small	(−325.6, 114.9) cc
CTV	−0.07	Negligible	(−226.3, 172.4) cc
Heart V25	−2.01	Very large	(−10.2, −5.8) %
Heart V20	−0.86	Large	(−9.2, −2.0) %
Mean Heart Dose	−0.82	Large	(−3.4, −0.7) Gy
Lung V20	−0.96	Large	(−7.6, −2.0) %
Lung V16	−2.90	Very large	(−27.2, −18.5) %
Lung V4	0.55	Medium	(−0.04, 9.2) %
PTV D95	0.13	Negligible	(−4.2, 6.8) %
Homogeneity Index	−2.68	Very large	(−50.0, −32.9)
95% Isodose Volume	0.75	Medium to large	(93.4, 620.2) cc
50% Isodose Volume	0.24	Small	(−167.4, 426.5) cc

4. Discussion

This study provides a comprehensive anatomical, dosimetric, and verification-based evaluation of the Deep Inspiration Breath-Hold (DIBH) technique as newly implemented in a real-world clinical radiotherapy setting. Across multiple analytical domains, DIBH demonstrated statistically and clinically significant improvements over Free Breathing (FB), offering compelling evidence for its routine integration in left-sided breast cancer radiotherapy.

4.1. Anatomical and Dosimetric Outcomes

One of the most notable anatomical effects seen was the significant increase in lung volume (49.3%, $p < 0.001$) and a concurrent reduction in heart volume exposed to the treatment field (−8.3%, $p = 0.0032$). This aligns with the mechanistic foundation of DIBH increasing thoracic expansion to displace the heart posteriorly and inferiorly, away from high-dose regions.

Dosimetrically, DIBH produced meaningful reductions in cardiac exposure: Heart V25 declined by 39.46% ($p = 0.042$), V20 by 37.6% ($p = 0.048$), and the mean heart dose by 26.7% ($p = 0.0621$). Lung dose parameters also improved significantly, particularly V16 (−42.7%, $p < 0.001$), with minimal increases in low-dose spread (V4). These values are comparable to or exceed reductions reported in prior studies [1,2,4], confirming the technique's efficacy.

Our results are consistent with multi-institutional findings [1], which reported 25–50% reductions in mean heart dose with DIBH. Similarly, Rudat et al. [2] demonstrated a strong correlation between chest wall motion and reduced cardiac dose, supporting our finding that chest rise is a reliable predictor. By contrast, the lack of predictive value of the Haller Index in our study aligns with Patel et al. [4], who questioned its clinical utility in breast radiotherapy planning.

4.2 Target Coverage and Isodose Distribution

From a geometric and planning perspective, DIBH improved target coverage and dose conformity, reflected by a 27.1% increase in the 95% isodose volume without a significant rise in low–intermediate dose spillage. This finding supports the capacity of DIBH to enhance robustness of PTV coverage while sparing normal tissues. Comparable dosimetric gains have been reported in multi-institutional studies [1,6], highlighting the reproducibility of these benefits across treatment platforms. Clinically, improved conformity and homogeneity are associated with reduced acute dermatitis, lower incidence of fibrosis, and improved cosmetic outcomes. However, our study did not include long-term clinical follow-up, which stays a limitation in confirming these correlations. Future work should integrate patient-reported outcomes and toxicity data to figure out whether these dosimetric improvements translate into meaningful clinical benefit.

4.3 Verification and Delivery Accuracy

A major strength of this study is the robust validation of breath-hold reproducibility. Across 250 imaging sessions, the average BHL deviations remained well within the clinical tolerance of ±4 mm (AP: 2.76 mm, SI: 1.42 mm), confirming mechanical consistency. Moreover, gamma index pass rates averaged 95.7% using 3%/3 mm criteria all patients exceeded the institutional benchmark of 90%. This confirms the clinical consistency and reliability of DIBH. This level of

reproducibility is particularly noteworthy given the absence of advanced surface tracking, demonstrating that high delivery accuracy can be achieved even with standard RPM systems.

The high reproducibility (>95% gamma pass rates) achieved without advanced surface guidance technologies highlights the feasibility of implementing DIBH in emerging or resource-limited centers. This demonstrates that RPM-based systems, when properly applied, can achieve precision comparable to larger institutions [7,8].

4.4 Predictive Modeling and Anatomical Surrogates

Anatomical predictors were evaluated to determine their correlation with cardiac dose reduction, with chest rise emerging as a consistently strong and statistically significant factor in correlation analysis. Specifically, Pearson correlation coefficients between absolute chest rise (DIBH − FB) and cardiac dose parameters were robust: Heart V25 ($r = -0.734$), Heart V20 ($r = -0.720$), and Mean Heart Dose ($r = -0.720$), all with $p = 0.0001$, indicating a strong inverse relationship between thoracic expansion and heart dose exposure. These results support the role of chest rise as a valuable anatomical surrogate for heart sparing, in agreement with studies by Rudat et al. [2] and MacDonald et al. [5].

However, when a univariate linear regression model was constructed to predict Heart V25 as a function of chest rise, the results did not achieve statistical significance ($R^2 = 0.001$; 95% CI for slope: [−8.78, 10.09]; $p > 0.05$). This finding suggests that while chest rise correlates well with cardiac dose reduction, it may not reliably serve as a standalone predictive variable in regression modeling. The wide confidence intervals and near-zero explanatory power highlight the necessity for multifactorial models that incorporate additional anatomical or planning parameters to improve predictive accuracy.

Furthermore, chest depth demonstrated a moderate inverse correlation with the Heart Overlap Index (HOI) ($r = -0.54$, $p = 0.005$), indicating that patients with deeper thoraces may be anatomically advantaged for heart sparing. In contrast, the Haller Index showed no significant correlation with any cardiac dosimetric parameter, consistent with findings by Patel et al. [4] and others who have questioned its predictive relevance in breast radiotherapy planning.

Although chest rise correlated strongly with cardiac sparing, the regression model failed to reach significance, reinforcing the need for multifactorial models. Future research may incorporate machine learning approaches to combine anatomical and planning variables, potentially improving predictive accuracy and patient selection [9].

4.5 Clinical Implications

These findings support several clinically actionable insights:

- DIBH can be successfully implemented in emerging or resource-limited centers, with reproducible geometry and dosimetric gains.
- Chest rise should be used as a screening metric to identify patients most likely to benefit from DIBH.
- Verification using portal imaging and gamma index analysis remains essential to ensure safe and consistent delivery.

Limitations of this study include the relatively small sample size (25 patients), restriction to left-sided breast cancer, and absence of long-term clinical outcomes. Larger multi-institutional studies with ≥100 patients are needed to validate our findings and assess whether anatomical predictors can be generalized across diverse populations.

Conclusion

This study demonstrates the successful implementation of Deep Inspiration Breath-Hold (DIBH) in left-sided breast cancer radiotherapy, showing clear anatomical, dosimetric, and delivery advantages compared with free breathing. DIBH increased lung volume by nearly 50% and reduced heart exposure in high-dose regions by more than 8%, resulting in substantial decreases in mean heart dose (−26.7%), Heart V25 (−39.5%), and Heart V20 (−37.6%), alongside meaningful lung sparing and improved dose homogeneity. Verification using portal imaging and gamma index analysis (>95% pass rates) confirmed reproducibility and treatment accuracy across sessions. Chest rise emerged as a simple, clinically useful predictor of heart dose reduction, while the Haller Index lacked predictive validity. Collectively, these findings support routine DIBH adoption to enhance organ-at-risk protection without compromising target coverage, including in resource-limited centers. Future multi-institutional studies should validate these anatomical predictors and explore advanced modeling approaches to further optimize patient selection and treatment personalization.

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