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Benefits of Radiotherapy with Indigenous Tools Aiding Deep Inspiration Breath Holding Technique Compared to Free Breathing Technique among Breast Cancer Patients in Bangladesh

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Abstract

Background: Post-operative breast radiotherapy is used to reduce recurrence. The aim of this study was to investigate the outcomes of Deep Inspiration Breath-Hold (DIBH) technique with indigenous breath holding indicator scale in 3DCRT for breast cancer radiotherapy over Free Breathing (FB) technique. **Methods:** An observational study conducted at the Department of Radiation Oncology at National Institute of Cancer Research and Hospital, Dhaka and Square Hospital Limited, Dhaka, Bangladesh from June 2015 to May 2016. A total of 60 confirmed breast cancer patients who underwent adjuvant radiotherapy were included. An indigenous reproducible plastic tool (Perspex) was used as breath holding indicator scale with DIBH technique in 3DCRT. Paired sample t-test was used to compare with FB technique. **Results:** The mean age of patients was 47.32 (SD ± 8.33) years. In FB technique, Mean Heart Dose (MHD) was 413.27 cGy while in DIBH technique, it was 254.91 cGy ($P < 0.001$). The mean heart V20 and V30 were 5.5%, 4.37% in FB and 3.13%, 2.36% in DIBH respectively. In FB technique LADMD, LAD 0.2 cm^3, ILMD and ILV20 were 1698.17 cGy, 2852.53 cGy, 1155.31 cGy and 28.62% while in DIBH technique, it was reduced to 1164.01 cGy, 2132.24 cGy, 1007.98 cGy and 23.39% respectively. Similarly, the lung-CLMD and breast-CLMD were reduced from 38.37 cGy and 55.18 cGy to 24.64 cGy and 33.82 cGy respectively ($P < 0.001$). The mean difference for breast-CLMD was

21.36 cGy. **Conclusion:** The use of indigenous breath holding indicator scale with DIBH had better outcomes on breast cancer radiotherapy.

Keywords

Breast-Cancer, Radiotherapy, DIBH, Breath Holding Indicator Scale

1. Introduction

With the advances of mammography, breast cancer is being detected at an earlier stage thus preventing spread as well as supporting in rapid cure [1]. Subsequently, the homogenous radiotherapy dose distribution has significant impact on prevention of spread and treatment process. The post-operative breast radiotherapy classically utilizes tangential fields to encompass the entire chest wall volume and wedge compensation to ensure homogeneous dose distribution. The radiation in breast cancer is usually attributed to the target motion due to respiration [2]. The breathing adapted radiotherapy seems to reduce radiation doses to Organs at Risk (OARs) without compromising Clinical Target Volume (CTV) coverage [3]. Revised sentence: Irradiation techniques which utilize motion management strategies results in better dose homogeneity [2]. The radiation beam is being turned on during a pre-specified phase or amplitude of the respiratory cycle, thus modifying the target position and lung density within the field aperture. Several studies reported an appreciable reduction in cardiac volume within tangential radiation portals for left-sided breast cancer through deep inspiration using breath-hold techniques or forced breath-hold [4] [5] [6] [7] [8]. Additionally, they also reported on pulmonary tissue sparing for both left and right-sided cancers [6] [8]. However, the problems with breath-hold reproducibility as well as patient's non-cooperation are limiting the feasibility of this approach. Thus, the optimal parameters of breathing control have not been established yet.

A study investigated the possibility of decreasing chest wall excursion during breath-hold by coaching the patient using audio-visual display [8]. Another study found the better impact of coaching the patients to minimize inter-session variability [9]. Different studies have been conducted for the benefits of radiotherapy and patients compliance. A study demonstrated that during Deep Inspiration Breath-Hold (DIBH) technique, the left sided breast and heart were separated thus excluding substantial heart volume from radiation effect [10]. The post-operative radiotherapy for breast cancer can significantly reduce the risk of recurrence as well as improving long-term survival [11] [12]. However, breast radiotherapy has the risk of mortality and morbidity particularly with cardiac complication [13] [14]. Several studies with conventional techniques concluded with recommendations to lower the heart dose and to use modern techniques to reduce heart dose. Unfortunately cardiac side effects still exist even while utilizing modern techniques for breast cancer radiotherapy [15] [16]. Therefore, researchers felt the necessity to reduce the risk of cardiovascular complications particularly by irradiation to heart through dose-volume reduction or other methods. As DIBH technique allows to maximize the distance between target volume and heart, it allows us to provide adequate dose to the chest wall while minimizing dose to the heart. [17] [18]. However, there are very few studies and limited data on dosimetric evaluation of critical organs with Deep Inspiration Breath Holding (DIBH) technique in Bangladesh. In Bangladesh, usually a patient with breast cancer is treated postoperatively with 3DCRT in Free Breathing (FB) technique. So, the researcher purposively designed this study to investigate the potential benefits of Deep Inspiration Breath-Hold (DIBH) technique with 3DCRT over Free Breathing (FB) technique.

2. Materials and Methods

Study setting

This was an open label observational study conducted at the Department of Radiation Oncology in the National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka and Square Hospital Limited (SHL), Dhaka, Bangladesh from June 2015 to May 2016. A total of 60 histologically confirmed breast cancer patients who admitted at the mentioned hospitals for adjuvant radiotherapy were included in this study. The patients were selected randomly irrespective of site involved. Inclusion criteria were histologically confirmed breast cancer who need post-operative radiotherapy with aged 18 years and above, female and who had optimum Karnofsky performance score (KPS) ≥ 60. Patients with KPS < 60, inadequate bone marrow reserve (hemoglobin < 10 g/dL, inadequate neutrophil < 1500/μL, and platelet count < 100,000/μL), poor medical condition and those \who were not able to keep breath hold for at least 15 second were excluded. Since this is a pilot study only 60 consecutive patients who were willing to participate in the study were included.

Consent and study approval

The objective of the study as well as procedure, risks and benefits of this study were properly explained to the patients in local native language which was easily understandable to all. Patients were included in the study only after the informed consent document was signed. This study has been approved by both the institutional review/Ethics board. Approval reference number was: NICRH/Ethics/2015/154

Study procedure

A new device was applied externally to patients which were made with transparent plastic (Perspex) to measure the maximum expansion of the chest during DIBH simulation. Researchers locally developed and applied the device for the benefits of the patients as breath holding indicator scale. The DIBH data were collected with this indigenous simple, cost-effective, reliable and reproducible tool (Breath Holding Indicator Scale) for this study to aid breath hold during radiotherapy. For each patient, both free breathing (FB) and DIBH computed tomography (CT) scan was planned to measure and compare accordingly. However, before applying, patients were trained about the deep inspiration and hold their breath for at least 15 seconds. It was recorded with appropriate marking to achieve the same expansibility by the same patient during the course of action.

Diagrammatic figure of the device showed to each patient. They were trained on how to hold their breath in the supine position with the left arm kept above the head in a customized arm support using a breast board to ensure that the sternum was in a horizontal position. For all patients, the positions of screw A and B were correctly reproduced every time on the patient as indices above the contra lateral breast. Patients had been instructed to hold their breath at the end of inspiration and asked to practice breath holding by repeating the instructions "breathe in, out, and stop". The middle screw C was fixed at the junction of upper 2/3rd and lower 1/3rd of the distance between Suprasternal Notch (SSN) to Xiphisternum. During last respiration session at the upper most expansion, the position of middle screw C was stopped at that point. So the screw level C was fixed and marked as deep inspiration breath hold (**Figure 1**). If the position screw C varied considerably or if the patient could hold her breath for only a few seconds even after repeated training, the use of the system was discontinued for that patient.

The planning CT scan was taken in Siemens CT simulator and treatment planning and plan evaluation was performed with Eclipse 8.6 (Varian USA). Two opposing 6- or 10-MV tangential conformal fields with multileaf collimators. PTV received a dose prescription of 50 Gy in 25 fractions. The parameters such as Heart Mean Dose (HMD), the volume of the heart receiving 20 Gy and 30 Gy (heart V20 and V30), mean LAD dose (LADMD), the maximal dose to 0.2 cm^3 of the LAD, the mean right/left lung dose and the volume of the right/left lung receiving 20 Gy (left lung V20). Since LAD is a serial organ, we felt that maximal dose to 0.2 cc of LAD is more relevant that of LAD maximum dose. Usually 0.2 cc of LAD corresponds to 1 cm length of vessel when contoured [19].

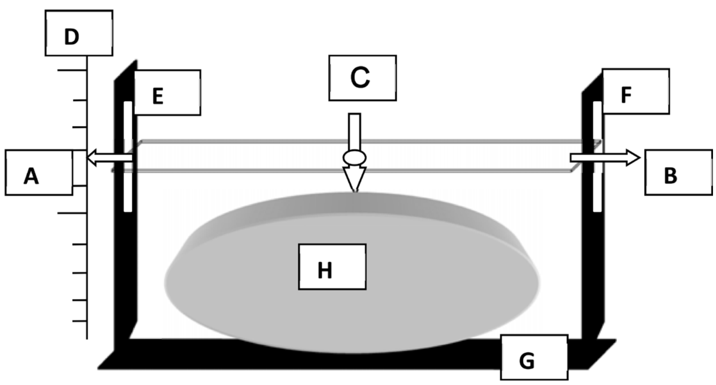

Figure 1. Device for the determination of max expansion of chest wall at sternal point during DIBH.A = Adjustable Screw, B = Adjustable Screw, C = Midline Screw for depth determination, D = Measuring scale, E = Horizontal column with adjustable screw level, F = Horizontal column with adjustable screw level, G = Base plate for the horizontal column, H = Patient Body.

All the patients were assessed weekly during RT for skin reactions with Radiation-Induced Skin Reaction Assessment Scale (RISRAS). During treatment, a completed blood count (CBC) was performed weekly and blood chemistry monthly up to final evaluation.

Data analysis

The data were recorded carefully and analyzed using SPSS, IBM version 23.0. Categorical data were expressed as number and percentage using Chi-square test. Continuous data were expressed as mean ± SD and were compared using paired "t" test. The value, $P < 0.05$ was considered as significant level.

3. Results

It was an observational comparative study between free breathing (FB) and deep inspiration breath-hold (DIBH) technique. In this study, the mean age of the patient was 47.32 (SD ± 8.33) years. Majority of the patients (65%) were in the $5^{th}/6^{th}$ decade and 25% of patients were <40 yrs. (Table 1). Out of 60 patients, 60% patients were suffering from the left sided breast cancer while remaining

Table 1. Age, site involved, severity, types of cancer and surgery underwent by patients.

Age group	Number of patients	%
≤40 years	15	25.0
40 - 50 years	25	41.7
51 - 60 years	15	25.0
≥60 years	05	08.3
Affected sites		
Left sided breast cancer	36	60.0
Right sided breast cancer	24	40.0
Both sided breast cancer	00	00.0
Severity according to stage		
No stage	24	40.0
Stage I	00	00.0
Stage II	23	38.3
Stage III	13	21.7
Type of breast cancer		
Invasive duct cell carcinoma	55	91.7
Lobular cell carcinoma	2	03.3
Medullary carcinoma	2	03.3
Mucinous carcinoma	1	01.7
Type of surgery		
Mastectomy	45	75.0
Lumpectomy	15	25.0

patients had right sided breast cancer. However, there was no bilateral breast cancer (Table 1). As for the surgical technique, 75% of the patients had underwent MRM and 25% of the patients had breast conservation surgery with axillary clearance.

According to severity of disease, more than one-third (>38%) of patients had stage II and prominent portion of patients (>21%) also had stage III. A significant percentage of patients (40%) were received radiotherapy from outside without having appropriate staging. Most of the patients (>91%) had invasive duct cell carcinoma (Table 1). In our study, boost was given only to those who had breast conservation surgery.

In free breathing technique, the heart mean dose (HMD) was 413.27 cGy while in deep inspiration breath holding technique, the HMD went down to only 254.91 cGy. The mean difference was 158.36 cGy which was statistically significant ($P < 0.001$) (Table 2).

Similarly, heart volume receiving 20% and 30% volume of prescribed dose was higher in FB than DIBH technique. The mean difference in both volumes was highly significant ($P < 0.001$). The left anterior descending mean dose (LADMD) was also found to be high in FB than DIBH and the difference was found to be highly significant ($P < 0.001$) (Table 2).

In free breathing technique, the Lung Ipsilateral Mean Dose (ILMD) was 1155.31 cGy while in deep inspiration breath holding technique, it was 1007.98 cGy. The mean difference was statistically significant ($P < 0.001$). Subsequently, the Lung Ipsilateral V20% (ILV20) in two techniques was 28.62% and 23.39% respectively which was also significant ($P > 0.05$). Consequently, the Lung Contralateral Mean Dose (lung-CLMD) and Breast Contralateral Mean Dose (breast-CLMD) were significantly higher (38.37 cGy and 55.18 cGy) in FB than DIBH (24.64 cGy and 33.82 cGy) (Table 2).

Table 2. Heart Mean Dose, Heart V20%, V30% and LAD mean dose and other differences in two techniques (t-test).

Organ Type	Parameter	cGy			t-statistic	df	P-value
		Free Breathing	Deep Inspiration Breath Hold	Mean difference			
Heart	Heart Mean Dose (HMD)	413.27	254.91	158.36	7.643	59	<0.001
	Heart V20	550	313	2.37	6.271	59	<0.001
	Heart V30	434	236	1.98	5.993	59	<0.001
	LAD mean dose (LADMD)	1698.17	1164.01	534.16	6.895	59	<0.001
	LAD 0.02 cm^3	2852.53	2132.24	720.29	6.192	59	<0.001
Lung	Lung Ipsilateral mean Dose (Lung-ILMD)	1155.31	1007.98	147.33	9.563	59	<0.001
	Lung ipsilateral V20	286.2	233.9.	52.3	1.745	59	<0.086
	Lung contralateral mean dose (Lung-CLMD)	38.37	24.64	13.73	3.896	59	<0.001
Breast	Breast contralateral mean dose (Breast-CLMD)	55.18	33.82	21.36	4.314	59	<0.001

*FB: Free breathing and DIBH: Deep Inspiration Breath-Hold, HMD: Heart Mean Dose, V20: received 20% of prescribed dose, V30: received 30% of prescribed dose, LAD: Left Anterior Descending, df: degree of freedom, tech.: technique.

The indigenous tool, customized device for determination of chest expansion, plane image of both FB and DIBH technique and dose volume histogram on heart dose are figure out with images (Figures 1-4).

Figure 2. Customized device under the "Breast Board" and Single view for determination of chest expansion during the DIBH scan.

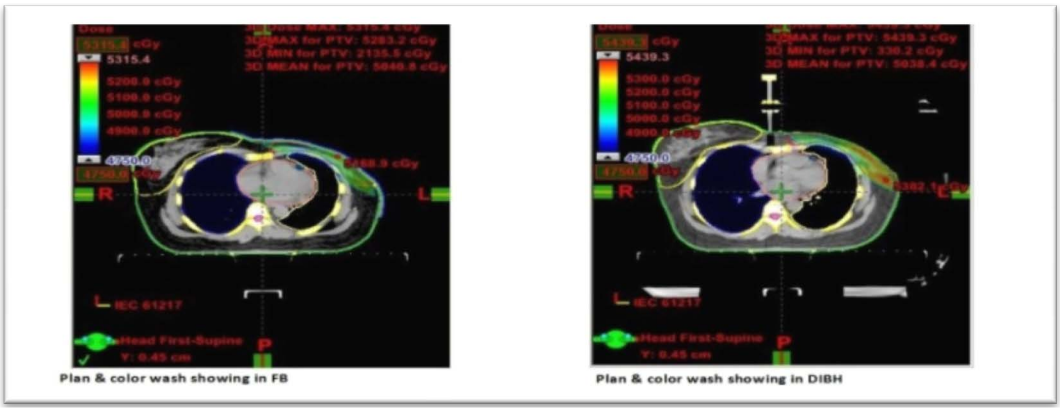

Figure 3. Plane image with color wash in FB & DIBH in a case of post mastectomy left sided breast carcinoma patient. In DIBH scan Screw C is showing touching the skin of chest wall over sternum.

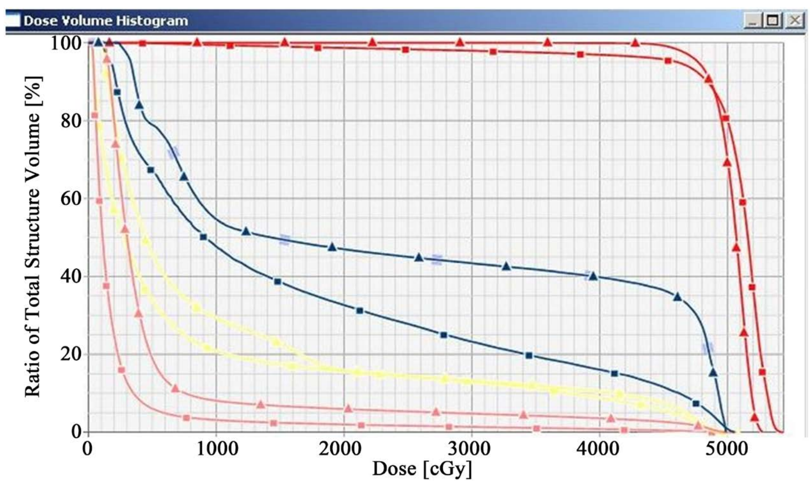

Figure 4. Dose volume histogram of Left Sided Breast Case in FB (▲) and DIBH (■) technique (n = 60) Color Code: Orange: Heart doses, Yellow: Lung doses, Blue: LAD doses, Red: PTV coverage.

4. Discussion

In our study, we found breast cancer patients of either side (left: 36; right: 24) who needed adjuvant radiotherapy. The mean age of the patients was 47.32 (SD ± 8.33) years. These findings are consistent with literatures. One of the studies also described that breast cancer mainly affects the middle-aged population [20]. Majority of the study subjects (45.75%) underwent mastectomy followed by breast conservation surgery commonly called lumpectomy (15.25%). However, most of the patients were suffering from invasive duct cell carcinoma (86.7%). We counseled and trained each of the patients on the use of devices, systems and timing. This is an important component of a clinical program that uses breath-hold respiratory gating for treatment [21]. In our study, the duration of the training session was 30 minutes with indigenous tool. Using the tool, the lung inflation during inspiration increases the absolute lung volume and decreases the percentage irradiated lung volume which is depicted in our study findings. In FB technique, the Ipsilateral Lung Mean Dose (ILMD) was 1155.31 cGy while in DIBH technique, it was 1007.98 cGy, which indicates the lower dose effect in DIBH. Similarly, in FB technique, the lung ILV 20% was 28.62% while in DIBH technique that value went down to 23.39%. Though the difference was not significant ($P > 0.05$), it was lower than FB technique. A study reported that in 7 out of 8 patients, the increase in absolute lung volume (ALV) overcompensated the increase in Irradiated Lung Volume (ILV). Thus, they recommend decreasing of mean lung dose. However, the differences between DIBH and FB in their study showed only a trend (P-value = 0.05). We found a significant advantage of DIBH using our indigenous tool to decrease the heart volume thus decreasing both the mean and the maximum dose of heart. In our study, we found Heart Mean Dose (HMD) 413.27 cGy and 254.91 cGy in FB and DIBH techniques respectively. Similarly we found better results in DIBH over FB technique for mean Heart V20 and V30. Several studies in different countries show similar results using DIBH technique [22]-[27].

However, we found that with the usage of our indigenous tool with DIBH technique in breast contralateral mean dose (CLMD), left anterior descending 0.2 cm^3 (LAD) and left anterior descending mean dose can be decreased significantly when compared to FB technique.

Since the dose gradient is very steep on the internal side of the photon field, the increase of the distance between the target and the heart was very effective at decreasing the LAD maximum dose. These findings support the other study findings. A study explained that a reduction of at least 16% in lung mean dose and at least 20% in irradiated pulmonary volumes was observed when DIBH was applied [3].

The current study was conducted to find out the difference of critical organ doses of 3DCRT in free breathing (FB) and in deep inspiration breath-hold (DIBH) technique. Our results suggest that in DIBH, with indigenous tool, proper counselling and training would be a practical and achievable solution for minimizing respiratory-induced target motion during simulation. Though DIBH technique requires comparatively complex set-up and prolonged time, it would be of great potential to get positive outcomes particularly on dosimetric and clinical benefits of radiotherapy with patient's satisfaction. With our indigenously developed toolto aid DIBH technique, we could significantly reduce doses to heart, LAD and lungs, due to increased distance between target and heart. The radiation oncologists would feel easy to adopt this technique as it is easy to administer, cost effective and environment friendly. Further in-depth and large-scale longitudinal study may validate our findings to establish its impact globally.

5. Limitation of the Study

Due to scarcity of motivated patients, sample size was low. In addition, we have only documented the dosimetric advantages. This needs to be tried on prospective cohort of patients to validate the results. As cohort findings are not yet evaluated, the real treatment benefits of the competing techniques could not be ascertained.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

DIBH: Deep Inspiration Breath Holding
3DCRT: 3D Conformal Radiation Therapy
FB: Free Breathing
MHD: Heart Mean Dose
KPS: Karnofsky Performance Score
LADMD: Left Anterior Descending Mean Dose
ILMD: Ipsilateral Lung Mean Dose (ILMD)
RISRAS: Radiation-Induced Skin Reaction Assessment Scale
CBC: Completed Blood Count