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Right Deep Inspiration Breath Hold Technique: An Effective Way of Treatment In Right Breast Radiotherapy For Sparing Of Normal Organ At Risk: A Treatment Planning Study

Dr Mayuresh D Virkar[1], Dr Kharde Anup[2*]

1. Consultant Radiation Oncologist, Radiation Oncology, HCG-MANAVTA CANCER CENTRE, Nashik, Maharashtra.
2. Professor Zydus Medical College & Hospital Dahod Gujarat.

*Corresponding Author

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ABSTRACT

Women with early-stage breast cancer undergo breast-conserving surgery followed by irradiation to whole breast, resulting decrease in rate of local recurrence. Though adjuvant radiation therapy has survival and local control effects many have questioned with the associated toxicities and resulting mortality may actually nullify some of the survival benefit It is found that the mortality is specifically related to cardiac mortality, and studies have shown the cardiac mortality is more seen in patients who receive radiation therapy for left-sided breast Due to limited availability of data present study was planned to quantify the dose-sparing benefits of Right Deep Inspiration Breath Hold Technique (DIBH) compared to free breathing (FB) for right-sided breast radiotherapy **Method:** This was descriptive cross sectional study was carried out on secondary data of 40 patients of radiotherapy plans in FB and DIBH technique of forty patients who was originally receiving adjuvant radiotherapy to Right intact breast/chest wall with or without ipsilateral supraclavicular node and/or internal mammary node. **Results:** In present study out of 40 patients 25 patients had undergone Breast conservative surgery (BCS) and 15 undergone Modified radical mastectomy (MRM). For all cohorts there was significant ipsilateral lung sparing effect was seen in DIBH with Mean Lung = 0.72 ± 1.87 and V20Gy = 2.60 ± 6.45 showing statistically significance (p=0.02,p=0.015 respectively). There was significant dose sparing to contra lateral breast in DIBH for both the cohort i.e. BCS and MRM 0.10 ± 0.16

(p=0.00). Cardiac sparing effect was seen in DIBH for both BCS and MRM with Heart Mean dose 0.37 ± 0.96 (p=0.01) and Heart Max 1.52 ± 4.99 (p=0.06). In addition, a significant dose reduction in DIBH is seen in RCA Mean dose = 0.97 ± 1.84 (p=0.00) and RCA Max dose = 1.68 ± 2.68 (p=0.00). **Conclusion:** DIBH is a promising approach which could lead to sparing of normal-tissue during radiotherapy for right sided breast cancer patients, particularly sparing of heart and lungs.

Keywords: Right Deep Inspiration Breath Hold Technique, Free breathing, breast cancer**,** radiotherapy

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INTRODUCTION

Women with early-stage breast cancer undergo breast-conserving surgery followed by irradiation to whole breast, resulting decrease in rate of local recurrence.[1-3] Radiotherapy to the chest wall and regional lymph nodes which is termed as regional nodal irradiation, is commonly used in women with node-positive breast cancer after mastectomy and adjuvant systemic therapy, which reduces loco-regional and distant recurrence and improves overall survival.[4-6] With the survival benefits and local control effects with adjuvant radiation therapy[7,8] many have questioned with the associated toxicities and resulting mortality may actually nullify some of the survival benefit [9,10] It is found that the mortality is specifically related to cardiac mortality, and studies have shown the cardiac mortality is more seen in patients who receive radiation therapy for left-sided breast[11,12]. In fact, cardiac deaths and coronary events is correlated with mean radiation dose to the heart[13-15] The cardiac events is estimated to increase 4–7% for each 1 Gy in mean heart dose, and there does not appear to be a minimum dose threshold below which there is no risk of cardiac events [16-18].

Deep inspiration breath-hold (DIBH) is a respiratory manoeuvre predominantly used to decrease the risk of late cardiac toxicity along with lung sparing benefits for women receiving radiotherapy left-breast irradiation, with or without regional nodal irradiation (RNI)[9-15].Despite the widespread implementation of DIBH for left-breast radiotherapy, it is rarely used for right sided treatment and there are few studies exploring the possible dosimetric advantages. However few studies show cardiac and pulmonary benefits for right-breast cancer patients when RNI is also prescribed [17,18]. Liver-sparing is also reported, but data remains limited. The

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aim of this study is to quantify the dose-sparing benefits of DIBH compared to free breathing (FB) for right-sided breast radiotherapy, with and without irradiation of the regional nodes and also to evaluate Dose distributions to the lungs, heart, left anterior descending (LAD) artery and right coronary artery (RCA).

METHODS

Secondary data was analyzed retrospectively for Free-breathing and DIBH computed tomography (CT) scans were obtained from forty (40) patients, who was originally receiving adjuvant radiotherapy to Right intact breast/chest wall with or without ipsilateral supraclavicular node and/or internal mammary node from May 2021 to April 2022. No extra imaging was required for the study. All the patients were treated in free breathing position as per the standard of care radiotherapy.

Patients were scanned in a supine position with arms raised over head and supported by a breast board. Patients did not change position between the FB and DIBH scans. Verbal coaching was received from radiation therapists to the patients during the DIBH scan. The Active Breathing Coordinator (ABC) system (Aktina Medical Corporation, NY 10920) was used to monitor breathing during both FB and DIBH scans via ABC mouth piece. All patients were able to hold their breath for greater than twenty seconds to accommodate the scan during DIBH. The CT scan length was from the level of the C3 vertebra to 5 cm inferior to the infra-mammary fold with a CT slice thickness of 3 mm. Scans were imported into the Monaco^{TM} (Elekta) planning system for volume delineation and treatment planning. Target volume and organ at risk delineation.

Target volumes were delineated by one radiation oncologist and independently peer reviewed by a second radiation oncologist prior to treatment planning. The target volumes delineation was defined according to ESTRO consensus guidelines. The breast CTV was defined as the visible breast tissue on CT cropped 5mm from the skin surface. The planning target volume (PTV) was a 5mm isotropic expansion of the CTV which was subsequently cropped 5mm from the skin surface. Contours for both lungs were generated using an automated segmentation tool and adjusted manually where necessary. The contra lateral breast, the heart, LAD, LCA, LCC and RCA were contoured manually as per RTOG 1106 contouring atlas.

Treatment planning

Contouring and treatment planning for Free Breath (FB) and Deep Inspiration Breath (DIBH) treatment plans were generated for each patient by Radiation Oncologist and Radiation Physicist, where it was performed with the TPS Monaco Version 5.11.02 (Elekta, Stockholm, Sweden). The prescription dose for all plans was 41.5Gy in 15 fractions (for patients who had undergone mastectomy) followed by electron boost with dose of 12.5 Gy in 5 fractions for patients undergone breast conservative surgery. Dose Calculation was done with the Collapsed Cone (CC). Target coverage was evaluated as per ICRU recommendations, following are the recommendations; Coverage of the PTV by the 95% isodose, mean dose to the PTV between 100 and 102% of the prescription dose, maximum dose not exceeding 107% of the prescribed dose. Whole breast with supra clavicular fossa (SCF) & Breast only plans were planned with a Field in Field technique using a tangential beam arrangement, predominantly using a 6 MV photon beam energy, however, for coverage of SCF 8 x 8cm2field size with the anterior field was used. The dose-volume objectives for the Organs at Risk like heart and lungs were aligned to QUANTEC guidelines as follows; heart- V30Gy <46%, and mean dose < 26 Gy, lung-V20Gy < 30% and mean dose <20Gy. The maximum dose to the heart was to be kept as low as possible. The mean dose to the contra lateral left breast was restricted to less than 2 Gy.

Plan evaluation and statistical analysis

For plan evaluation dose volume histogram generated from all target volumes and organ at risk on both free breath and deep inspiration breath hold image database, following recording were recorded for organs at risk and target volumes:Dose to ipsilateral lung: mean, volume receiving 20Gy, 5Gy of dose, mean and maximum dose to heart, mean dose and volume receiving 95% of prescription dose to PTV, mean and max dose to opposite breast, mean dose to contra lateral lung, mean and max dose to RCA, LCA, LAD and LCC respectively.All analyses were performed using SPSS software, Data was presented as Mean values ± standard deviation (SD). Paired sample T-test were used to compare dose volume constraints achieved between FB and DIBH were P<0.05 was considered significant.

RESULTS

Comparison of Dose volumetric for target volumes and OARs are summarized in (Table:1). Two sets of data were collected for comparison of DIBH V/S FB i.e.

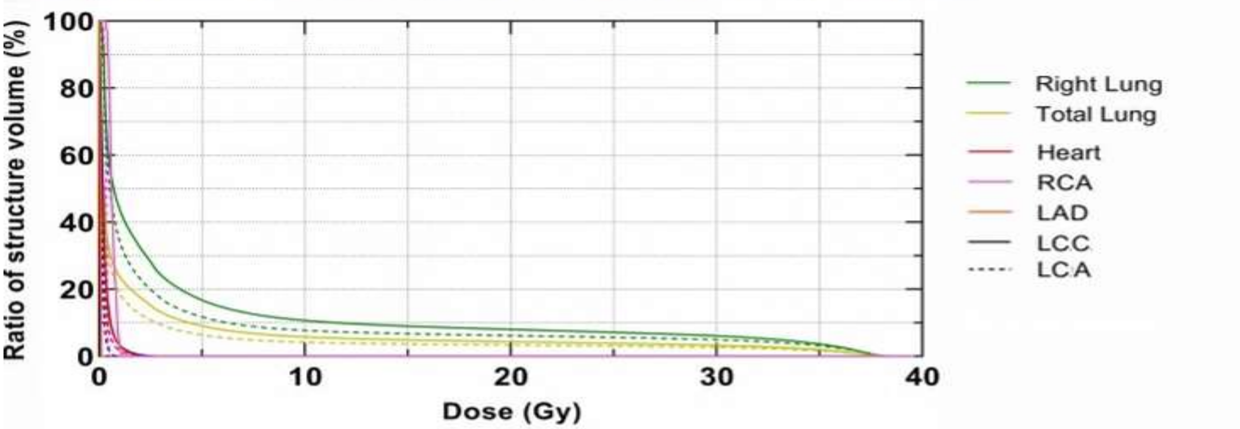
1. Patients who was undergone Breast conservative surgery (BCS) (n=25)
2. Patients who was undergone Modified radical mastectomy (MRM)(n=15).

Table 1: Paired Samples Test for 40 patients

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	LungipsimeanFB - LungipsimeanDIBH	.72115	1.87436	.29636	.12170	1.32060	2.433	39	.020
Pair 2	Lungipsiv20FB - Lungipsiv20DIBH	2.60125	6.45205	1.02016	.53778	4.66472	2.550	39	.015
Pair 3	Lungipsiv5FB - Lungipsiv5DIBH	1.42175	5.55258	.87794	-.35405	3.19755	1.619	39	.113
Pair 4	HeartmaxFB - HeartmaxDIBH	1.52235	4.99694	.79009	-.07575	3.12045	1.927	39	.061
Pair 5	HeartmeanFB - HeartmeanDIBH	.37590	.96612	.15276	.06692	.68488	2.461	39	.018
Pair 6	PTVmeanFB - PTVmeanDIBH	.09175	.30993	.04900	-.00737	.19087	1.872	39	.069
Pair 7	PTVv95FB - PTVv95DIBH	.67950	4.27951	.67665	-.68916	2.04816	1.004	39	.321
Pair 8	BreastcontrameanFB - BreastcontrameanDIBH	.10658	.16615	.02627	.05344	.15971	4.057	39	.000
Pair 9	RCAmaxFB - RCAmaxDIBH	1.68975	2.68861	.42511	.82989	2.54961	3.975	39	.000
Pair 10	RCAmeanFB - RCAmeanDIBH	.97025	1.84139	.29115	.38134	1.55916	3.332	39	.002
Pair 11	LCAmaxFB - LCAmaxDIBH	.10200	.23056	.03646	.02826	.17574	2.798	39	.008
Pair 12	LCAmeanFB - LCAmeanDIBH	.04075	.20773	.03284	-.02568	.10718	1.241	39	.222

Pair 13	LADmaxFB - LADmaxDIBH	.13775	.44673	.07063	-.00512	.28062	1.950	39	.058
Pair 14	LADmeanFB - LADmeanDIBH	.34725	1.69652	.26824	-.19532	.88982	1.295	39	.203
Pair 15	LungcontrameanFB - LungcontrameanDIBH	-.02628	.22852	.03613	-.09936	.04681	-.727	39	.471
Pair 16	LCCmaxFB - LCCmaxDIBH	.06450	.18347	.02901	.00582	.12318	2.223	39	.032
Pair 17	LCCmeanFB - LCCmeanDIBH	.03225	.13271	.02098	-.01019	.07469	1.537	39	.132

Fig:1 Dose-volume metrics for DIBH and FB treatment plans



ABBREVIATIONS:

(DIBH) Deep inspiration breath-hold
(ABC) The Active Breathing Coordinator
(FB) Free Breathing
(CC) Collapsed Cone
(RT) Radiation Therapy

(CT) Computed Tomography

(CTV) Clinical Target Volume

(PTV) Planning Target Volume

(SD) Standard Deviation

(LAD) Left Anterior Descending

(RCA) Right Coronary Artery

(SCF) Supra Clavicular Fossa

(BCS) Breast Conservative Surgery

(MRM) Modified Radical Mastectomy

(RP) Radiation-Induced Pneumonitis

For the comparison DVHs of both FB and DIBH was used (Fig1). There was no difference in plan quality for target coverage between DIBH and FB in both the group i.e. MRM and BCS patients. Thus all under both breathing condition meet the optimal target coverage (Table1). For all cohorts there was significant ipsilateral lung sparing effect was seen in DIBH with Mean Lung = 0.72 ± 1.87 and V20Gy = 2.60 ± 6.45 showing statistically significance (p=0.02,p=0.015 respectively).However there was no benefits was seen in low dose exposure in ipsilateral lung for V5Gy = 1.42 ± 5.55 (p=0.11). On subgroup analysis between BCS and MRM patients there was no significant ipsilateral lung sparing effects seen in MRM patients.

There was significant dose sparing to contra lateral breast in DIBH for both the cohort i.e. BCS and MRM 0.10 ± 0.16 (p=0.00).Cardiac sparing effect was seen in DIBH for both BCS and MRM with Heart Mean dose 0.37 ± 0.96 (p=0.01) and Heart Max 1.52 ± 4.99 (p=0.06).In addition, a significant dose reduction in DIBH is seen in RCA Mean dose = 0.97 ± 1.84 (p=0.00) and RCA Max dose = 1.68 ± 2.68 (p=0.00).There was no significant difference to dose to LAD and LCC in both FB and DIBH for both cohorts. However there was significant difference to dose to max point of LCC = 0.06± 0.18 (p=0.03).

DISCUSSION

This study supports the use of Deep inspiration breath-hold (DIBH) technique for right-sided breast cancer patients with due respect to its cardiac sparing and lung sparing benefits. In the modern era of radiation therapy, the rate of radiation-induced pneumonitis (RP) following breast radiotherapy in the modern era is low (1 to 5%) with reductions in lung-function being more common [19,20]. In right- sided breast radiotherapy DIBH not only reduces percentage of volume of lung (i.e. V20 and V5), but also reduces lung tissue density. [21] As per Zurl et al [22] reported that when compared to free breath technique, the use of deep inspiration breath-hold technique in breast cancer patients can reduce the mean lung dose by 15% and the lung V20 by 17%. Essers et al. [23] and Conway et al.[24] showed an absolute reduction in ipsilateral lung V20Gy of 7.5% and of 7.8%, respectively. In our study the dose reduction in ipsilateral lung volume of 20 Gy (V20) and Mean lung dose was statistically significant (p=0.02, p=0.015 respectively). One of the major determinable factors for the effect of radiotherapy in survival is radiation induced cardio-toxicity. However with the use of adjuvant cardio-toxic chemotherapy, it is necessary to achieve as low as radiation dose to heart. Cardiac sparing effect is most relevant to left breast radiotherapy, however use of DIBH in right breast radiotherapy have shown promising results. Vincent et al[25] reported that a reduction in radiation dose can be achieved in patient's breast cancer using an ABC device. Darby et al.[26] demonstrated that increase in per Gray dose increases the risk of major coronary events with rate of 7.4% per Gray, with no threshold dose. In our Study cardiac sparing effect was seen in both BCS and MRM cases with mean and max heart dose (p=0.01 and p=0.06 respectively) Nilsson et al [27] recently published study that correlated sites of coronary artery stenosis to RT fields. They correlated patients in Swedish breast cancer registries who had subsequently undergone coronary angiography. The breast cancer patients were subdivided into who have high-risk RT (RT field to internal mammary nodes that may have irradiated the RCA, and tangential left breast/chest wall fields that may have irradiated distal branches of the LAD) and low-risk RT (right tangential breast/chest wall, supraclavicular/axillary and those Breast cancer patient who did not receive Radiotherapy. These subgroups were compared with each other and also with a reference group that had undergone coronary angiography but had no history of breast cancer. Their analysis revealed that the patients with high-risk RT had higher frequency of coronary stenosis in the arteries that were irradiated, namely the RCA and the distal branches of the LAD and with low-risk RT had a distribution of coronary stenosis sites similar to the reference patients. In our study there was significant dose sparing with mean and max to RCA (p=0.01and p=0.00 respectively) and max to LCC (p=0.03), Altinok et al.[28] suggests that use of high doses to the proximal RCA could predisposes to coronary artery Disease. Thus, it further provides support for implementing DIBH technique for Right sided breast radiotherapy. There is limitation in our study which should be noted first the results presented in our studies are specific to dose prescription and the planning technique standard to our department, the magnitude of dosimetric benefits will vary between different planning techniques. Second only one radiation therapist generated the treatment plans for all patients, which gives the advantage of eliminating inter-planner variation (error) between treatment plans, there may still be the possibility for planning bias between different patients. Last, Further prospective studies with larger cohorts is needed in order to support DIBH technique to right-breast radiotherapy as this was a retrospective study with a relatively small number of patients.

CONCLUSION

We have shown that DIBH is a promising approach which could lead to sparing of normal-tissue during radiotherapy for right sided breast cancer patients, particularly sparing of heart and lungs to prevent late and early complications.

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