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Original Research Article

To Evaluate and Compare the Dosimetric Effects of Deep Inspiratory Breath-Hold Technique with Free Breathing Technique With Respect To Target Coverage and Organs at Risk in Patients of Left Sided Breast Cancer Treated By External Beam Radiotherapy

Pandita Sumit[1], Sharma Manish[2], Mandal Avik[2], Patel Arvind[3]

[1]DNB Radiation Oncology, Junior Consultant Radiation Oncology, Batra Hospital and Medical Research Centre, New Delhi.
[2]DNB Radiation Oncology, Senior Resident Radiation Oncology, Batra Hospital and Medical Research Centre, New Delhi.
[3]M.Sc Physics, Physicist, Batra Hospital and Medical Research Centre, New Delhi.

Corresponding Author: Pandita Sumit

ABSTRACT

Context: Radiotherapy techniques in breast cancer treatment have improved over years but have also raised concerns over subsequent acute and late effects. One such late complication, cardiac toxicity has led to much interest and optimisation in treatment delivery.
Aims: The aim of this study was to compare dose received by the target and organs at risk in left sided breast cancer patients undergoing post-operative radiotherapy with Deep Inspiratory Breath Hold (DIBH) technique and to compare its results with Conventional Free Breathing (FB) technique.
Materials and Methods: 24 patients of left-sided breast cancer requiring post-operative were taken for study after proper breath-hold training. CT-simulation was done in both free breathing and deep inspiration breath-hold pattern. The treatment plans were generated for both FB and DIBH. Dosimetric values were recorded and compared for both the plans.
Design of Study: A Prospective Observational Study.
Statistical analysis used: Statistical analysis was done using IBM SPSS statistical software version 16.0. Paired t-tests were used for statistical analysis of the differences.
Results: In our study, DIBH plans resulted in significant reduction in heart doses including Dmean (4.84 vs 3.93 Gy), V5 (19.33 vs 16.23), V10 (16.33 vs 13.59), V20 (13.87 vs 12.07), V30 (10.88 vs 9.90) and V40 (0.67 vs 0.41). DIBH also resulted in a significant reduction in all the LAD parameters including Dmax (45.26 vs 43.55 Gy), Dmean (25.54 vs 23.91 Gy), V5 (65.53 vs 59.06), V10 (52.51 vs 40.11), V20 (40.79 vs 28.16), V30 (28.05 vs 16.24) and V40 (14.95 vs 5.24). For LAD maximum relative reduction was observed for V40 (64.9%) and the minimum relative reduction was for Dmax. Compared with FB, DIBH resulted in a significant reduction in lung dose parameters including Dmean (3.85 vs 2.69 Gy), V20 (5.92 vs 3.54) and V40 (2.97 vs 1.61).
Conclusion: In our study dosimetric comparison between FB and DIBH plans showed significantly lower doses to heart, lung and LAD without compromising target coverage. Further prospective studies with longer follow-up are required to evaluate the cardiac and pulmonary toxicity.
Keywords: Deep inspiratory breath-hold (DIBH), Maximum heart distance (MHD), Central lung distance (CLD).

INTRODUCTION

In recent years, considerable effort has been exerted to identify techniques that reduce the dose to the heart in patients receiving postoperative radiotherapy for breast cancer. The newest techniques include breathing adapted radiotherapy, which takes advantage of the change in the patients anatomy during the respiratory cycle, such that the patients only receive radiation when they are at deep inspiration, so as to inflate the lungs, increasing the distance between chest wall and heart to maximum at or near deep inspiration, moving heart postero-inferiorly and pushing the heart out of the radiation field. Treatment delivery only at deep inspiration reduces the area of the heart that receives a high dose. [1,2] It is, however, still unclear what the mechanisms of cardiac radiation induced toxicity really are, and what dose levels are relevant. Moreover, the whole heart is often the only organ volume included in retrospective dose evaluation studies. However, the dose distribution in the heart is not homogenous and the highest doses are likely to be delivered to the anterior heart, including the left anterior descending artery (LADCA). This is a concern since new studies suggest that arteries are particularly sensitive to radiation, and the LADCA is one of the typical sites of origin for ischemic heart disease. [3] In this context, it is appropriate to ensure that radiation treatments for breast cancer patients are designed to minimise the dose to cardiovascular structures while still ensuring a proper irradiation of the target volume (breast and associated lymph nodes).

For patients treated with left sided tangential irradiation, maximum heart distance (MHD) was a good predictor of mean heart dose and gave an appropriate estimate of dose to the heart and LADCA. Maximum heart distance (MHD) is defined as the maximum distance between the anterior cardiac contour and the posterior tangential field edge as displayed on a beam's eye view of a treatment field. It is assumed that every 1 cm increase in maximum heart depth on a beam's eye view, roughly correlates with increase in mean heart dose by 3 Gy. [4] A relationship can generally be established between the volume of a healthy organ getting high radiation doses and the probability of side effects. Increasing irradiation of the heart leads to increased risk of ischemic heart disease, [3] and it has been shown that patients with left-sided breast carcinoma had a higher risk of cardiac morbidity than patients with right-sided breast carcinoma. [5] It has been suggested that if 5% of the heart receives 40 Gy, the risk of cardiac mortality exceeds 2%. [6]

Consequently, in the adjuvant setting it is pivotal to minimise radiation to the heart since breast cancer survivors have a good prognosis for cancer-free survival and may live several decades after treatment. The Danish Breast Cancer Cooperative Group recommends that considering the future risk of cardiac morbidity, the volume of heart receiving more than 40 Gy is to be kept below 5%, as well as the volume receiving more than 20 Gy be kept under 10%. [7]

Not many studies have been conducted in Indian population to assess the dose to critical structures. In view of this, the present study works to assess and compare the radiation dose delivered to the heart, lung and the LADCA in free breathing and deep inspiration breath-hold phase of respiration in left-sided breast cancer patients while keeping similar target coverage, thereby establishing the role of DIBH for patient with left-sided carcinoma breast.

MATERIALS AND METHODS

Twenty and recording four left sided breast cancer patients post-surgery undergoing radiotherapy were included in this study. The study was approved by Institutional review board and Ethics committee. Informed consent was taken from the patients and their relatives. They underwent breath-hold training before the CT-simulation along with monitoring and recording the baseline respiratory waveform generated with the help of an infrared marker box and infrared camera. The breathing amplitudes were recorded and stored each time the patients were trained. The recorded amplitudes were assessed for their reproducibility. After proper training, patients were taken for CT-simulation with intravenous contrast in both free breathing and deep inspiration breath-hold (instructed by audio command) and subsequent respiratory waveforms were recorded and taken as baseline reference. The simulation scans were transferred to the treatment planning software for contouring. Contouring of the target volumes and organs at risk was performed in accordance with the guidelines published by the Radiation Therapy Oncology Group (RTOG). The Left Anterior Descending Artery (LAD) was delineated in the anterior inter-ventricular groove from its initiation down to the apex of heart. Contouring was done in both the DIBH and FB simulation CT-scans. Heart, lungs and LAD were contoured. The prescription dose was 46 Gy in 23 fractions to the chest wall for mastectomy cases whereas for breast conservative surgery cases this was further followed by boost of 12.5 Gy to the lumpectomy cavity. However for the purpose of this study, boost plans were excluded from the comparison. The treatment plans were generated for both FB and DIBH and plan optimisation was such that a minimum of 95% of the target volume was to be covered by the 95% isodose line (V95≥95%). The dosimetric values for both the plans were recorded for each patient. Treatment plans were generated with Field-in-Field (FiF) 3D conformal radiotherapy technique to avoid hotspots exceeding 110%. Two opposing 6MV tangential conformal fields with a multi-leaf collimator were used. The dose to normal organs was kept as low as possible without compromising the target volume dose. The maximum heart distance in FB and DIBH phase was compared along with mean dose, maximum dose and percentage of heart and LADCA receiving 5, 10, 20, 30, 40 Gy (V5, V10, V20, V30, V40) were analysed. The mean dose to total lungs as well as volume receiving 20 Gy and 40 Gy were also recorded for both the plans.

Ethics: The present study was approved by the Institutional Scientific and Ethical committee.

Statistics: Statistical analysis was done using IBM SPSS statistical software version 16.0. Dose-volume histograms were extracted and compared for each of the DIBH and FB plans. For the heart, V5-V40 Gy, as well as the mean heart dose (Dmean) and maximum heart dose (Dmax) were measured. For the LAD, the Dmax and Dmean and V5-V40 Gy were determined. For Lung Dmean, V20 and V40 were compared. Paired t-tests were used for statistical analysis of the differences. Data were considered statistically significant at p-value<0.05.

RESULTS

The maximum heart distance in the tangential field was reduced from 2.38 cm in FB plan to 2.14 cm in DIBH plan with a relative reduction of 10.1% [Table-1] along with significant reduction in all other heart parameters including Dmax (46.59 vs 44.62 Gy), Dmean (4.84 vs 3.93 Gy), V5 (19.33 vs 16.23), V10 (16.33 vs 13.59), V20 (13.87 vs 12.07), V30 (10.88 vs 9.90) and V40 (0.67 vs 0.41) [Table- 2]. DIBH also resulted in a significant reduction in all the LAD parameters including Dmax (45.26 vs 43.55 Gy), Dmean (25.54 vs 23.91 Gy), V5 (63.53 vs 59.06), V10 (52.51 vs 40.11), V20 (40.79 vs 28.16), V30 (28.05 vs 16.24) and V40 (14.95 vs 5.24). For LAD maximum relative reduction was observed for V40 (64.9%) and the minimum relative reduction was for Dmax [Table-3]. Compared with FB, DIBH resulted in a significant reduction in lung dose parameters including Dmean (3.85 vs 2.69 Gy), V20 (5.92 vs 3.54) and V40 (2.97 vs 1.61) [Table-4].

Table-1: Comparison of Maximum Heart Distance (MHD) in cm between FB and DIBH

Approach	MHD [cm] (Mean±SD)
FB	2.38±0.54 cm
DIBH	2.14±0.49 cm
p-value[1]	0.0001*
Relative reduction (%)	10.1 %

[1]Paired t-test, *Significant

Table-1 shows the comparison of Maximum heart distance (MHD) in FB vs DIBH approach. Compared with FB (2.38±0.54), DIBH (2.14±0.49) resulted in a significant (p=0.0001) reduction in MHD with a relative reduction of 10.1%.

Table-2: Dosimetric comparison of Heart Radiation Doses

Heart	FB (n=24)	DIBH (n=24)	p-value[1]	Relative reduction (%)
Dmax (Gy)	46.59±2.18	44.62±2.52	0.0001*	4.2
Dmean(GY)	4.84±1.36	3.93±1.30	0.0001*	18.8
V5 (%)	19.33±1.64	16.23±2.15	0.0001*	16.0
V10 (%)	16.33±2.27	13.59±2.20	0.0001*	16.8
V20 (%)	13.87±1.78	12.07±1.92	0.0001*	13.0
V30 (%)	10.88±1.70	9.90±1.75	0.0001*	9.0
V40 (%)	0.67±0.37	0.41±0.32	0.0001*	38.8

[1]Paired t-test, *Significant

Table-2 shows the Dosimetric comparison of heart radiation doses. Compared with FB, DIBH resulted in a significant (p=0.0001) reduction in all the heart parameters. The maximum relative reduction was observed for V40 (38.8%) and the minimum relative reduction was for Dmax (Gy) (4.2%).

Table-3: Dosimetric comparison of LAD Radiation doses

LAD	FB (n=24)	DIBH (n=24)	p-value[1]	Relative reduction (%)
Dmax (Gy)	45.26±2.10	43.55±2.42	0.0001*	3.8
Dmean(GY)	25.54±2.78	23.91±3.18	0.0001*	6.4
V5 (%)	65.53±2.49	59.06±2.17	0.0001*	9.9
V10 (%)	52.51±1.71	40.11±1.67	0.0001*	23.6
V20 (%)	40.79±2.39	28.16±1.55	0.0001*	31.0
V30 (%)	28.05±1.51	16.24±1.83	0.0001*	42.1
V40 (%)	14.95±2.34	5.24±2.01	0.0001*	64.9

[1]Paired t-test, *Significant

Table-3 shows the Dosimetric comparison of LAD radiation doses. Compared with FB, DIBH resulted in a significant (p=0.0001) reduction in all the LAD parameters. The maximum relative reduction was observed for V40 (64.9%) and the minimum relative reduction was for Dmax (Gy).

Table-4: Dosimetric comparison of Irradiated Lung Volumes

LUNG	FB (n=24)	DIBH (n=24)	p-value[1]	Relative reduction (%)
Dmean	3.85±0.73	2.69±0.65	0.0001*	43.1
V20 (%)	5.92±1.37	3.54±0.95	0.0001*	67.2
V40 (%)	2.97±0.74	1.61±0.66	0.0001*	84.5

[1]Paired t-test, *Significant

Table-4 shows the Dosimetric comparison of irradiated lung volumes. Compared with FB, DIBH resulted in a significant (p=0.0001) reduction in Dmean (3.85±0.73 vs 2.69±0.65), V20 (5.92±1.37 vs 3.54±0.95) and V40 (2.97±0.74 vs 1.61±0.66). The relative reduction was observed to be highest for V40 (84.5%) compared to V20 (67.2%) and Dmean (43.1%).

Table-5: Target coverage comparison between the FB and DIBH plan

Target Coverage	FB (n=24)	DIBH (n=24)	p-value[1]	Relative reduction (%)
D95 (Gy)	41.89±8.08	43.64±0.37	0.31	-4.2
D98 (Gy)	41.60±0.30	41.54±0.25	0.26	0.1
V<93	2.83±0.89	3.01±0.84	0.10	-6.4

[1]Paired t-test

Table-5 shows the target coverage comparison between FB and DIBH. There was no significance (p>0.05) difference in target coverage between FB and DIBH.

DISCUSSION

In the past few years, cardiac toxicity following radiotherapy for breast cancer has been recognised as an important issue. In the meta-analysis by the Early Breast Cancer Trialist's Collaborative Group including 78 randomised trials, an excess risk of mortality from heart disease (HR 1.27) was found in patients who received adjuvant radiotherapy. [8] Even though it is well known fact that radiation of chest wall is associated with long term cardiac effects, no consistent dose-volume correlations exists. This is likely due to the lack of detailed dosimetric studies with consistent cardiac sub-structure volume delineation.

In a study by Joo JH et al., [9] it was observed that DIBH resulted in significant reduction in the average mean cardiac dose from 7.24 Gy in FB to 2.79 Gy in DIBH (61%). The average heart distance in the tangential field was also reduced from 2.1 cm in FB to 0.7 cm in DIBH. The relative heart volume irradiated with 10-50 Gy was also consistently reduced with DIBH. The mean dose to the LAD coronary artery and ipsilateral lung volume receiving 20 Gy or more and 40 Gy or more was reduced by 2.2% in both cases. The estimated risks of coronary events at 10 years were 4.03% and 2.55% for RT with FB and DIBH, respectively (p<0.001). Hence, it was concluded that the use of DIBH during RT of the left sided breast results in significant reduction in doses delivered to the heart and LAD artery.

Swanson et al. [10] included 99 patients with left sided breast cancer and they were evaluated for reduction in cardiac dose during breast irradiation. They used moderate deep inspiration breath-hold (mDIBH), using an Active Breathing Control device. Of all the patients, 87 patients were treated with mDIBH and rest with free breathing technique. Plans for both the FB and mDIBH were evaluated and analysed for dose to the heart and ipsilateral lung, comparing results for mDIBH vs FB plans. They reported that there was a significant decrease in all DVH parameters evaluated, favouring the delivery of mDIBH over FB plans. Further mDIBH plans had reported a mean heart dose reduction from 4.2 Gy with FB to 2.5 Gy (40%). In addition, there were significant reductions in all other heart parameters evaluated (volume of heart treated, V5, V10, V20, V30 and V40).

Vikstrom et al. [2] showed that compared to FB, the DIBH plans obtained lower cardiac and pulmonary doses, with equal coverage of PTV. The average mean heart dose was reduced from 18.1 Gy in FB to 6.4 Gy in DIBH. They concluded that respiratory gating with DIBH, utilising audio-visual guidance, reduced cardio-pulmonary doses for tangentially treated left sided breast cancer patients without compromising the target coverage.

In the present study with the aim of achieving similar dosimetric coverage within the target, for both DIBH and FB plans for all the patients, it was observed that the heart and LAD coronary artery dose parameters were significantly reduced by using RPM guided breathing adapted radiotherapy. It was observed that the reduced heart and LAD doses in DIBH plans also correlated with maximum heart distance. The average heart distance in the tangential field was reduced from 2.38 cm in FB plan to 2.14 cm in DIBH plan. The mean heart dose was reduced from 4.84 Gy to 3.93 Gy (relative reduction of 18.8%).

In the present study, the mean dose received by Total lung in DIBH (2.69 +/- 0.65 Gy) was reduced compared to FB plans (3.85 +/- 0.73 Gy). Similarly the V20 and V40 were alsoreducedfor DIBH [(3.54 +/- 0.95 Gy0, (1.61 +/- 0.66 Gy)] compared to FB plans [(5.92 +/- 1.37 Gy), (2.97 +/- 0.74 Gy)]. This is in accordance with the previous study by Joo et al. [9] which showed that the average mean heart dose was reduced from 7.24 Gy to 2.79 Gy using DIBH (p<0.001) and the relative heart volume receiving 10-50 Gy was consistently reduced. The mean dose to the LADCA was reduced from 40.79 Gy to 23.68 Gy (p<0.001). It was observed that the average mean pulmonary dose was reduced with DIBH, from10.18 Gy (range 4.88-15.16 Gy) to 9.43 Gy (range 5.05-13.86 Gy) (p=0.001). Similarly, for the average ipsilateral lung volume receiving 20 Gy or more, the V20, was reduced from 18.9% (range 8.3-30.9%) to 16.7% (range 9.2-24.7%) (p<0.001). The V40 was also reduced from 14.1% (range 5.8-23.8%) to 11.9% (range 6.3-19.2%) with DIBH (p<0.001). This is because even though the Central Lung Distance (CLD) in radiation portal increased considerably in DIBH plans compared to FB plans, the total lung volume increased considerably during the DIBH plans. Thus the relative volume of lung irradiated decreased. Also CLD as a parameter to suggest the chances of pneumonitis cannot be used for DIBH plans as the irradiated lung volume decreases, suggesting lower pulmonary complication post treatment.

Hence, in the present study we concluded that DIBH is a better alternative compared to conventional free breathing technique ensuring lower doses to nearby vital structures without compromising dose to target thereby causing lesser post-radiotherapy cardiac and pulmonary morbidity. The study duration was limited so a large number of patients could not be taken up for the present study. So, it is recommended that a larger study be undertaken with similar technique with long term clinical follow-up for evaluation of cardiac and pulmonary toxicity.

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