

Dosimetric Outcomes of Deep Inspiration Breath-Hold (DIBH) Technique in Terms of Normal Tissue Sparing for Right-Sided Breast Cancer Irradiation: A Single-Institution Experience

Research Article

Raka Banerjee*, Koustav Mazumder, Poonam Ray, Amitabh Ray, Sayan Kundu, Chandrani Mallik, Bodhisattwa Dutta, Dilip Kumar Ray

Chittaranjan National Cancer Institute, Kolkata, West Bengal India

Received 24 April 2025; Accepted 10 July 2025

Abstract: **Introduction:** Deep inspiration breath-hold (DIBH) technique is commonly used in left breast cancer irradiation as it has shown to reduce cardiac and pulmonary doses. DIBH technique has also shown to reduce critical organ doses in right-sided breast cancer patients. This study aimed to demonstrate the single-institution experience of dosimetric benefits of DIBH technique in irradiation of right breast carcinoma patients.

Materials and Method: Twenty consecutive patients who underwent adjuvant locoregional radiotherapy by DIBH technique for right-sided breast carcinoma were included retrospectively for analysis. Indications for use of DIBH for right-sided disease in our institution included presence of breast implant or need for irradiation of axillary and/or internal mammary nodal basin. For all these patients, planning computed tomography (CT) was obtained in both free breathing (FB) and deep inspiration breath hold (DIBH) using indexed breast board. Treatment was replanned in the FB planning CT slices, and dosimetric endpoints in terms of differences in PTV coverage and doses to lungs, heart, liver, and contralateral breast were compared. Radiation was delivered using either volumetric modulated arc therapy or intensity-modulated radiotherapy technique.

Results: There was no significant difference in PTV coverage between FB and DIBH scans showing similar plan qualities. The ipsilateral lung volume showed significant increase with subsequent decrease in the mean dose with DIBH compared to FB (from 14 Gy in the FB plan to 12 Gy with DIBH, p -value 0.01). Technique of DIBH significantly lowered the mean hepatic dose compared to FB technique (3.8 vs. 7.9 Gy, p -value: 0.0001). Contralateral lung mean dose also showed reduction of statistical significance in DIBH. There was significant difference in the mean dose to the heart between the two techniques, as well as in the max dose, which was reduced significantly with DIBH. Contralateral breast mean dose was also reduced with DIBH, though the difference was not statistically significant.

Conclusion: DIBH technique showed significant dosimetric benefit in terms of reduced critical organ doses, providing a potential for incorporation into radiotherapy of right-sided breast carcinoma.

Keywords: Breast cancer • radiotherapy • deep inspiration breath hold (DIBH) • dosimetry

1. Introduction

Postoperative whole-breast or chest wall radiotherapy has been documented to improve both locoregional disease control and overall survival in breast carcinoma patients.^[1,2,3] Despite the benefits, radiation-induced toxicity is a major concern due to the observed long-term survival of breast carcinoma patients. An increased risk of long-term cardiac morbidity following adjuvant

radiotherapy for left-sided breast carcinoma has been shown in studies using conventional radiotherapy techniques.^[4,5]

In recent years, multiple attempts have been made to devise modifications in radiotherapy techniques to reduce critical organ doses, particularly pulmonary and cardiac doses, during adjuvant radiotherapy for breast carcinoma. Among the various radiotherapy

* E-mail: introraka218@gmail.com

techniques aimed at reducing adjacent normal tissue doses, particularly doses to the heart and lungs, the deep inspiration breath-hold (DIBH) technique is the most studied. DIBH is achieved using either the Elekta Active Breathing Coordinator™ or the Varian RPM (Real Time Position Management) System, and studies have shown that both techniques produce comparable results in terms of reproducibility and normal tissue sparing.^[6]

Several studies have demonstrated the significant benefits of DIBH in sparing the heart and other structures, such as the left anterior descending artery, with appreciable reductions in mean heart dose compared to older radiotherapy techniques.^[7,8,9] In addition, DIBH significantly reduces ipsilateral lung mean doses.^[10,11,12] Although DIBH increases the absolute volume of the lung, it spares the lung tissue by reducing the relative volume of the lung irradiated.

Multiple studies have proven the benefit of DIBH in left-sided radiotherapy in terms of critical organ sparing. However, studies and clinical practices remain limited in the case of right-sided breast or chest wall irradiation. The few studies on right-sided radiotherapy using DIBH have primarily focused on cardiac and lung benefits, with limited data available on liver dose reduction despite the liver being an important organ at risk in right breast carcinoma adjuvant radiotherapy.^[13,14,15,16]

The subsequent use of systemic therapy in breast cancer treatment for recurrence or distant metastasis, particularly targeted therapy and immunotherapy, which can affect organ function, including hepatic function, makes hepatic tissue sparing during radiotherapy even more critical alongside other normal tissue dose reductions.

This study aimed to demonstrate a single institution's experience with the dosimetric benefits of the DIBH technique in the irradiation of right breast carcinoma patients, focusing on sparing the heart, bilateral lungs, and liver while maintaining acceptable target volume coverage.

2. Materials and Methodology

2.1. Patient Population and Study Design:

The study was carried out in the Radiotherapy Department of Chittaranjan National Cancer Institute, Kolkata, India. Twenty consecutive patients with right-sided breast carcinoma undergoing adjuvant whole-breast or chest wall radiotherapy using the DIBH technique were retrospectively included in the study. Trial was not funded and was conducted according to ethical guidelines established by the Declaration of

Helsinki and other guidelines like Good Clinical Practice Guidelines and those established by the Indian Council of Medical Research.

Indications for the use of DIBH for right-sided breast carcinoma adjuvant radiotherapy in our institution included the presence of a breast implant or the need for irradiation of the axillary and/or internal mammary lymph nodal area. All patients were treated using the DIBH technique. An indexed breast board was used, with both arms placed above the head and the head rotated to the opposite side. Planning scans were obtained in both free breathing (FB) and DIBH for all patients using a wide-bore computed tomography (CT) simulator (GE 128 Wide Bore CT). During DIBH, respiratory motion was tracked using the Varian RGSC (Respiratory Gating for Scanners) gating system (Varian Medical System) with a surrogate block placed over the diaphragm, which provided a signal to the RGSC camera. Both planning scans for each patient were obtained with a 2.5-mm slice separation, with the patient in the same position and covering the same length, from the mentum to full coverage of the liver. The planning scans were then transferred to the Varian Treatment Planning System for target and normal tissue delineation and treatment planning.

2.2. Target and Organ-at-Risk Delineation:

Targets and organs at risk were contoured in both planning scans using the same contouring method. Whole-breast or chest wall Clinical Target Volume (CTV) were delineated using the Radiation Therapy Oncology Group, RTOGBreast Contouring Atlas.^[17] Regional lymph nodes, when indicated, were contoured using the same guidelines.^[17] For whole-breast and chest wall CTVs, no Planning Target Volume (PTV) margin was added, with the dose prescribed directly to CTV (CTV=PTV) after cropping it 3 mm from the skin. For nodal CTVs, a 5-mm isotropic PTV margin was added, which was then cropped 3 mm from the skin. Both lungs were contoured using an automated segmentation tool, while the remaining normal tissues were contoured manually in both scans using the RTOG normal tissue contouring guidelines.^[17]

2.3. Treatment Planning and Treatment Delivery

Treatment planning was performed in Eclipse v16 (Varian Medical Systems). The prescribed dose was either 40 Gy in 15 fractions or 50 Gy in 25 fractions (in cases with implant-based reconstruction or internal mammary chain irradiation), with dose prescribed to

whole-breast or chest wall with/without regional lymph nodes. For patients undergoing breast conservation surgery, sequential tumor bed boost was delivered with dose prescription of 12 Gy in four fractions. Treatment plans were generated using 6 MV photon beams with either static intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) technique. All patients were treated using the DIBH plan, but treatment was replanned using the FB scan with the same dose prescription and technique. Dose coverage was maintained as per ICRU (International Commission on Radiation Units and Measurements) recommendations.^[18] Normal tissue doses were maintained within their documented tolerance limits as per QUANTEC (Quantitative Analysis of Normal Tissue Effects in the Clinic) guidelines.^[19]

The normal tissue constraints followed during plan approval included the following:

- Hypofractionated dose (40 Gy/15 fractions)
 - Heart – Dmean $\leq$ 6 Gy; V4 $\leq$ 40%; V20 $\leq$ 10%
 - Ipsilateral lung – Dmean $\leq$ 12 Gy; V4 $\leq$ 60%; V16 $\leq$ 30%
 - Contralateral lung – Dmean $\leq$ 3 Gy; V4 $\leq$ 10%
 - Contralateral breast – Dmean $\leq$ 3 Gy; V10 $\leq$ 5%

Conventional fractionated dose (50 Gy/25 fractions)

- Heart – Dmean $\leq$ 8 Gy; V5 $\leq$ 40%; V25 $\leq$ 10 Gy
- Ipsilateral lung – Dmean $\leq$ 16 Gy; V5 $\leq$ 60%; V20 $\leq$ 30%
- Contralateral lung – Dmean $\leq$ 4 Gy; V5 $\leq$ 10%
- Contralateral breast – Dmean $\leq$ 4 Gy; V10 $\leq$ 10%

The treatment was delivered using a Varian TrueBeam Linear Accelerator. Patients undergoing post-mastectomy chest wall irradiation were treated with a 5-mm-thick bolus over the chest wall on alternate days. Before treatment delivery, patients were repositioned according to the fiducial reference points from CT simulation, and image verification with kV-CBCT (kilovoltage cone-beam computed tomography) was performed for the first three consecutive days, followed by weekly verification.

2.4. Dosimetric Analysis

The dosimetric objectives of the study included PTV coverage and dose metrics for the liver, ipsilateral and contralateral lungs, heart, and contralateral breast. These metrics were obtained for both FB and DIBH plans and compared. Dosimetric endpoints for the heart included mean dose, maximum dose, and the percentage of volume receiving 2, 5, 10, 20, and 25 Gy, as well as the total volume of the heart included in the portal. For the ipsilateral lung, data were collected

regarding the maximum point dose, mean dose, and volume receiving 5, 16, and 20 Gy. For the contralateral lung, mean and maximum point doses were recorded. Dosimetric data collected for the liver included the volume of liver, mean and maximum point doses, and the volume of liver covered by the 30 Gy, 10%, 50%, and 90% isodose curves. Mean dose and volume receiving 5 Gy for the contralateral breast were also documented and compared between the two plans.^[20]

2.5. Statistical Analysis

Statistical calculations included relative differences and absolute differences between DIBH and FB plans for all dosimetric endpoints, which were summarized as median and range values. Relative differences were calculated using the formula $100 \times [(DIBH - FB)/FB]$, and absolute differences were calculated using the formula $(DIBH - FB)$.^[20] Dosimetric outcomes obtained for FB and DIBH scans were compared using the Wilcoxon signed-rank test to determine the presence of any statistically significant differences. All statistical calculations were carried out using Microsoft Excel version 2021.

3. Results

3.1. Patient and Treatment Characteristics

The patient and tumor characteristics included in the study are summarized in Table 1. The median age of the patients analyzed in the study was 45.5 years (standard deviation [SD] = 10.68), with the youngest patient being 24 years old and the oldest being 66 years old.

Sixty-five percent (65%) of the included patients had stage III disease, while the remaining presented with stage II disease. Most of the patients (90%) had undergone modified radical mastectomy (MRM) followed by post-mastectomy chest wall irradiation. Implant-based reconstruction was performed in nine patients during MRM, while the remaining MRM patients underwent simple wound closure with or without flap-based reconstruction.

Nodal irradiation to the axillary nodes, internal mammary nodes, or both was prescribed in 16 patients (80%), while four patients were irradiated using the DIBH technique solely due to the presence of implant-based reconstruction.

The total radiation dose prescribed was 50 Gy in 25 fractions for 60% of patients, while a hypofractionated dose of 40 Gy in 15 fractions was prescribed for 40%

Table 1: Distribution of Patient and Treatment Characteristics.

CHARACTERISTICS		NUMBER	PERCENTAGE (%)
Clinical T stage	T1	0	0
	T2	9	45
	T3	6	30
	T4	5	25
Clinical N stage	N0	4	20
	N1	5	25
	N2	7	35
	N3	4	20
Composite stage	IIA	3	15
	IIB	4	20
	IIIA	5	25
	IIIB	4	20
Type of surgery	IIIC	4	20
	MRM	18	90
	BCS + ALND	2	10
	Yes	9	45
Presence of implant	No	11	55
	Axillary nodes	13	65
Nodal irradiation	IMN nodes	5	25
	No nodal RT	1	5
Radiation dose	50 Gy in 25#	12	60
	40 Gy in 15#	8	40
Tumor bed boost	Yes	2	10
	No	18	90
Radiation technique	VMAT	10	50
	IMRT	10	50

IMRT: intensity-modulated radiotherapy, MRM: modified radical mastectomy, VMAT: volumetric modulated arc therapy, BCS: Breast conservation surgery, IMN: Internal mammary nodes, RT: radiotherapy, ALND: Axillary lymph node dissection, #: radiation fractions.

of patients. Radiation was delivered using the VMAT technique in 10 patients and the IMRT technique in the remaining 10 patients.

In all the tables, the dosimetric endpoints are presented as median and range for DIBH plan, FB plan, and for absolute and relative differences between the two treatment methods. The dosimetric variables were compared between DIBH and FB plans using Wilcoxon signed-rank test to calculate the *p*-value.

3.2. PTV Coverage

Dose–volume data for target volume coverage between FB and DIBH plans are summarized in Table 2. There was no difference in plan quality between the FB and

DIBH plans in terms of target volume coverage. The target volume criteria were met for both FB and DIBH plans.

A less than 1% absolute difference in mean PTV coverage was observed in terms of V95% and V90% between the two breathing patterns of irradiation. This indicated that, regardless of the treatment technique, target volume coverage did not need to be compromised to meet normal tissue constraints.

3.3. Cardiac Dose

Dosimetric parameters of the heart in DIBH and FB plans are presented in Table 3. Although the cardiac volume was larger in the FB breathing pattern, with an absolute difference of 42 ml, the difference from the DIBH plan did not reach statistical significance.

Both the mean dose and the percentage of cardiac volume covered by the 2-Gy isodose were lower with DIBH (mean absolute difference of 85.8 cGy and 12.8%, respectively) compared to FB, and this difference was statistically significant (*p*-value: 0.0002 and 0.02, respectively).

In addition, the percentage of cardiac volume covered by the 5-Gy and 10-Gy isodoses was significantly reduced with the DIBH technique compared to FB.

The study also found a significantly reduced cardiac Dmax in favor of the DIBH plan, with a mean absolute difference of 708.6 cGy (*p*-value: 0.0003).

3.4. Ipsilateral Lung Dose

All dose–volume parameters of the ipsilateral lung showed significant normal tissue dose sparing with the DIBH technique of irradiation, as shown in Table 4. The DIBH technique nearly doubled the lung volume, as evident in the planning scan, compared to the FB technique (1710 vs. 1024.7 ml, *p*-value: <0.0001).

The dose–volume parameters of the ipsilateral lung also favored the DIBH technique. The mean dose to the ipsilateral lung decreased from 14 Gy in the FB plan to 12 Gy with DIBH (*p*-value: 0.01). Other dose–volume metrics, including V5 Gy, V16 Gy, and V20 Gy, all showed a significantly lower percentage of lung volume irradiated with the DIBH technique compared to FB.

The maximum dose to the ipsilateral lung in the DIBH plan differed by an average absolute value of 534.1 cGy from the FB technique, which proved statistically significant in favor of the DIBH plan.

Table 2: Summary of Target Volume Coverage in DIBH- or FB-Based Treatment Planning.

TARGET VOLUME COVERAGE		DIBH	FB	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	p-VALUE
V95% (%)	Median	97	97	0	0	0.662492922
	Range	88	88	-0.6	-0.621118012	
		99	99	0.4	0.421052632	
V90% (%)	Median	98.5	99.1	-0.8	-1.204819277	0.139625473
	Range	95	90.4	-1.2	-1.210898083	
		99.9	99.9	4.6	5.088495575	

DIBH: deep inspiration breath hold, FB: free breathing

Table 3: Summary of Dosimetric Findings of OAR (Organ at Risk) Heart Between DIBH and FB Techniques of Irradiation.

HEART VARIABLES		DIBH	FB	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	p-VALUE
Volume (ml)	Median	520.5	537.95	18.15	3.18936175	0.622128586
	Range	403.1	381.1	-1076.5	-72.75615031	
		681.7	1479.6	102.6	25.07331378	
Mean dose (cGy)	Median	359.5	472.15	-78.1	-17.48974806	0.000218629
	Range	79.7	97.4	-235	-43.63163758	
		755	805	22.4	17.63779528	
V2 Gy (%)	Median	65.25	80.45	-10.3	-12.85026338	0.024153571
	Range	17.37	33.1	-34.3	-66.00782779	
		95.7	100	4.1	4.475982533	
V5 Gy (%)	Median	18.7	35.425	-13.9	-42.24616432	0.001596809
	Range	1.2	6.78	-35.5	-86.26609442	
		63.5	67.7	-2.3	-5.793450882	
V10 Gy (%)	Median	0.795	5.3	-3.85	-82.81993532	0.0001
	Range	0	0.26	-11.83	-100	
		23.5	27.4	11.62	2472.340426	
V20 Gy (%)	Median	0	0	0	0	0.193353996
	Range	0	0	-8.83	-100	
		2.73	9.66	0.11	66.66666667	
V25 Gy (%)	Median	0	0	0	0	0.088106998
	Range	0	0	-1.6	-100	
		0.7	1.6	0.001	14.28571429	
Max dose (cGy)	Median	1987	2930.3	-796.1	-32.19124322	0.000397958 0.05
	Range	663.7	1503.5	-1309	-55.85633522	
		2657	3706	-607.7	-28.30545062	

DIBH: deep inspiration breath hold, FB: free breathing

3.5. Contralateral Lung and Contralateral Breast Dose Parameters

Dosimetric outcomes for the contralateral lung and breast are summarized in Tables 5 and 6, respectively. The DIBH technique resulted in a statistically significant

reduction in contralateral lung mean doses compared to the FB technique, implying a meaningful dose-sparing effect of breath hold in radiotherapy (207.9 vs. 319.3, p-value: 0.03). The maximum dose to the contralateral lung was also reduced with the DIBH technique, but the difference did not reach statistical significance.

Table 4: Summary of Dosimetric Findings of OAR Ipsilateral Lung between DIBH and FB Techniques of Irradiation.

IPSILATERAL LUNG VARIABLES		DIBH	FB	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	p-VALUE
Volume (ml)	Median	1807.75	1005.95	741.8	72.93396796	<0.0001
	Range	951.9	605.4	22.3	1.868610692	
		2234.1	1344	1216	119.4381691	
Mean dose (cGy)	Median	1191.4	1415.45	-141.85	-8.529702109	0.010001072
	Range	774.1	926.3	-572.9	-42.5315516	
		1587	1725.8	50	3.253090436	
V5 Gy (%)	Median	57.35	72.85	-11.89	-17.91653481	<0.0001
	Range	32.5	49.5	-43.4	-49.09502262	
		82.4	88.4	4.4	5.641025641	
V16 Gy (%)	Median	21.265	32.7	-9.15	-31.35642415	0.000397958
	Range	10.3	13.6	-28.2	-68.20987654	
		36.7	44.7	4.2	30.88235294	
V20 Gy (%)	Median	19.315	25.05	-6.11	-26.41222344	0.00111909
	Range	10.1	6.3	-12.67	-49.24623116	
		29.3	33.1	6.9	109.5238095	
Max dose (cGy)	Median	4012.65	4569.35	-429.55	-10.24967229	0.002666834
	Range	2924.6	3980.4	-1401.8	-31.27482082	
		5828.4	6184.8	4	0.099226037	

DIBH: deep inspiration breath hold, FB: free breathing

Table 5: Summary of Dosimetric Findings of OAR Contralateral Lung between DIBH And FB Techniques of Irradiation.

CONTRALATERAL LUNG VARIABLES		DIBH	FB	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	p-VALUE
Max dose (cGy)	Median	1578.45	1773	-202.9	-12.39397995	0.061554407
	Range	470.6	460.3	-875.9	-34.09763314	
		2444.2	2741.8	146.3	11.40655106	
Mean dose (cGy)	Median	229.8	321.85	-63.75	-20.52377012	0.032927742
	Range	38	40.4	-882.7	-73.3505069	
		342	1203.4	56.4	20.35366294	

DIBH: deep inspiration breath hold, FB: free breathing

The mean dose to the contralateral breast and V5 Gy were reduced with the DIBH technique, with an average absolute difference of 12.6 cGy and 1.01%, respectively. However, the difference did not reach statistical significance (Dmean *p*-value: 0.28 and V5 Gy *p*-value: 0.55). These dose-volume metrics also favored the DIBH technique in reducing contralateral breast dose, although no statistically significant difference was found compared to the FB technique.

3.6. Liver Dose

Use of the DIBH technique for the irradiation of the right whole-breast or chest wall resulted in a significant reduction in all hepatic dose-volume metrics, as shown in Table 7. There was a significant increase in hepatic volume with DIBH compared to FB (mean volume: 1503.8 vs. 1374.39 ml, *p*-value: 0.04).

Table 6: Summary of Dosimetric Findings of OAR Contralateral Breast Between DIBH and FB Techniques of Irradiation.

CONTRALATERAL BREAST VARIABLES		DIBH	FB	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	p-VALUE
Mean dose (cGy)	Median	306.35	297.7	-1.2	-0.283243356	0.284999874
	Range	31.9	26.8	-148.6	-49.30325149	
		448.2	506.6	89.4	101.6233766	
V5 Gy (%)	Median	15.3	14.95	-0.105	-2.77459486	0.553793068
	Range	0.25	0.01	-17.4	-68.99696049	
		32	36.5	15.9	2400	

DIBH: deep inspiration breath hold, FB: free breathing

Table 7: Summary of Dosimetric Findings of OAR Liver Between DIBH and FB Techniques of Irradiation.

LIVER VARIABLES		DIBH	FB	ABSOLUTE DIFFERENCE	RELATIVE DIFFERENCE	p-VALUE
Volume (ml)	Median	1462.2	1318.45	153.8	9.552907368	0.046760925
	Range	1066.9	1000.2	-129.3	-5.304615385	
		2308.2	2437.5	402.8	31.8948452	
Mean dose (cGy)	Median	271.65	783.6	-453.5	-62.26498393	<0.0001
	Range	54.8	201.6	-875.3	-91.38674884	
		582.7	1344.7	-146.8	-38.69565217	
Max dose (cGy)	Median	3952.35	4965.2	-917.45	-19.42725463	0.001022183
	Range	1081.6	2984.5	-3590.7	-72.77167525	
		5765.1	6217.6	-28.3	-0.713835288	
V30 Gy Isodose (%)	Median	0.885	3.405	-2.48	-68.82016467	0.00206989
	Range	0	0	-8	-100	
		4.72	11.4	0.02	200	
V30 Gy Isodose (ml)	Median	16.675	47.515	-31.6	-66.86010887	0.002253843
	Range	0	0	-109.38	-100	
		70.3	179.68	0.3	150	
V10% isodose (%)	Median	15.55	49.35	-31.2	-65.46855922	<0.0001
	Range	0.01	4.02	-727	-99.75124378	
		35.4	755.2	-4.01	-31.16062521	
V10% isodose (ml)	Median	170.45	578	-357.3	-64.1423338	<0.0001
	Range	0.25	71.3	-1180.5	-99.64936886	
		575.1	1280.16	230.1	305.1724138	
V50% isodose (ml)	Median	31.7	114.945	-63.115	-72.51538516	<0.0001
	Range	0	9.7	-242.4	-100	
		120	306.3	8.08	83.29896907	
V90% isodose (%)	Median	0.045	0.625	-0.285	-89.94968553	0.000740489
	Range	0	0	-4.02	-100	
		0.97	4.5	0	0	
V90% isodose (ml)	Median	0.6	7.955	-3.9955	-89.38940265	0.000775787
	Range	0	0	-42.27	-100	
		11.3	48.5	0	0	

DIBH: deep inspiration breath hold, FB: free breathing

The mean hepatic dose was significantly reduced with the use of DIBH (3.8 vs. 7.9 Gy, p -value: 0.0001), as was Dmax, when compared to the FB technique (36.7 vs. 46.3 Gy, p -value: 0.001). The volume of liver receiving 30 Gy, as well as the volume irradiated by the 50% and 90% isodoses, also showed a significant reduction with DIBH, with a relative difference of more than 50% in all dose–volume coverages compared to the FB technique.

Besides the high-dose volume, DIBH also resulted in a significantly lower volume of the liver irradiated by the 10% isodose, with a relative difference of 68% (16.6% vs. 79.8%, p -value: 0.0001) from the low-dose coverage of the FB plan.

Thus, this study demonstrated that the use of DIBH for right-sided breast or chest wall irradiation led to a significant reduction in both high- and low-dose volumes compared to the FB technique of irradiation.

4. Discussion

This study presented the dosimetric outcomes of DIBH in adjuvant radiotherapy for right-sided breast carcinoma patients by comparing the dose–volume metrics of the technique with that of the FB technique. The observations showed significant improvements in all dosimetric endpoints, suggesting the dose-sparing efficacy of DIBH for the lungs, heart, and liver during irradiation of right-sided breast carcinoma.

However, this study included patients undergoing both right-sided whole-breast irradiation and right-sided chest wall irradiation. Mader et al.^[20] and Pandeli et al.^[21] included only patients undergoing localized right-sided breast radiotherapy post-lumpectomy. In contrast, Haji et al.^[22] included patients undergoing post-mastectomy chest wall radiotherapy for right-sided breast carcinoma in their analysis.

In this study, radiotherapy was delivered using VMAT for 10 patients, while the remaining 10 patients received treatment via static field IMRT. Borgonovo et al.^[15] also used both VMAT and IMRT plans, with five patients in each group, while Mader et al.^[20] and Dumane et al.^[8] used only VMAT plans with DIBH for radiotherapy. Three-dimensional conformal radiotherapy with tangential beams was the radiotherapy planning technique used in the studies conducted by Pandeli et al.^[21]

In the present study, both the mean dose and the percentage volume covered by the 2-Gy isodose were lower with DIBH (mean absolute difference of 85.8 cGy and 12.8%, respectively) compared to FB, reaching statistical significance (p -value: 0.0002 and 0.02, respectively). In addition, the percentage volume

of the heart covered by 5 Gy and 10 Gy isodoses was significantly reduced with the DIBH technique compared to FB. Furthermore, there was a significantly reduced cardiac Dmax in favor of the DIBH plan, with a mean absolute difference of 708.6 cGy (p -value: 0.0003).

Borgonovo et al.^[15] reported a 2.2 Gy reduction in heart Dmean with the DIBH technique compared to FB, along with a 25.2% reduction in V5 Gy and a significant reduction in heart Dmax, favoring DIBH. Similarly, Mader et al.^[20] observed a statistically significant reduction in cardiac Dmax with DIBH compared to the FB plan.

All dose–volume parameters of the ipsilateral lung demonstrated significant normal tissue dose sparing with the DIBH technique. While DIBH nearly doubled the lung volume compared to FB, the dose–volume parameters of the ipsilateral lung still favored DIBH. The mean dose to the ipsilateral lung decreased from 14 Gy in the FB plan to 12 Gy with DIBH (p -value: 0.01). Other dose–volume metrics such as V5 Gy, V16 Gy, and V20 Gy showed significantly lower percentages of irradiated volume when using the DIBH technique compared to FB. The maximum dose to the ipsilateral lung in the DIBH plan differed by an average absolute value of 534.1 cGy from the FB technique, proving statistical significance in favor of the DIBH plan.

Mader et al.^[20] documented a significant reduction in ipsilateral lung mean dose and V20 Gy with the DIBH technique, despite the significantly increased lung volume when irradiated using DIBH. Borgonovo et al.^[15] also reported a reduction in ipsilateral lung mean dose and V20 Gy with DIBH, along with an increase in lung volume compared to FB, though the difference was not statistically significant. In addition, Haji et al.^[22] reported a significant reduction in ipsilateral lung mean dose, V20 Gy, and V30 Gy, along with a significant increase in lung volume when using DIBH for right chest wall radiotherapy. Pandeli et al.^[21] also observed significant ipsilateral lung dose sparing with DIBH, as evidenced by a significantly reduced ipsilateral lung mean dose, V5 Gy, and V20 Gy compared to FB in patients undergoing right-sided breast radiotherapy with or without regional lymph node irradiation.

Using the DIBH technique for irradiation of the right whole breast or chest wall resulted in a significant reduction in all hepatic dose–volume metrics. There was a significant increase in hepatic volume with DIBH compared to FB (mean volume: 1503.8 vs. 1374.39 ml, p -value: 0.04). The mean hepatic dose was significantly reduced with DIBH (3.8 vs. 7.9 Gy, p -value: 0.0001), as was Dmax (36.7 vs. 46.3 Gy, p -value: 0.001). The volume of the liver receiving 30 Gy and the volume irradiated by the 50% and 90% isodoses also showed significant reductions with DIBH, with a relative difference of more

than 50% in all dose–volume coverages compared to FB.

In addition, DIBH significantly reduced the volume of the liver irradiated by the 10% isodose, with a relative difference of 68% (16.6% vs. 79.8%, p -value: 0.0001) compared to the low-dose coverage of the FB plan. Thus, this study demonstrated that the use of DIBH for right-sided breast or chest wall irradiation led to a significant reduction in both high- and low-dose volumes compared to the FB technique.

In the study conducted by Haji et al.,^[22] the DIBH technique for right chest wall irradiation resulted in a significant reduction in liver mean dose, liver V20 Gy, and liver V10 Gy compared to the FB technique. In another study by Pandeli et al.,^[21] evaluating dosimetric outcomes of DIBH in adjuvant irradiation of the intact right breast, statistically significant reductions were observed in liver V20 Gy and maximum liver dose compared to FB, with the greatest reduction seen in patients receiving whole-breast plus regional lymph node irradiation. Mader et al.^[20] found that DIBH significantly reduced hepatic mean and maximum doses as well as the low-dose volume of the liver covered by the 10% isodose level, further establishing the beneficial organ-sparing effects of DIBH compared to FB.

The DIBH technique resulted in a statistically significant reduction in contralateral lung mean doses compared to FB (p -value: 0.03), implying a meaningful dose-sparing effect of breath-hold radiotherapy. The contralateral lung maximum dose was also reduced by DIBH, though the difference did not reach statistical significance (p -value: 0.06). Contralateral breast mean dose and V5 Gy were lower with DIBH, with an average absolute difference of 12.6 cGy and 1.01%, respectively.

5. Conclusion

This study thus demonstrated significant normal tissue sparing with the addition of DIBH in adjuvant radiotherapy for right-sided breast carcinoma, as evident by the reduction in high- and low-dose

volumes for the ipsilateral lung, heart, and liver. However, this study included a small cohort of patients, making it difficult to predict whether these dosimetric findings would ultimately translate into significant clinical benefits. Nevertheless, in terms of dosimetric parameters, the DIBH technique in right-sided breast cancer radiotherapy demonstrated a clear advantage. Therefore, DIBH should be incorporated into right breast carcinoma radiotherapy where available to help reduce potential late normal tissue toxicities in breast carcinoma patients.

Funding

No funding was obtained for the study.

Conflict of Interest

There was no conflict of interest encountered in the conduct of this study.

Data Sharing Perspective

Individual de-identified patient treatment and follow-up data will be made available on reasonable request from Dr. Raka Banerjee (email id: introraka218@gmail.com), starting from the date of publication until 10 years after publication. Beyond this timeframe, requests for data sharing will be considered from case to case basis.

Author Contributions

Study conception and design: RB, KM; Data collection: RB, KM, PR; Data analysis and interpretation: RB, KM; Drafting the article: RB, KM; Critical revision of the article: KM, AR, SK, BD, CM, DKR; Final approval of the version to be published: all authors.

References

- [1] Kwong DL, McGale P, Taylor C, Correa C, Cutter D, Duane F, Ewertz M, Gray R, Mannu G, Peto R, Whelan T. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *The Lancet*. 2014.
- [2] Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, Jeong JH, Wolmark N. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *New England Journal of Medicine*. 2002 Oct 17;347(16):1233-41.

- [3] Speers C, Pierce LJ. Postoperative Radiotherapy After Breast-Conserving Surgery for Early-Stage Breast Cancer: A Review. *JAMA Oncol.* 2016 Aug 1;2(8):1075-82. doi: 10.1001/jamaoncol.2015.5805. PMID: 27243924.
- [4] Senkus-Konefka E, Jassem J. Cardiovascular effects of breast cancer radiotherapy. *Cancer treatment reviews.* 2007 Oct 1;33(6):578-93.
- [5] Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Brønnum D, Correa C, Cutter D, Gagliardi G, Gigante B, Jensen MB. Risk of ischemic heart disease in women after radiotherapy for breast cancer. *New England Journal of Medicine.* 2013 Mar 14;368(11):987-98.
- [6] Bartlett FR, Colgan RM, Carr K, Donovan EM, McNair HA, Locke I, Evans PM, Haviland JS, Yarnold JR, Kirby AM. The UK HeartSpare Study: randomised evaluation of voluntary deep-inspiratory breath-hold in women undergoing breast radiotherapy. *Radiotherapy and Oncology.* 2013 Aug 1;108(2):242-7.
- [7] Swanson T, Grills IS, Ye H, Entwistle A, Teahan M, Letts N, Yan D, Duquette J, Vicini FA. Six-year experience routinely using moderate deep inspiration breath-hold for the reduction of cardiac dose in left-sided breast irradiation for patients with early-stage or locally advanced breast cancer. *American journal of clinical oncology.* 2013 Feb 1;36(1):24-30.
- [8] Dumane VA, Saksornchai K, Zhou Y, Hong L, Powell S, Ho AY. Reduction in low-dose to normal tissue with the addition of deep inspiration breath hold (DIBH) to volumetric modulated arc therapy (VMAT) in breast cancer patients with implant reconstruction receiving regional nodal irradiation. *Radiation oncology.* 2018 Dec;13:1-7.
- [9] Simonetto C, Eidemüller M, Gaasch A, Pazos M, Schönecker S, Reitz D, Käab S, Braun M, Harbeck N, Niyazi M, Belka C. Does deep inspiration breath-hold prolong life? Individual risk estimates of ischaemic heart disease after breast cancer radiotherapy. *Radiotherapy and Oncology.* 2019 Feb 1;131:202-7.
- [10] Marks LB, Bentzen SM, Deasy JO, Bradley JD, Vogelius IS, El Naqa I, Hubbs JL, Lebesque JV, Timmerman RD, Martel MK, Jackson A. Radiation dose-volume effects in the lung. *International Journal of Radiation Oncology* Biology* Physics.* 2010 Mar 1;76(3):S70-6.
- [11] Choi J, Kim YB, Shin KH, Ahn SJ, Lee HS, Park W, Kim SS, Kim JH, Lee KC, Kim DW, Suh HS. Radiation pneumonitis in association with internal mammary node irradiation in breast cancer patients: an ancillary result from the KROG 08-06 study. *Journal of Breast Cancer.* 2016 Sep 1;19(3):275-82.
- [12] Osman SO, Hol S, Poortmans PM, Essers M. Volumetric modulated arc therapy and breath-hold in image-guided locoregional left-sided breast irradiation. *Radiotherapy and Oncology.* 2014 Jul 1;112(1):17-22.
- [13] Essers M, Poortmans PM, Verschueren K, Hol S, Cobben DC. Should breathing adapted radiotherapy also be applied for right-sided breast irradiation?. *Acta oncologica.* 2016 Apr 2;55(4):460-5
- [14] Conway JL, Conroy L, Harper L, Scheifele M, Li H, Smith WL, Graham T, Phan T, Olivetto IA. Deep inspiration breath-hold produces a clinically meaningful reduction in ipsilateral lung dose during locoregional radiation therapy for some women with right-sided breast cancer. *Practical radiation oncology.* 2017 May 1;7(3):147-53.
- [15] Borgonovo G, Paulicelli E, Daniele D, Presilla S, Richetti A, Valli M. Deep inspiration breath hold in post-operative radiotherapy for right breast cancer: a retrospective analysis. *reports of practical Oncology and radiotherapy.* 2022;27(4):717-23.
- [16] Rice L, Harris S, Green MM, Price PM. Deep inspiration breath-hold (DIBH) technique applied in right breast radiotherapy to minimize liver radiation. *BJR| case reports.* 2015 May 8;1(2):20150038.
- [17] <http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx>.
- [18] International Commission on Radiation Units and Measurements. Prescribing, Recording, and Reporting Photon Beam Therapy. International Commission on Radiation Units and Measurements; 1999.
- [19] Marks L.B., Yorke E.D., Jackson A., et al. Use of normal tissue complication probability models in the clinic. *Int J Radiat Oncol Biol Phys.* 2010;76(3 SUPPL.) doi: 10.1016/j.ijrobp.2009.07.1754.
- [20] Mader T, Pace R, da Silva RT, Adam LE, Näf G, Winter CC, Aspradakis MM, Radovic M, Spyridonidis A, Hayoz S, Baumert BG. Deep inspirational breast hold (DIBH) for right breast irradiation: Improved sparing of liver and lung tissue. *Clinical and Translational Radiation Oncology.* 2024 Mar 1;45:100731
- [21] Pandeli C, Smyth LM, David S, See AW. Dose reduction to organs at risk with deep-inspiration breath-hold during right breast radiotherapy: a treatment planning study. *Radiation Oncology.* 2019 Dec 10;14(1):223.
- [22] Haji G, Nabizade U, Kazimov K, Guliyeva N, Isayev I. Liver dose reduction by deep inspiration breath hold technique in right-sided breast irradiation. *Radiation Oncology Journal.* 2019 Dec;37(4):254.