Research Article

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Journal of Neoplasm
ISSN 2576-3903

2019
Vol.4 No.1:9

Reduction of Heart Dose using Voluntary Deep Inspiration Breath-Holding Technique in Left Breast Cancer Patients Treated by Hypo Fractionated Radiation Therapy

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Citation: Elbadawy S, Attia H, Eltagy R, Mahmoud M (2019) Reduction of Heart Dose using Voluntary Deep Inspiration Breath-Holding Technique in Left Breast Cancer Patients Treated by Hypo Fractionated Radiation Therapy . J Neoplasm Vol.4 No.1:9.

Abstract

Aim: This study aims to compare between conventional FB simulation technique and Deep-Inspiration Breath Holding (DIBH) technique regarding doses to the heart and ipsilateral lung.

Patients and Methods: Sixty-six patients with left-sided breast cancer who presented to the radiotherapy department at National Cancer Institute, Cairo, Egypt between November 2015 and December 2016 were accrued. Patients were planned by 3D conformal radiotherapy technique with a dose of 4005 cGy/15 fx to left breast/chest wall ± supraclavicular lymph nodes. All patients were simulated during free breathing and after voluntary Deep Inspiration Breath Holding.

Result: In this study, whether patients had undergone CBS or MRM, all heart, and Left Anterior Descending (LAD) artery doses, were lower with high statistical significance (p-value<0.001), and left lung doses were lower with statistical significance (p-value<0.05) using DIBH technique compared to FB technique.

Conclusion: The Deep Inspiration Breath Hold (DIBH) technique can be associated with lower radiation exposure to the heart, Left Anterior Descending (LAD) Artery, and ipsilateral lung without compromising coverage of the breast or chest wall.

Keywords: Deep inspiration breath hold; Free-breathing; Left anterior descending

Received: August 01, 2019; **Accepted:** August 13, 2019; **Published:** August 19, 2019

Introduction

Breast cancer is the most common malignancy among females, and one of the leading causes of cancer mortality [1]. Management of primary breast cancer embraces a multi-modality approach including surgery, chemotherapy, and radiation therapy [2].

Adjuvant radiotherapy is known to reduce local recurrence, which in turn increases breast cancer-specific survival and overall survival [3]. With most patients now living long after their breast cancer diagnosis, the medical community bears increased responsibility to minimize long-term side-effects of treatment for breast cancer. This is particularly true in regards to reducing late cardiac and pulmonary side effects of Radiotherapy.

In 2013, New England Journal of Medicine published an article reporting on cardiac toxicity incurred in 2168 women treated for breast cancer in Sweden and Denmark between 1958 and 2001 [4]. In this group, 963 women suffered major coronary events and 1205 were used as controls. They found that rates of major coronary events increased linearly with mean dose to the heart by a relative rate of 7.4% per Gy [4] the risk was noted to start within five years of treatment and to continue for at least 20 years [4].

Respiratory motion studies in the past have demonstrated that deep inspiration results in increased distance between the heart and left anterior chest wall. Breath holding, accomplished by having the patient take and hold a deep inspiration during CT simulation and during treatment each day, has been shown to significantly reduce heart dose [5,6].

Previously, all breast cancer patients at the National Cancer Institute of Egypt, the largest and most populated cancer research center in Egypt, have been treated using free-breathing technique. Thus, this exploratory study aims to compare doses to critical organs at risk mean heart dose, V10-heart, V20-heart, V25-heart, Left Anterior Descending (LAD) artery, and lungs

between conventional free-breathing simulation technique and Deep-Inspiration Breath Holding (DIBH) technique. Also the study aims at assessing the feasibility of DIBH technique in lowering the radiation exposure to the heart without compromising coverage of left breast or chest wall.

Patients and Methods

Sixty-six patients with left-sided breast cancer who presented to the radiotherapy department at National Cancer Institute, Cairo, Egypt between November 2015 and December 2016 were accrued.

Inclusion criteria included patients with non-metastatic left breast cancer after undergoing breast conserving surgery or mastectomy who are candidates for post-operative radiotherapy with or without chemotherapy.

Exclusion criteria included patients with pre-existing chest conditions, including but not limited to, TB, severe bronchial asthma, and interstitial pulmonary fibrosis, patients with uncontrolled co-morbidities as diabetes and hypertension, patients with ischemic heart disease, and patients not able to hold deep inspiration for duration of CT simulation (~ 20 seconds).

CT simulation

The patients were positioned in supine decubitus with their arms above their heads on breast board. Thin metallic wires were placed along the midline (medial) and mid-axillary line (lateral) at the time of image acquisition. The area of CT scanning included the clavicular head (cranial) and contralateral inferior breast border (caudal). Spiral CT scans were performed on General Electric CT with 2.5 mm slice thicknesses for breathing conditions, free-breathing, and deep inspiration breath-holding. The CT image data sets were then transferred to the treatment planning system where target and organs at risk were contoured according to RTOG protocols.

LAD arteries were contoured according to the University of Michigan cardiac atlas by Feng et al. [7]. The heart contour included the ventricles, atria, auricles, and pericardium and excluded the root of the aorta, the pulmonary artery and veins, and the vena cava. To achieve optimal comparability between FB and DIBH volumes, the LAD was contoured with a standardized 5 mm diameter from its origin at the left aortic sinus down to the cardiac apex in all cases.

3D-conformal planning was done, and doses calculated using hypofractionated dose of 40Gy/15 fractions in all cases. Dose-Volume Histograms were then prepared and compared between free-breathing volumes and vDIBH volumes regarding doses to critical organs at risk (mean heart dose, V10-heart, V20-heart, V25-heart, (LAD) artery, contralateral breast, and lungs), and planning target volume (PTV).

Statistical analysis of raw data was performed utilizing IBM SPSS® 20.0. Paired-T tests were used to compare between FB and DIBH techniques regarding heart, LAD artery and left lung doses in respects to mean, laterality, type of surgery, axillary/SCV irradiation and Internal Mammary nodal irradiation.

Result

In this study, 66 patients were accrued from Nov. 2015 to Dec. 2016 at the Radiotherapy Department at National Cancer Institute, Egypt.

Mean heart doses ranged from 99 cGy to 613 cGy with the average being 330 cGy. According to RTOG 1005 protocol, used for the purpose of this study, 3 patients had unacceptable mean heart doses of more than 500 cGy, while 14 patients had unideal but acceptable mean heart dose between 400 to 500 cGy **Figure 1**.

In the deep inspiration breathe holding (DIBH) technique

Mean heart doses ranged from 74 cGy to 407 cGy with the average being 210 cGy. According to RTOG 1005 protocol, used for the purpose of this study, none of the patients had unacceptable mean heart doses of more than 500 cGy, while 1 patient had an unideal but acceptable mean heart dose between 400 to 500 cGy **Figure 2**.

Using the DIBH technique, all patients, with the exception of one, had lower heart and LAD artery doses with highly statistically significant difference (p-value<0.001) **Table 1**.

Left lung doses highly statistically significantly with DIBH than FB (p-value <0.001) **(Table 1)**.

In this study, whether patients had undergone MRM or CBS, heart, and LAD artery, highly statistically significantly (p-value <0.001), and left lung doses were statistically significantly lower

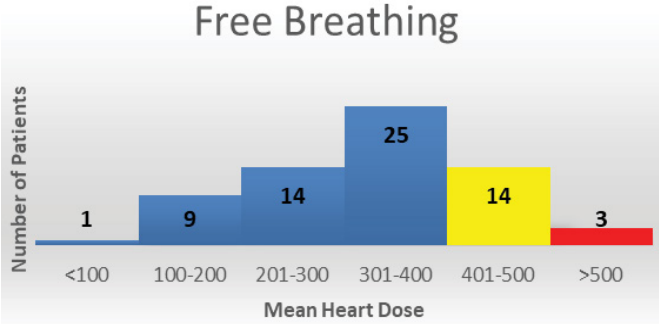

Figure 1 Mean heart dose in free-breathing setup.

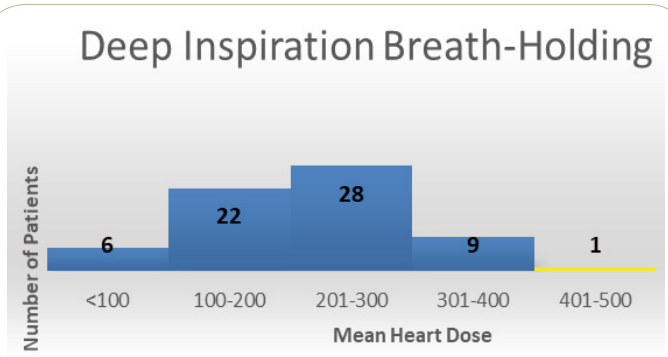

Figure 2 Mean heart dose in DIBH setup.

Table 1: Comparison between the different heart and lung parameters in FB and DIBH techniques.

		Mean	SD of mean	Difference	p-value
Mean Heart Dose (cGy)	FB	330	113.422	36.40%	<0.001
	DIBH	210	82.187		
V10-Heart (%)	FB	7.38	3.459	43.90%	<0.001
	DIBH	4.14	2.583		
V20-Heart (%)	FB	5.26	2.879	51.30%	<0.001
	DIBH	2.56	1.923		
V25-Heart (%)	FB	4.27	2.447	57.10%	<0.001
	DIBH	1.83	1.669		
Maximum LAD (Gy)	FB	20.85	8.709	33.40%	<0.001
	DIBH	13.89	4.724		
Mean LAD (Gy)	FB	5.3	2.17	33.65%	<0.001
	DIBH	3.52	1.327		
V20-Lung (%)	FB	20.47	2.255	8.40%	<0.001
	DIBH	18.76	2.877		

Table 2: Different heart and lung parameters in patients who underwent MRM.

MRM (n=41)		Mean	SD of mean	p-value
Mean Heart Dose (cGy)	FB	324.66	117.555	<0.001
	DIBH	207.54	83.169	
V10-Heart (%)	FB	7.2	3.544	<0.001
	DIBH	4.02	2.485	
V20-Heart (%)	FB	5.17	3.065	<0.001
	DIBH	2.44	1.803	
V25-Heart (%)	FB	4.15	2.545	<0.001
	DIBH	1.73	1.613	
Maximum LAD (Gy)	FB	20.32	8.184	<0.001
	DIBH	13.71	4.734	
Mean LAD (Gy)	FB	5.44	2.409	<0.001
	DIBH	3.46	1.267	
V20-Lung (%)	FB	20.24	1.868	0.001
	DIBH	18.85	2.555	

Table 3: Different heart and lung parameters in patients who underwent CBS.

CBS (n=25)		Mean	SD of mean	p-value
Mean Heart Dose (cGy)	FB	340.96	107.877	<0.001
	DIBH	215.04	82.03	
V10-Heart (%)	FB	7.68	3.363	<0.001
	DIBH	4.32	2.779	
V20-Heart (%)	FB	5.4	2.598	<0.001
	DIBH	2.76	2.126	
V25-Heart (%)	FB	4.48	2.311	<0.001
	DIBH	2	1.779	
Maximum LAD (Gy)	FB	21.72	9.619	<0.001
	DIBH	14.2	4.787	
Mean LAD (Gy)	FB	5.08	1.73	<0.001
	DIBH	3.6	1.443	
V20-Lung (%)	FB	20.84	2.779	0.006
	DIBH	18.6	3.391	

(p-value <0.05) using DIBH technique (i.e. both groups of patients benefited) **Tables 2 and 3**.

Patients who received left axillary/SCV irradiation had highly significant lower ipsilateral (left) lung doses using DIBH technique than free-breathing technique (p-value<0.001). Patients who didn't receive axillary/SCV nodal irradiation had statistically

Table 4: Differences in V20- lung in patients who received left axillary/SCV irradiation.

Axilla/SCV (n=51)		Mean	SD of mean	p-value
V20-Lung (%)	FB	20.27	2.474	0.001
	DIBH	18.8	2.608	
NUMBER (n=15)		**Mean**	**SD of mean**	**p-value**
V20-Lung (%)	FB	21.13	1.06	0.02
	DIBH	18.6	3.757	

significant differences between left lung doses (p-value<0.05) as shown in **Table 4**.

Discussion

This study, as far as we know, is the first of its kind in Egypt. However, some limitations should be acknowledged, the lack of different patient characteristics such as body BMI and smoking history which may have an impact on breath-holding were not included in the statistical analysis. Furthermore, the sample size may be considered small; however, this is an exploratory study to assess the value of DIBH at our high-density institute. This study included only women with left-sided breast cancer. Patients were planned by 3D conformal radiotherapy technique with a dose of 40 Gray in 15 fractions to left breast/chest wall ± supraclavicular lymph nodes. All patients were simulated during free breathing and after voluntary Deep Inspiration Breath Holding.

Regarding mean heart dose

In the present study, in the Free Breathing (FB) technique, mean heart doses ranged from 99 cGy to 613 cGy with the average being 330 cGy. While, in the Voluntary Deep Inspiration Breath Hold (vDIBH) technique, mean heart doses ranged from 74cGy to 407 cGy with the average being 210 cGy. This corresponds to an absolute mean heart dose reduction of 120 cGy and a relative dose reduction of 36.4% favoring vDIBH. These results are highly statistically significant (p-value<0.001).

This is similar to what was reported by the UK Heart Spare Study and Swanson et al. who reported a relative dose reduction by 41 % and 40 % respectively [7-9].

Although Rochet et al. and Borst et al. values appear to be noticeably higher than in our study, all were highly statistically significant. This difference could be attributed to a lower number of patients recruited in Rochet et al.'s study where 35 patients were included and Borst et al.'s study which included 19 patients only compared to 66 patients in our study [10,11].

Regarding left anterior descending artery dose

In the present study, in the FB technique, the maximum dose to Left Anterior Descending Artery (LAD) averaged at 20.8 Gy. While, in the vDIBH technique, maximum dose averaged at 13.9 Gy. This represents a relative dose reduction of 33.4% favoring vDIBH, (p-value<0.001).

This is coinciding with what was reported by The UK Heart Spare study [8] where there was a relative reduction of 32% and 55% for maximum and mean LAD doses respectively. Both values were highly significant.

Also our results are similar to those reported by Rochet et al. and

Wang et al. who reported a relative dose reduction of 56% and 73% for maximum and mean LAD respectively in the first study and a dose reduction of 63% and 71% for maximum and mean LAD doses Respectively in the second study [10,12]. Both values were highly significant.

Regarding ipsilateral lung dose

In our present study, the average V20 of the ipsilateral (left) lung was reduced from 20.5% to 18.8% between FB and vDIBH techniques. This represents a relative dose reduction of 8.4% which is highly statistically significant (p-value<0.001).

Similar findings were found by Swanson et al. and Comsa et al. where there was a relative decrease of 16% and 23% for V20 respectively in patients treated with 3-4 field technique, which was highly significant [9,13].

Regarding regional nodal irradiation

In the current study, Patients who received left axillary/supraclavicular (SCV) nodal irradiation had highly significant lower ipsilateral (left) lung doses using DIBH technique than free-breathing technique (p-value<0.001).

This result is comparable to Hjelstuen et al. who reported significant lower lung doses using DIBH technique in patients receiving axillary/SCV nodal irradiation [14].

Conclusion

We conclude that Deep Inspiration Breath Hold (DIBH) technique can be associated with lower radiation exposure to the heart, Left Anterior Descending (LAD) Artery, and ipsilateral lung without compromising coverage of the left breast or chest wall.

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