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Scientific Paper

# Comparison of cardiac and lung doses for breast cancer patients with free breathing and deep inspiration breath hold technique in 3 dimensional conformal radiotherapy - a dosimetric study

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## Abstract

Purpose: To investigate the cardio-pulmonary doses between Deep Inspiration Breath Hold (DIBH) and Free Breathing (FB) technique in left sided breast irradiation.
Materials & Methods: DIBH CT and FB CT were acquired for 10 left sided breast patients who underwent whole breast irradiation with or without nodal irradiation. Three fields single isocenter technique were used for patients with node positive patients along with two tangential conformal fields whereas only two tangential fields were used in node negative patients. All the critical structures like lungs, heart, esophagus, thyroid, etc., were delineated in both DIBH and FB scan. Both DIBH and FB scans were fused with the Dicom origin as they were acquired with the same Dicom coordinates. Plans were created in the DIBH scan for a dose range between 50 Gy in 25 fractions. Critical structures doses were recorded from the Dose Volume Histogram for both the DIBH and FB data set for evaluation.
Results: The average mean heart dose in DIBH vs FB was 13.18 Gy vs 6.97 Gy, ($p = 0.0063$) significantly with DIBH as compared to FB technique. The relative reduction in average mean heart dose was 47.12%. The relative V5 reduced by 14.70% (i.e. 34.42% vs 19.72%, $p = 0.0080$), V10 reduced by 13.83% (i.e. 27.79 % vs 13.96%, $p = 0.0073$). V20 reduced by 13.19% (i.e. 24.54 % vs 11.35%, $p = 0.0069$), V30 reduced by 12.38% (i.e. 22.27 % vs 9.89 %, $p = 0.0073$) significantly with DIBH as compared to FB. The average mean left lung dose reduced marginally by 1.43 Gy (13.73 Gy vs 12.30 Gy, $p = 0.4599$) but insignificantly with DIBH as compared to FB. Other left lung parameters (V5, V10, V20 and V30) shows marginal decreases in DIBH plans compare to FB plans.
Conclusion: DIBH shows a substantial reduction of cardiac doses but slight and insignificant reduction of pulmonary doses as compared with FB technique. Using the simple DIBH technique, we can effectively reduce the cardiac morbidity and at the same time radiation induced lung pneumonitis is unlikely to increase.

**Key words**: cardiac toxicity; lung toxicity; deep inspiration breath hold; free breathing; breast radiotherapy.

## Introduction

Breast cancer is the most common cancer in women worldwide. It is estimated that more than 1.7 million new cases of breast cancer occurred among women worldwide in 2012 (most recent data available) [1]. Breast cancer incidence rates around the world vary a great deal. In general, developed countries have higher rates than developing countries. The main types of treatment for breast cancer are surgery, radiation, chemotherapy, hormone therapy, targeted therapy, bone-directed therapy. In most instances, the local and regional extent of disease is treated by surgery and/or radiation therapy (RT). The distant disease risk is treated by systemic therapy including chemotherapy, endocrine therapy, biologic therapy, or any combination of these agents.

Radiotherapy to the breast cancers reduces the low recurrences and improves overall survival [2]. Left sided breast and chest wall radiotherapy results in considerable dose to heart, lung and coronary arteries. Radiation therapy is associated with an increased risk for cardiovascular disease, which included heart disease such as pericarditis, ischaemic heart disease and myocardial infarcation long after radiotherapy. It may happen many years or decades after the initial exposure. Rates of major coronary events increased linearly with the mean dose to the heart by 7.4% per gray, with no apparent threshold [3]. Chemotherapy is an integral part of the systemic therapy of breast cancer; Cardio-toxicity is one of the most important adverse reactions of chemotherapy, leading to an important increase of morbidity and mortality [4, 5].

Different breath hold techniques were used to reduce the cardiac and pulmonary toxicity during breast radiotherapy, few common methods were the real time position management (RPM) system (Varian Medical Systems, Palo Alto, CA) and the spirometry based active breathing coordinator (ABC) system (Elekta, Sweden). During the deep inspiration breath hold, the patients need to hold the breath for 15 to 20 sec on several occasion, during the breath hold process the chest expands and push heart down away from the chest wall, this process will enable us to minimize the doses to the heart and lung during radiotherapy.

A reproducible position of deep breath hold is always superior compared to free breathing in thoracic tumors, because of its advantage in reducing the respiratory tumor motion and varies the internal critical structure in a way it is often protected from the radiation beams [6].

## Materials and Methods

### Patient demographic

Ten patients with left breast cancer treated in our center with deep inspiration breath hold (DIBH) were included in this study. The median age of the 10 patients with left-sided breast cancers included in this dosimetric analysis is 52 years (range: 32 – 67 yrs). 60% patients were treated with breast-conserving surgery followed by whole breast radiotherapy and 40% underwent mastectomy and chest wall and nodal radiotherapy. The common co-morbidities are hypertension, chronic obstructive pulmonary disease (COPD) and heart disease.

### CT Simulation

All the patients underwent a Computed tomography (CT) simulation (GE Discovery 600 PET-CT) in supine position with arms above the head. A radio opaque brass wire was kept around the breast surface for the landmark identification. CT slices with 2.5 mm thickness were acquired using either ‘T’ grip wing board or MT-350 Breast board (M/S Civco, USA) as a positioning device depends upon the patient’s body geometry. Wing board was preferred, if the patient chest was flat without slope on a flat surface, otherwise breast board with 10 to 30 degree angle was used to make an entire chest flat. All the ten patients underwent DIBH and free breathing (FB) scan approach using a common Dicom origin. Real time position management (RPM) equipped with infra-red camera and 6 dot reflective markers, which are integrated with the GE CT was used for all the patients to obtain the DIBH scans (**Figure 1**). The DICOM images from the CT control console were transferred to the treatment planning system. The images were imported in the Eclipse treatment planning system (M/S Varian Medical System, Palo Alto, USA).

**Table 1. Age, Sex, status of surgery and associated co-morbidities of selected patients**

| S No. | Age | Sex | Surgery | Co-Morbidities |
|---|---|---|---|---|
| 1 | 44 | F | Lumpectomy | Hypertension |
| 2 | 62 | F | Mastectomy | COPD |
| 3 | 48 | F | Lumpectomy | Heart Disease |
| 4 | 53 | F | Mastectomy | - |
| 5 | 65 | F | Lumpectomy | Hypertension |
| 6 | 32 | F | Mastectomy | COPD |
| 7 | 51 | F | Lumpectomy | Heart Disease |
| 8 | 67 | F | Mastectomy | - |
| 9 | 49 | F | Lumpectomy | Heart Disease |
| 10 | 59 | F | Lumpectomy | - |

### Target and organ and risk delineation

All the target volumes and critical structures like heart, left lung, right lung, thyroid, esophagus and spinal cord were delineated in both DIBH and FB CT datasets individually. Entire left breast were delineated for breast conservation surgery patients and left chest wall were delineated for the mastectomy patients as a clinical target volumes (CTV). An additional margin of 5 mm isotropic margin was given around the CTV to generate planning target volume (PTV). CTV boost volume for the lumpectomy patients were delineated with the aid of surgical clips, cavity and other radiological and clinical information available for the patients. A PTV boost volume has been created by giving additional 5 mm isotropic margin around the CTV boost volume. **Figure 1** illustrates the target and OAR delineation in different planes.

### Treatment Planning

Two plans one with DIBH data set and other plan with FB dataset were created using 3DCRT technique. In plan 1, two tangential fields plus/minus supraclavicular field were used to produce adequate dose coverage for the left breast volume (PTV). Critical organs were shielded using MLC without compromising PTV coverage. Beam weights were adjusted until the optimum coverage and acceptable hot spots were achieved.

**Figure 1. CT simulation of breast patient with RPM.**

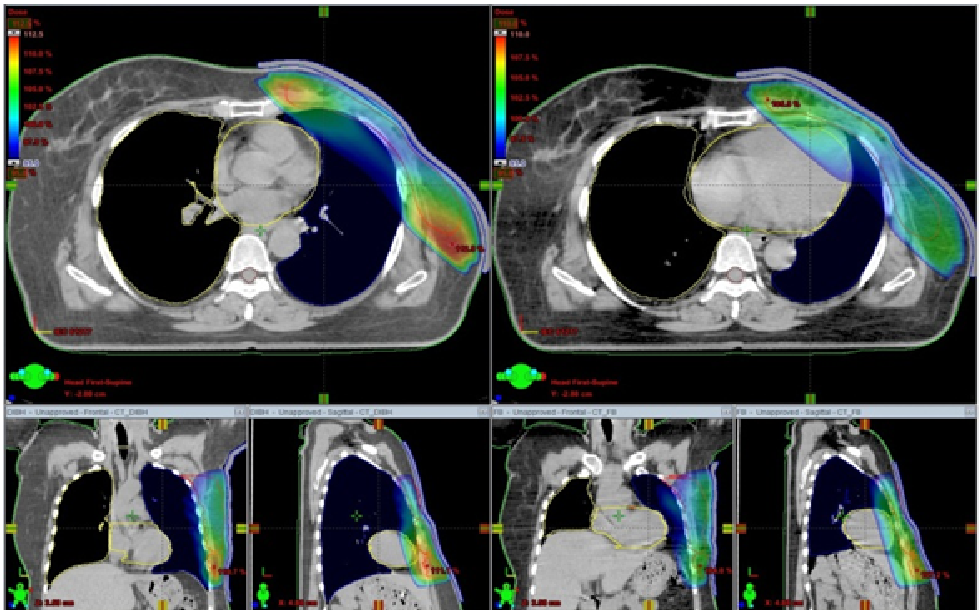


**Figure 2. Dose colors wash between the (a) Deep inspiration Breath Hold technique and (b) Free breathing technique.**

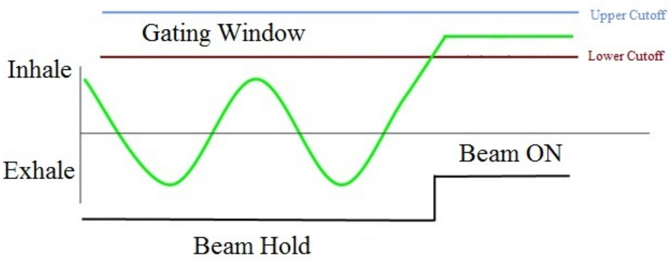


**Figure 3. Deep Inspiration Breath Hold example for data acquisition and dose delivery with upper and lower cutoff.**

Left breast set to receive at least 95% of the prescribed breast dose. Three fields using single isocenter technique were used for patients with node positive along with two tangential conformal fields whereas only two tangential fields were used in node negative patients. Enhanced dynamic wedges were used in all tangential fields to compensate for the breast surface and field in field technique also used whenever necessary to reduce the hot spots. Boluses were used for all mastectomy cases to increase the dose to the chest wall. All the plans for DIBH were planned with the dose rate of 600 MU/min, with a combination of 6 MV and 10MV were used depends on the requirements. Normally with 600 MU/min dose rate a patient with breath hold of 20 Sec is enough to complete one filed. The below **Figure 2** shows the sample of breath hold pattern of the patient for the CT scan acquisition and dose delivery. All the patients were planned with Eclipse treatment planning system and the dose calculation were done using anisotropic analytic algorithm (AAA) ver.11.0.

## Planning Evaluation

ICRU 83 report [6] released in 2010 used different concepts of plan evaluation parameters to evaluate the plans. To compare the DIBH and FB plans, we used the ICRU 83 definition to determine the dose conformity and RTOG definitions for dose homogeneity. Dose conformity and homogeneity are independent specifications of the quality of the absorbed dose distribution. Dose conformity characterizes the degree to which the high dose region conforms to the target volume whereas dose homogeneity characterizes the uniformity of the absorbed dose within the target volume.

### Homogeneity Index (HI)

$$\text{Homogeneity Index (HI)} = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \qquad \text{Eq. 1}$$

Where $D_{2\%}$, $D_{98\%}$ and $D_{50\%}$ are the are the doses received by 2%, 98% and 50% of the PTV volumes respectively. HI = 0 (zero) is ideal value.

### Conformity Index (CI)

In 1993, Radiation Therapy Oncology Group recommended conformity index (CI) as a ratio of the reference isodose volume to the target volume.

$$CI_{RTOG} = \frac{V_{RI}}{TV} \qquad \text{Eq. 2}$$

Where $V_{RI}$ is reference isodose volume, and TV is the target volume.

## Statistical Analysis

The statistical data were presented as the average of all the patients followed by the standard deviation ($\bar{x} \pm \sigma\bar{x}$). Both DIBH and FB technique results were compared using the paired sample t-test performed using the Microsoft Excel version 2010 with p-value < 0.05 considered as significant.

## Results and discussion

Both right and left lung volume of all the ten patients were measured and tabulated in the **Table 2** which shows the mean volume ± standard deviation ($\bar{x} \pm \sigma\bar{x}$) and range for right lung, left lung and heart volumes in FB and DIBH, respectively. Both lungs volume increased to almost double size during DIBH, whereas the mean heart volume were relatively same which shows that there is a good consistency in the heart delineation within the FB and DIBH data delineation.

The **Table 2** clearly illustrates that there is a relative increase of 1.8 and 2.0 fold increases in the right lung and left lung volume in the DIBH data compared to FB data set.

## Conformity index & dose homogeneity index

The treatment plan quality has been compared using dose conformity and dose homogeneity parameters of two techniques are performed using conformity index (CI) and homogeneity index (HI). The calculated HI and CI of the PTV for both two techniques DIBH and FB are tabulated in the **Table 3**. The average conformity index (CI) ($\bar{x} \pm \sigma\bar{x}$) values were 1.88 ± 0.38 for FB, 1.81 ± 0.29 for DIBH.

As shown in **Table 3**, the average minimum dose to PTV decreased (44.74 Gy vs 44.72 Gy, p = 0.286) insignificantly with DIBH as compared to FB. However, there is a slight increase in maximum dose (54.76 Gy vs 55.50 Gy, p = 0.104) to the PTV. As compared to FB, average mean dose to PTV decreased (51.30 Gy vs 50.980 Gy, p = 0.465) but insignificantly with DIBH technique. Also average modal dose decreased (51.72 Gy vs 50.05 Gy, p = 0.06) slightly in DIBH. Likewise average medial dose also decreased (51.50 Gy vs 51.05 Gy, p=0.322) slightly and insignificantly with DIBH. The conformity index is similar (1.88 in FB vs 1.81 in DIBH, p = 0.587) for both the techniques. Homogeneity index is slightly better (0.11 in FB vs 0.13 in DIBH, p = 0.024) for FB as compared to DIBH but they are comparable. Since all the dosimetric parameters including conformity index and homogeneity index for both the techniques do not show a significant change with techniques, FB and DIBH are comparable.

## Heart FB and DIBH plans dosimetric data comparison

**Figure 4** compares FB and DIBH Dose Volume Histograms (DVHs) for heart of a left breast mastectomy case. From the figure, it is obvious that higher relative volume of the heart is getting same dose in FB as compared to DIBH. This is more pronounced in low dose volumes that at higher doses regions.

As shown in **Table 4**, the average heart mean dose reduced by 6.21 Gy (13.18 Gy vs 6.97 Gy, p = 0.0063) significantly with DIBH as compared to FB technique. The average relative reduction in average heart mean dose was 47.12%. The relative V5 reduced by 14.70% (i.e. 34.42% vs 19.72%, p = 0.0080), V10 reduced by 13.83% (i.e. 27.79 % vs 13.96%, p = 0.0073). V20 reduced by 13.19% (i.e. 24.54 % vs 11.35%, p = 0.0069), V30 reduced by 12.38% (i.e. 22.27 % vs 9.89 %, p = 0.0073) significantly with DIBH as compared to FB.

## Left Lung FB and DIBH plans dosimetric data comparison

It is obvious from the **Figure 5** that higher relative volume of the left lung is getting the same dose in FB as compared to DIBH. This is more pronounced in low dose volumes that at higher doses regions.

As shown in **Table 5**, the average mean left lung dose reduced slightly (13.73 Gy vs 12.30 Gy, p = 0.4599) but insignificantly with DIBH as compared to FB. The absolute reduction in left lung average mean dose is 1.43 Gy. Relative V5 decreased by 1.26% (37.95 Vs 36.69, p = 0.0798) but insignificantly with DIBH as compared to FB. Similarly, relative V10 decreased by 2.71% (30.20 vs 27.49, p = 0.0539) but insignificantly with DIBH. Likewise relative V20 decreased by 3.14% (26.05 vs 22.91, p = 0.4451) but insignificantly with DIBH. Relative V30 decreased by 2.9% (23.75 vs 20.85, p = 0.4585) but insignificantly with DIBH.

**Table 2. Mean volume in cc and the range for right lung, left lung and heart during free breathing (FB) and deep inspiration breath-hold ( DIBH) for all 10 patients.**

| | FB(cc) | DIBH(cc) | Relative |
|---|---|---|---|
| Right Lung ($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | 971.92 ± 133.46 [755.95 - 1241.54] | 1765.41 ± 206.25 [1405.23 - 2095.84] | 1.816 |
| Left Lung ($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | 754.49 ± 88.83 [577.68 - 872.42] | 1515.124 ± 222.25 [1182.19 - 1849.11] | 2.008 |
| Heart ($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | 469.09 ± 93.48 [349.42 - 654.10] | 468.39 ± 91.84 [353.79 - 646.16] | 0.998 |

**Table 3. Comparison of Dosimetric Parameters (Min Dose, Max Dose, Mean Dose, Modal Dose, Median Dose, Conformity Index & Homogeneity index) during free breathing (FB) and deep inspiration breath-hold ( DIBH) for all 10 patients**

| Dosimetric Parameters | FB($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | DIBH($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | p-value |
|---|---|---|---|
| Minimum Dose (Gy) | 44.74 ± 2.26 [40.94 - 46.67] | 43.72 ± 1.83 [41.10 - 46.00] | 0.286 |
| Maximum Dose (Gy) | 54.76 ± 0.6856 [53.50 - 55.99] | 55.50 ± 1.16 [53.62 - 56.77] | 0.104 |
| Mean Dose (Gy) | 51.30 ± 1.13 [49.37 - 52.70] | 50.98 ± 0.78 [49.94 - 51.93] | 0.465 |
| Modal Dose (Gy) | 51.722±1.4306 [50.13-53.98] | 50.47 ± 1.36 [48.87 - 52.75] | 0.06 |
| Median Dose (Gy) | 51.50 ± 1.11 [49.96 - 53.06] | 51.05 ± 0.84 [49.80 - 52.752] | 0.322 |
| Conformity Index | 1.88 ± 0.38 [1.65 - 2.13] | 1.81 ± 0.29 [1.62 - 2.23] | 0.587 |
| Homogeneity Index | 0.11 ± 0.01 [0.01 - 0.14] | 0.13 ± 0.02 [0.09 - 0.18] | 0.024 |

**Table 4. Heart Mean dose, in Gy and relative V5, V10, V20 and V30 during free breathing (FB) and deep inspiration breath-hold (DIBH) for all 10 patients.**

| Heart | | FB (Gy) | DIBH (Gy) | p-value |
|---|---|---|---|---|
| Mean Dose ($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | | 13.18 ± 5.31 [3.64 - 20.98] | 6.97 ± 3.08 [2.12 - 11.16] | 0.0063 |
| Relative Volumes ($\bar{x} \pm \sigma_{\bar{x}}$) | V5 | 34.42 ± 12.91 | 19.72 ± 8.09 | 0.0080 |
| | V10 | 27.79 ± 12.15 | 13.96±7.02 | 0.0073 |
| | V20 | 24.54 ± 11.56 | 11.35±6.42 | 0.0069 |
| | V30 | 22.27 ± 10.99 | 9.89±5.87 | 0.0073 |

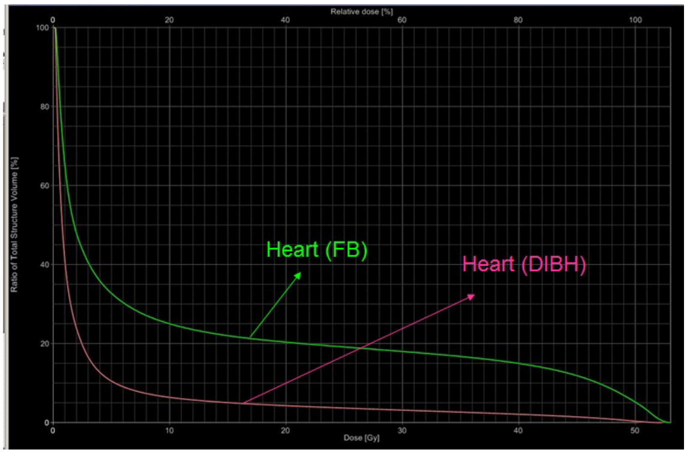


**Figure 4. FB and DIBH heart DVHs comparison.**

**Table 5. Left Lung Mean dose, in Gy and relative V5, V10, V20 and V30 during free breathing (FB) and deep inspiration breath-hold (DIBH) for all 10 patients.**

| Left Lung | | FB (Gy) | DIBH (Gy) | p-value |
|---|---|---|---|---|
| Mean Dose ($\bar{x} \pm \sigma_{\bar{x}}$) [Range] | | 13.7 3 ± 4.62 [3.85 - 20.376] | 12.30 ± 3.00 [5.61- 15.98] | 0.4599 |
| Relative Volumes ($\bar{x} \pm \sigma_{\bar{x}}$) | V5 | 37.95 ± 11.61 | 36.69 ± 10.08 | 0.0798 |
| | V10 | 30.20 ± 10.60 | 27.49 ± 8.61 | 0.0539 |
| | V20 | 26.05 ± 10.01 | 22.91 ± 7.79 | 0.4451 |
| | V30 | 23.75 ± 9.53 | 20.85 ± 7.43 | 0.4585 |

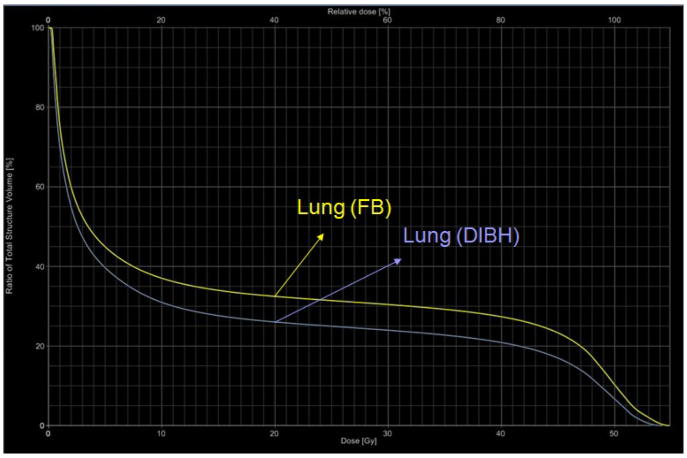


**Figure 5. Comparison of FB and DIBH Dose Volume Histograms (DVHs) of left lung for a left breast mastectomy case.**

## Discussion

In this study, DIBH technique significantly reduced the mean heart dose and V5, V10, V20 and V30 volumes compared to FB technique, on the other hand, there is slight but insignificant reduction in the left lung mean dose and V5, V10, V20 and V30. The DIBH mean heart dose decreased significantly to 6.21 Gy from 13.18 Gy as compared to FB technique. Similarly relative V5, V10, V20 and V30 of the heart, decreased significantly by 14.70%, 13.83%, 13.19% & 12.38% respectively. It implies that the risk of radiation-induced cardiac morbidity may reduce using the DIBH technique. However, the DIBH mean left lung dose decreased slightly and insignificantly by 1.43 Gy (12.30 Gy vs 13.73 Gy, p = 0.4599) as compared to FB, relative V5, V10, V20 and V30 of the left lung also decreased but insignificantly by 1.26%, 2.71%, 3.14% and 2.9% respectively. Hence the risk of radiation-induced pneumonitis is unlikely to increase using the DIBH. It has been demonstrated in several studies that breathing adaptation techniques can be used to reduce the irradiated heart and lung volumes, primarily by utilizing lung inflation which dilutes the amount of lung tissue in the radiation fields and spatially separates the heart from target. Although the absolute left lung volume appeared to have increased with DIBH, proportionately less of the left lung was irradiated. While lung volume may increase with deep inspiration, the lung density may decrease, resulting in irradiation of a reduced fraction of normal lung mass [7]. Therefore, implementing the DIBH technique using RPM system for all patients receiving left-sided breast radiotherapy was feasible, because the benefits were obvious for patients undergoing 3DCRT.

The reported heart doses may be influenced by variability in the method used to contour the heart between studies. However, several reports have documented the tolerability and inter-fraction reproducibility of the DIBH technique for supine position while with acceptable reproducibility but instability for prone position [8, 9]. We attempted to maintain consistency of volume measurements by employing the same radiation oncologist to perform all contouring. Even so, some minor variations in all contours may have occurred due to variation in the anatomy of the heart and lung between FB and DIBH scans. Our data are consistent with those of other published reports demonstrating significant reduction in the doses to the heart with DIBH technique using active breathing control and RPM systems. However, several factors may limit comparisons between studies.

In our experience to reduce the cardiac doses, 3DCRT utilizing DIBH technique with RPM system is relatively easy to achieve compare to 3DCRT utilizing FB technique for treatment of left breast cancer patients. Although IMRT has been favored as an alternative method to reduce cardiac and lung doses, it could only avoid high dose regions while the volume of low and medium cardiac, pulmonary and contralateral breast doses increase. Moreover, intra-fraction and inter-fraction positional accuracy studies have proved DIBH to be highly reproducible. Meantime, DIBH conformity index & homogeneity index being similar to that of FB CI and

HI confirmed the comparability of both techniques. Keeping in view all of these observations, 3DCRT utilizing DIBH technique is found to be better than FB technique in sparing cardiac morbidity and reducing late complications including pneumonitis slightly after irradiation of left breast cancer patients.

## Conclusion

Our study demonstrates that DIBH is an effective method to reduce cardiac doses and pulmonary doses is unlikely to increase. In case of heart, low and medium dose volumes decrease significantly while treating the left breast cancer patients under 3DCRT techniques. However, in case of left lung, these volumes decrease, but insignificantly. Based on the review of the studies, the reduction in mean dose to heart and low dose volumes are likely to result in reduced long-term cardiac risks. However, it's yet not clear about the benefit in reducing the risks to the left lung because although there is a reduction in mean dose to left lung, it is small and the change is insignificant. However, it is unlikely to increase the radiation risks to the left lung. Moreover, DIBH technique is substantially reproducible and stable during inter-fraction and intra-fraction treatments. The limitations inherent to this dosimetric study with expected errors during exact radiation delivery and clinical practice indicate the need for future research. It is important to explore the association and degree of dependence between dose volume parameters and long term cardiac and pulmonary morbidity and mortality.

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