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Deep inspiration breath hold (DIBH) for cardiac sparing in breast cancer radiotherapy

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► ***Original article***

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ABSTRACT

***Background*:** We aimed to assess the effect of the DIBH plan on cardiac and other organs at risk received dose during radiotherapy in left breast cancer patients. ***Materials and Methods*:** The study was carried out on 30 patients with left breast cancer with a history of mastectomy/lumpectomy surgery who were referred to the radiotherapy department of the Cancer Institute of Iran. Each patient underwent computed tomography (CT) simulations in two respiratory phases, including deep inspiration breath-hold (DIBH) and free-breathing (FB). In addition, the dose-volume histograms (DVHs) of the heart, lung, spinal cord, and breast of each respiratory phase were compared. ***Results*:** We observed a significantly higher mean of heart dose in FB in both lumpectomy and mastectomy groups (P value<0.05). We also compared the means of V25 and V30 heart between FB and DIBH—for both, the received dose was statistically higher in FB than DIBH. The mean dose received by the lung and spinal cord was higher in FB than DIHB. However, the observed difference was only significant in the lumpectomy group (P value<0.05). ***Conclusion*:** The DIBH is a viable method that could be suggested to reduce the mean dose of the heart during left breast cancer radiotherapy.

INTRODUCTION

Radiotherapy is one of the main aspects of breast cancer treatment. It is well-documented that radiotherapy is associated with decreased local recurrence and, consequently, leads to increased survival rates in breast cancer patients. However, radiation's effects on healthy tissue, particularly cardiac and pulmonary side-effects, limit the benefits of radiotherapy [1]. Some evidence highlights that the risk of mortality due to heart failure increases in patients with left breast cancer patients who underwent RT [2, 3,4]. It seems the incidence of heart ischemic diseases after RT is associated with the volume of heart irradiation and the radiation dose imposed on the cardiac tissue during RT for left breast cancer [5]. A critical concern associated with RT is matching and adapting the planning situation with the treatment situation. Adapting the radiation beam according to the respiratory changes can be valuable in RT, especially when dealing with tumors located in the thoracic and abdomen regions. Hence, several attempts have been made to reduce late cardiac and pulmonary side-effects of RT. Implementing deep inspiration breath hold (DIBH) during treatment planning and RT can change the position of internal organs in the chest. It has been reported that using breath-holding techniques can reduce the radiation dose of healthy tissues [6, 7].

According to the breath-holding techniques, the radiation beam is turned on only during the predetermined phase or amplitude in the respiratory cycle. Therefore, given the decreased displacement of the lung, breast displacement will also be reduced [8]. Different studies indicated that improvement of the results in these methods, whether performed simply and without monitoring, or together with monitoring, or in a complicated way such as the use of spirometry monitoring together with forced breath-hold lead to a decrease in the heart volume during the treatment period and even in the dose delivered to the lungs [9, 10,11].

Stranzi and Zurl [12] demonstrated that the left-sided breast and heart were separated during radiotherapy in the Deep Inspiration Breath-Hold (DIBH) technique, which excluded a considerable

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volume of the heart from the high-dose area. However, problems with patient cooperation and reproducibility, and verification of breath-hold level may limit the feasibility of this approach. As a result, no optimal parameters have been established yet for breathing control for breast cancer [9]. Therefore, the current study compared the received dose by critical organs at risk, including heart, lung, and spinal cord, between DIBH and free-breathing (FB).

The current study compared DIBH and free-breathing (FB) regarding the doses received by critical organs at risk, including the heart, lungs, and spinal cord.

MATERIALS AND METHODS

Patients selection

The sample comprised 30 female patients with left breast cancer who were referred to the radiotherapy department of the Cancer Institute of Iran between July 2018 and October 2019. The ethics committee approved the current study of the Tehran University of Medical Sciences in November 2018 (Ethics Approval Code; IR.TUMS.VCR.REC.1397.590).

CT investigations

All patients were imaged with GE high-speed 16 slice scanners (GE Healthcare, HiSpeed FX/i) with two breathing protocols, namely DIBH and FB. Scanning was carried out in a supine position on a breast board, and patients were asked to raise their arms overhead. DIBH images were acquired when the patient took a maximally comfortable inspiration. During FB and DIBH scanning, we asked patients to stay in the same position and not to change it—we closely monitored whether they did this successfully. Patients were also guided verbally by radiation therapists during DIBH. Spiral Imaging parameters were 130 kVp, Smart mA activated, 0.5-mm slice thickness, standard reconstruction kernel, 0.5 s rotation time, and a pitch of 0.984. Other imaging parameters were kept constant. In addition, tiny lead strings were placed as markers on each patient's skin during imaging to allow the researchers to locate the exact site of separation between the supra-clavicle fields from others. The images were then transferred to an Eclipse™ v13 TPS (Varian, Palo Alto, California, USA) treatment planning system (TPS) for contouring and dose calculations.

Delineation of target volume and organs at risk

A radiation oncologist delineated target volume according to ESTRO guidelines [13], and a second radiation oncologist peer-reviewed the delineated target volumes. The breast and lumpectomy cavity or chest wall were contoured following the 5-mm margins added to the breast or chest wall target to generate the planning target volume. We also used an automated segmentation tool to contour both lungs. The heart and spinal cord were contoured manually. Because we used a CT scan without contrast for simulation, Left Anterior Descending (LAD) and right coronary artery (RCA) was not contoured.

Treatment planning

We generated two consequential treatment plans for every patient (i.e., using the Free Breathing (FB) and Deep Inspiration Breath Hold (DIBH) CT image sets (figure 1). Medial and lateral non-divergent tangential fields designed to treat the entire left breast or chest wall were generated for each plan. In addition, a supraclavicular field was employed, using an anterior oblique field with a mono isocentric machine placed at the head of the clavicle. Goal coverage was 90% of the contoured target receiving the prescription dose. The total dose of 5000 cGy in 25 fractions (200 cGy per fraction) using 3-dimensional conformal photon arrangements was given to patients. We did not calculate the boost dose in this study.

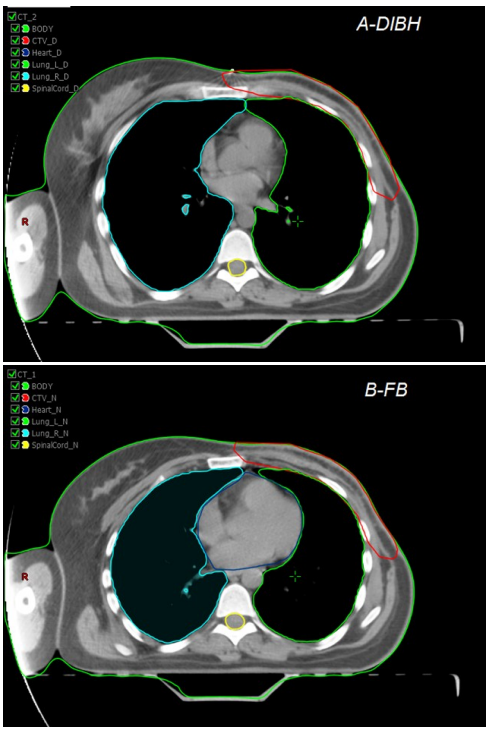

Figure 1. Radiotherapy plan for a patient in two consequential breathing phases; **(A)** Deep Inspiration Breath Hold (DIBH) **(B)** Free Breathing (FB).

Comparison criteria

Three critical organs at risk for all patients—the heart, spinal cord, and lung—were contoured to compare plans created according to the CT images acquired during two breathing phases. Meanwhile, the tumor dose per fraction and number of fractions were the same. Because of the communication role of the spinal cord, the maximum dose delivered to the spinal cord ($D_{max, SC}$) was based on treatment planning system (TPS) calculations. To assess the damage caused by radiation in heart quantities of the average dose received by the heart ($D_{mean,}$ Heart), volumes of the dose received by the heart of more than 25 Gy

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(V_{25}) and more than 30 Gy (V_{30}) were considered. We also measured the radiation dose of the spinal cord (SC) in terms of the average and maximum doses received by SC (D_{mean} & D_{Max}, SC) and the average dose received by the left lung (D_{mean}, Lung). These parameters were calculated in Eclipse software for all patients during two breathing phases.

Statistical analysis

We used The Kolmogorov-Smirnov (K-S) test to evaluate the normality of the data and the paired t-test to compare the breathing phases. In addition, a paired t-test was used to compare the variation in doses due to changing the breath phase between the two groups of patients with a history of mastectomy or lumpectomy. All statistical analyses were performed using SPSS software ver 22.0. A P value of < 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was (55 (Standard Error(SE)±10.2) and Mean Body Mass Index(BMI) (27.13 +/- SE 4.6). Fifteen patients underwent a lumpectomy, and another 15 underwent a mastectomy. According to the Kolmogorov-Smirnov test, we did not find any significant deviations from the normal data distribution; thus, the distribution was deemed normal (P value>0.05). The mean doses received by the heart were 9.7 (±3.7) in the FB group and 7.4 (±2.8) in the DIBH group. The difference between the two groups was statistically significant (table 1, figure 2). The difference remained statistically significant independent of surgery type for patients who underwent either lumpectomy or mastectomy. Predictably, patients who underwent lumpectomy have significantly lower heart mean dose than mastectomy patients ($D_{Mean\ Heart}$ 7.3+/- SE 0.61 vs. 9.8+SE/-0.61, respectively). However, in both groups, the dose received during the FB phase was higher than in DIBH (figure 3). We also compared FB, and DIBH approaches regarding V25 and V30 of the heart—in both comparisons, the mean of the received dose was higher in FB (V25=15.9 ±7.2, V30=15.0 ±7.1) than in DIBH (V25= 11.6±6.0, V30=10.8±5.9) (P=0.044) (table 1, figure 2).

The mean overall doses received by the lung in the FB and DIBH phases were 16.8 (±2.7) and 15.8 (±2.2), respectively. However, this difference was not statistically significant (P value=0.032). The average dose received was significantly higher in FB than in DIBH in patients who underwent lumpectomy (Mean FB vs. DIBH=16.4±3.0 vs. 14.5±1.8) (P=0.032) (table 1).

No statistically significant difference was found regarding the overall Vmax dose received by the spinal cord between FB and DIBH breathing phases (P=0.221) (table 1).

Table 1. Comparing Dose- Volume metrics for Deep Inspiration Breath Hold (DIBH) and Free Breathing (FB) treatment plan.

	Mastectomy			Lumpectomy			Overall		
	FB	DIBH	P value	FB	DIBH	P value	FB	DIBH	P-value
Heart									
Mean V25 (SD)	18.5 (6.7)	14.4 (5.7)	0.040	13.2 (7.0)	8.6 (5.0)	0.029	15.9 (7.2)	11.6 (6.0)	0.008
Mean V30 (SD)	17.6 (6.7)	13.5 (5.7)	0.044	12.3 (6.8)	7.8 (4.8)	0.029	15.0 (7.1)	10.8 (5.9)	0.009
Mean Dose Gy (SD)	10.8 (3.6)	8.7 (2.7)	0.038	8.5 (3.5)	6.0 (2.4)	0.019	9.7 (3.7)	7.4 (2.8)	0.005
Lung									
Mean Dose Gy (SD)	17.2 (2.5)	16.9 (2.0)	0.347	16.4 (3.0)	14.5 (1.8)	0.032	16.8 (2.7)	15.8 (2.2)	0.060
Spinal cord									
Mean Vmax Gy (SD)	33.1 (7.6)	32.6 (9.4)	0.430	41.2 (3.4)	38.6 (4.2)	0.043	37.0 (7.1)	35.5 (7.8)	0.221

SD: Standard Deviation, FB: Free Breathing DIBH: Deep Inspiration Breath Hold

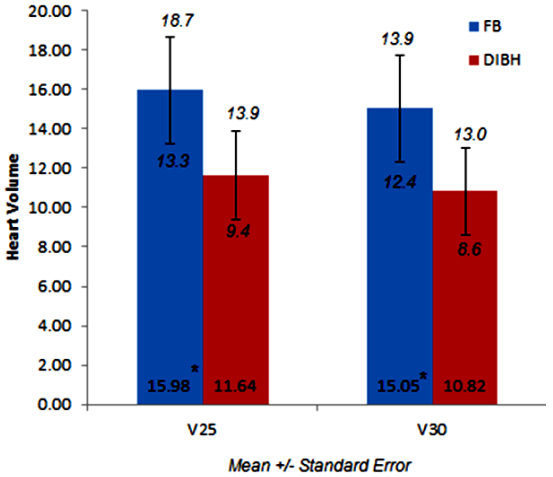

Figure 2. Comparing V25 and V30 in radiation therapy of breast in two types of breaths phases (for Deep Inspiration Breath Hold (DIBH) and Free Breathing (FB)).V25 (15.9 +/- SE (2.7) Vs. 11.6 +/- SE(2.2))and V30 (15.0 +/- SE (2.6) vs. 10.8 +/- SE(2.2)), significantly reduced in DIBH Technique. *P_{Value} < 0.05).

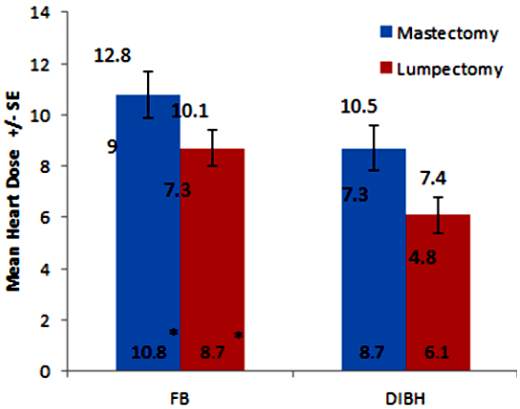

Figure 3. Mean heart dose in FB and DIBH breathing phases in patients who underwent breast lumpectomy or mastectomy surgery, Mean Heart dose is significantly lower with DIBH technique, either in Lumpectomy (6.0 SD (2.4) vs. 8.5 SD(3.5), Pvalue;0.005) or Mastectomy(8.7 SD (2.7) vs. 10.8 SD(3.6)), Pvalue;0.038) group.

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DISCUSSION

Radiotherapy plays a crucial role in treating breast cancer and reducing breast cancer mortality [14]. However, evidence points to long-term cardiac complications after RT, mainly due to damaged cardiac vessels [15, 16]. Radiotherapy is usually administrated in conjunction with cardiotoxic pharmaceuticals, which increases the risk of Heart Failure (HF) after treatment. In addition, the damage to vascular tissues usually leads to defects in cardiac perfusion, especially in the left anterior descent coronary artery [17], which can be reduced by heart dose reduction [18].

In the current study, we aimed to assess the effects of the DIBH approach on reducing doses received by the heart and other organs at risk during radiotherapy among left breast cancer patients. The probability of cardiac dose reduction by DIBH has been reported previously [6, 7,19, 20]. According to our findings, DIBH is associated with a significant reduction in mean heart dose ((9.7 (±3.7) vs. 7.4 (±2.8), P=0.005) FB group vs. the DIBH group respectively) (table1 & figure3).In addition, we found a significant Improvement in V25 and V30 for Heart in patients treated with the DIBH method, irrespective of the Surgery method (figure 2). Nissen *et al.* [21]reported similar results before, and V20 and V40 Significantly improved from 7.8% to 2.3% and from 3.4% to 0.3% in the DIBH group. Our study followed several previous dosimeter pieces of research that have documented the effectiveness of DIBH regarding cardiac dose reduction [22-24]. In the current study, we observed that the mean heart dose associated with the DIBH method was 23.8% lower than with free breathing (9.7 (±3.7) vs. 7.4 (±2.8), P=0.005). These findings were comparable to previous studies that reported 23-67% decreases in cardiac dose in DIBH compared to patients who underwent a free-breathing treatment plan [25]. In a large community-based retrospective study, Hong *et al.* treated patients with DIBH, which significantly improved mean heart dose compared to free-breathing [26]. Several internal thoracic anatomic changes due to DIBH, such as increased spatial separation between the heart and the target organ, are associated with reduced heart volume within the tangential fields. These anatomic alterations consequently decrease the dose received by the heart [27, 28]. During DIBH, the heart moves toward the inferior and posterior, and the distance between the heart and the tangential field margin increases. This tissue-sparing allows us to formulate a plan with a lower cardiac dose [29, 30].

DIBH is well-tolerated by most patients. Therefore, it could be used to reduce the mean heart doses in patients who receive radiotherapy. However, some patient-related factors, such as the ability to tolerate the technique, cost, patient convenience, as well as some tumor-related factors, including tumor size, location, and type of tumor, must be taken into account before case selection [25].

We also compared the doses received by the lung and spinal cord between DIBH and free-breathing and observed no statistically significant differences, although it was slightly higher in the free-breathing phase. One reason for this finding is that the parameter of the maximum dose was measured as a dispersion factor. This parameter is rigid to changes in the dose-volume histogram, perhaps due to the less noticeable changes in the irradiation field. The left lung average dose was similar in both breath phases, with only a negligible 6% change in the average dose (16.8+/-SD 2.7 vs. 15.8+/- SD2.2 FB vs. DIBH respectively P=0.06) (table 1).

Previous studies reported significantly lower doses received by organs at risks, such as the lung and spinal cord, in DIBH [31, 32]. For example, Wilson *et al.* reported that treating patients with DIBH decreased the mean dose of the lung by 6.4% and produced a significant reduction in the dose received by the spinal cord [33]. However, Pedersen et al. reported the same result regarding a reduction in the mean dose received by the lung, which is in contrast to our findings [7]. Our small sample size could be considered as the main reason for this discrepancy. Perhaps having a larger sample would alter the results. Thus, the primary limitation of the current study was the small sample size. Additionally, as we used CT without contrast, we could not contour heart arteries, including LAD and RCA.

CONCLUSION

The DIBH is a viable technique for reducing the mean doses received by the heart and other organs at risk.

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Author contribution*:* All authors contributed in Designing and Conducting the research in addition to writing the article.

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