PROSPECTIVE OBSERVATIONAL STUDY OF DEEP INSPIRATION BREATH HOLD (DIBH) IN RADIOTHERAPY FOR LEFT-SIDED BREAST CANCER

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Abstract

Objective: The objective of this study was to prospectively collect and report treatment planning data in terms of organs at risk (OARs) sparing effect between deep inspiration breath hold (DIBH) and free breathing (FB) computed tomography (CT) scans. This study also aims to identify potential planning parameters that could help in selecting patients most likely to benefit from DIBH.

Methods: Thirty-eight patients with left-sided breast malignancy indicated for adjuvant radiotherapy underwent DIBH and FB CT simulation. All patients were planned with a three-dimensional conformal radiation therapy (3D-CRT) for both scans. Comparisons of dosimetric variables include heart D_{mean}, left anterior descending coronary artery (LAD) D_{mean}/D_{max}, left lung V_{30Gy}, V_{20Gy}, V_{10Gy}, V_{5Gy}, FB axial cardiac contact distance (FB-CCDax) and parasagittal CCD (FB-CCDps).

Results: DIBH resulted in a statistically significant reduction of heart D_{mean}, LAD D_{mean} and $D_{max.}$ When DIBH was compared with FB, heart D_{mean} was 1.62 Gy versus 2.65 Gy; for LAD D_{mean}, 6.81 Gy versus 11.57 Gy; and for LAD D_{max}, 22.66 Gy versus 31.93 Gy. Left lung dosimetry results consistently showed all the volume parameters of V_{5Gy} to V_{30Gy} for FB were significantly higher than that of DIBH. There was a significant positive correlation between FB-CCDax/FB-CCDps and mean heart absolute dose reduction. A meaningful positive correlation was observed for FB-CCDps beyond the cutoff length of 2cm.

Conclusion: Our study has confirmed the benefit of DIBH in reducing mean heart and lung dose in left-sided breast/chest wall radiotherapy. FB-CCDps is a potentially reliable parameter to guide us in selecting patients whom would benefit most for DIBH.

Keywords: DIBH, Left Breast Radiotherapy, FB-CCD, Mean Heart Dose

Introduction

Adjuvant whole breast or chest wall irradiation is an integral part of breast cancer management. Patients with left-sided breast cancers receiving postoperative radiotherapy are potentially at risk of long-term cardiac morbidity and mortality many years after treatment due to the inclusion of the heart within the radiotherapy field (1, 2). Recent literature review report an estimated 40% increased risk of cardiac mortality, with a relative risk of cardiac mortality of 1.22 (95% confidence intervals (CI): 1.08 - 1.37) in left-sided breast radiotherapy patients as compared to those receiving right-sided treatment (3). The rates of major coronary events increase linearly with increase in the mean heart dose (MHD) at the rate of 7.4% per Gray (Gy) of radiation with no apparent safe threshold (4).

Cardiac sparing techniques are now mandated as standard of care in the UK guidelines for postoperative radiotherapy for breast cancer by the Faculty of Clinical Oncology, Royal College of Radiologists and are strongly recommended in the American Society for Radiation Oncology (ASTRO) evidence-based guideline for radiation therapy for whole breast (5, 6). The UK HeartSpare Study demonstrated that deep inspiration breath hold (DIBH) as a motion management strategy is accepted as an effective measure for reducing cardiac dose and sparing organs at risk (OAR) (7). This technique is utilised in the radiotherapy treatment of various tumours, including thoracic and mediastinal tumours, as well as left-sided breast cancers. DIBH technique has now been widely adopted by many international cancer centres for left breast radiotherapy. The clinical and dosimetric advantages, as well as the safety and efficacy of the DIBH technique have been documented in numerous publications (8 - 10).

There are various commercial products that are designed for use for DIBH technique, including the Active Breathing Coordinator (ABC) system, specific for use with Elekta linear accelerators. This system uses a spirometer to track a patient's actual lung volume. Treatment will only be delivered when the patient has reached the minimum set threshold. The distance between chest wall and heart increases during inspiration, hence the heart moves away from the treatment area, which will decrease, or completely omit the cardiac volume within radiation field (Figure 1) (8 - 10).

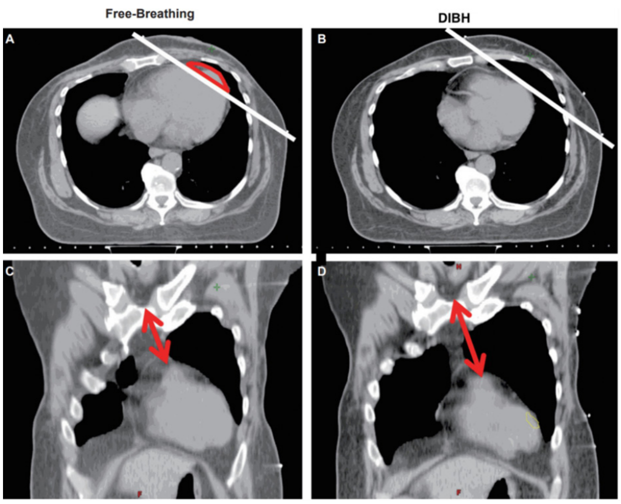

Figure 1: Impact of deep inspiration on cardiac dose sparing during postoperative radiotherapy using 3D-CRT for left-sided breast cancer; CT simulation axial and coronal images of (A) and (C): FB scan; (B) and (D): DIBH scan

We have implemented DIBH technique in radiotherapy treatment of left-sided breast cancer in University Malaya Medical Centre (UMMC). However, incorporating the use of DIBH into routine treatment requires significantly more time and resource commitments (11). Whilst there is good data to support the benefit of DIBH, not all patients are going to derive a benefit from the use of DIBH. There are currently no guidelines on how to select for patients that are most likely to benefit from DIBH. Few studies have demonstrated patient-specific factors such as anatomical variations, that may factor into patient selection for DIBH (12, 13). We aim to prospectively collect data on left-sided breast cancer patients being treated with the DIBH technique, including demographic and dosimetric data, to compare with published international data. This study also aims to identify parameters which could help in selecting patients most likely to benefit from DIBH.

Materials and Methods

Patient selection

This is a single institution prospective observational study carried out in UMMC from June 2019 to March 2020. Ethical approval was granted by the institutional review board. Eligible patients were women or men aged at least 18 years old with left-sided invasive breast carcinoma or ductal carcinoma in situ (DCIS) who have undergone breast conserving surgery or mastectomy and are indicated for adjuvant radiotherapy to breast or chest wall with or without regional nodal irradiation. Patients who failed to hold their breath for at least 20 seconds will not proceed with DIBH.

CT simulation

Patients identified for this study were scheduled to receive a coaching session lasting 1.5 to 2 hours at least one day prior to the actual CT simulation session. They were instructed on how to perform DIBH in the actual set-up position using the ABC machine. Patients were told to hold their breath for at least 20 seconds, once their individually determined lung volume threshold was achieved. They must be able to reliably reproduce two consecutive breath holds to be considered as suitable candidates for this technique. Patients who failed the coaching session will not proceed with DIBH. During CT simulation, patients were positioned supine with arms up on a breast-board. Radio-opaque wires were placed at the surgical scars and also at the field borders. Two scans were acquired for each patient, a DIBH CT and FB CT, at 5mm slice spacing to include all treatment area on a Big Bore 16 slice CT Simulator (Philips, Amsterdam, Netherlands).

Treatment planning

All patients were planned for a three-dimensional conformal radiation therapy (3D-CRT) technique utilising tangential beams for the breast and chest wall in the Elekta Monaco treatment planning system version 5.51. An anterior supraclavicular fossa (SCF) field was added, with posterior axilla boost field if indicated.

The breast or chest wall clinical target volume (CTV) as well as the regional nodal CTV, planning target volume (PTV) and all organs at risk (OARs) were delineated by the oncology trainee and checked by the treating oncologist, using the Radiation Therapy Oncology Group (RTOG) Breast Cancer Atlas as a reference (14).

All patients were prescribed 40 Gy in 15 fractions with an additional tumour bed boost of 10-16 Gy in 5-8 fractions as indicated by the treating clinician. Breast boost was treated either with electrons or reduced field tangential photons. The breast boost dosimetry was excluded from dosimetric comparisons in this study.

All patients had a plan each generated and optimised for the DIBH and FB CT, both plans were evaluated and approved by the treating oncologist, but only the DIBH plan was used for treatment.

Treatment

All patients were treated in DIBH, with the DIBH approved plan on the Elekta Versa HD linear accelerator (Stockholm, Sweden).

Data analysis

Patient demographics and oncological treatments were recorded. For both the DIBH and FB plans, the doses to the OARs including to heart and lungs were recorded: Mean heart dose (heart D_{mean}), Left Anterior descending artery mean dose (LAD D_{mean}) and maximum dose (LAD D_{max}), Left Lung V_{30Gy}, V_{20Gy}, V_{10Gy} and $V_{5Gy.}$

The cardiac contact distances of the axial (FB-CCDax) and parasagittal (FB-CCDps) planes are anatomic metrics measured on the FB CT scan described by Rochet et al. (2015) (12). These parameters are potentially helpful in selecting patients who would benefit most from DIBH when correlated with heart doses. Both FB-CCDax and FB-CCDps were measured as shown in Figure 2. FB-CCDax was measured as the shortest linear distance from the points of contact of the cardiac silhouette with the chest wall, at the level of the dome of the right diaphragm, in the axial plane of the CT scan. FB-CCDps was measured in a parasagittal plane at the midpoint of the left hemithorax as determined in the transverse and coronal plane. FB-CCDps was defined as the linear distance of direct contact by the heart with the chest wall (12).

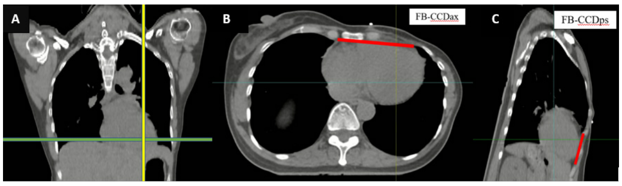

Figure 2: (A) Measurement of axial and parasagittal cardiac contact distance in coronal slice; (B) Measurement of FB-CCDax in axial slice and (C) Measurement of FB-CCDps in parasagittal slice, respectively; red lines)

Outcomes

The primary endpoint was to compare the OARs sparing effects in terms of heart and lung dosimetry parameters between DIBH and FB CT scans.

The key secondary endpoints were to determine correlations between cardiac contact distances (FB-CCDax/ FB-CCDps) and mean heart dose reduction to help identify patient and dosimetric factors that may select for patients most likely to benefit from DIBH.

Statistical analysis

All the relevant data was collected and tabulated in the data collection sheet in Microsoft Excel format. Patients' information was kept confidential. Paired Student t test, Wilcoxon Signed Rank test, Pearson correlation coefficient test, Spearman's rho correlation test and Linear Regression analysis were used for statistical comparison and analysis. All analyses were performed using SPSS version 25.0. A *p* value<0.05 was considered statistically significant in this study.

Results

From June 2019 to March 2020, we identified 38 eligible patients. The study cohort comprised of 37 female patients and 1 male patient. Patient and tumour characteristics were demonstrated in Table 1. Mean age was 50.9 years (range 33-74 years). Twenty patients (52.6%) had breast conserving surgery whereas 18 patients (47.4%) had mastectomy. Twenty-three patients (60.5%) received SCF irradiation, and one patient also received radiotherapy to the axilla. No patient received internal mammary irradiation.

Table 1: Patient and tumour characteristics (n=38)

Variables	Number (%)
Mean age (range)	50.9 (33-74)
T category	
Tis	1 (2.6%)
T1	15 (39.5%)
T2	16 (42.1%)
T3	4 (10.5%)
T4	2 (5.3%)
Nodal category	
N0	15 (39.5%)
N+	23 (60.5%)
Surgery	
Breast Conserving Surgery	20 (52.6%)
Mastectomy	18 (47.4%)
Radiation treatment fields	
Breast/Chest wall	15 (39.5%)
Breast/Chest wall + SCF	22 (57.9%)
Chest wall + SCF +axilla	1 (2.6%)
Boost	
Yes	10 (26.3%)
No	28 (73.7%)
Systemic treatment	
Neoadjuvant Chemotherapy	
Yes	13 (34.2%)
No	25 (65.8%)
Adjuvant Chemotherapy	
Yes	20 (52.6%)
No	18 (47.4%)
Trastuzumab	
Yes	7 (18.4%)
No	31 (81.6%)

Dosimetry parameters between DIBH and FB CT scans were tabulated in Table 2. When compared with FB, DIBH resulted in a statistically significant reduction of both heart D_{mean} and LAD D_{mean}. FB heart D_{mean} was 2.65 Gy whereas DIBH heart D_{mean} was 1.62 Gy ($p < 0.01$). FB LAD D_{mean} was 11.57 Gy whereas DIBH LAD D_{mean} was 6.81 Gy ($p < 0.01$). FB LAD D_{max} was significantly higher compared to DIBH D_{max}, 31.93 Gy and 22.66 Gy respectively ($p < 0.01$). In-field heart volume was numerically lower in DIBH scan compared to FB scan but statistically not significant ($p = 0.25$), whereas left lung volume was significantly larger in DIBH scan compared to FB scan ($p < 0.01$). Left lung dosimetry results consistently showed all the volume parameters of V_{5Gy} to V_{30Gy} for FB were significantly higher than that of DIBH ($p < 0.01$).

Table 2: Comparisons of Heart D_{mean}, LAD D_{mean}, LAD D_{max}, Left lung V_{5Gy}, V_{10Gy}, V_{20Gy}, V_{30Gy}, left lung volume and in-field heart volume between FB and DIBH scans

Parameters	FB		DIBH		*p* value
	Mean	SD	Mean	SD	
Heart D_{mean} (Gy)	2.65	1.05	1.62	0.67	<0.01*
LAD D_{mean} (Gy)	11.57	6.95	6.81	5.25	<0.01*
LAD D_{max} (Gy)	31.93	11.20	22.66	13.90	<0.01*
Left Lung (%)					
V_{5Gy}	32.95	10.52	27.99	8.07	<0.01
V_{10Gy}	25.52	9.08	20.90	6.79	<0.01
V_{20Gy}	19.71	7.25	15.44	5.59	<0.01
V_{30Gy}	11.64	4.84	9.04	3.49	<0.01
In-Field Heart Volume (cm^3)	547.50	108.60	522.30	131.10	0.25
Left Lung Volume (cm^3)	1039.60	253.30	1611.62	327.40	<0.01

DIBH: deep inspiration breath hold, FB: free breathing, LAD: left anterior descending coronary artery, SD: standard deviation

Paired Student t-test used for statistical mean comparisons

*Wilcoxon signed rank test used for mean comparisons for non-normal distribution

Left lung dosimetry and heart D_{mean} were analysed separately in those with or without nodal irradiation as presented in Table 3 and Table 4. In patients who have received nodal irradiation (n=23), left lung volume parameters of V_{5Gy} to V_{30Gy} for FB were significantly higher than that of DIBH ($p < 0.01$). Although the volume parameters of V_{5Gy} to V_{30Gy} were all numerically lower in DIBH for patients receiving breast or chest wall irradiation only, the only V_{20Gy} ($p = 0.01$) was significant. Heart D_{mean} was significantly lower in DIBH compared to FB with or without regional nodal radiotherapy ($p < 0.01$).

Table 3: Subgroup comparisons of left lung V_{5Gy}, V_{10Gy}, V_{20Gy}, V_{30Gy} and Heart D_{mean} between FB and DIBH scans in patients who received nodal irradiation (n=23)

Parameters	FB		DIBH		*p* value
	Mean	SD	Mean	SD	
Left Lung (%)					
V_{5Gy}	40.05	6.01	33.49	4.70	<0.01
V_{10Gy}	31.32	5.76	25.28	4.61	<0.01
V_{20Gy}	24.01	5.37	18.78	4.32	<0.01
V_{30Gy}	13.33	4.58	10.28	3.53	<0.01
Heart D_{mean} (Gy)	2.74	1.14	1.75	0.65	<0.01*

DIBH: deep inspiration breath hold, FB: free breathing, SD: standard deviation

Paired Student t-test used for statistical mean comparisons

**Wilcoxon signed rank test used for mean comparisons for non-normal distribution*

Table 4: Subgroup comparisons of left lung V_{5Gy}, V_{10Gy}, V_{20Gy}, V_{30Gy} between FB and DIBH scans in patients who did not receive nodal irradiation (n=15)

Parameters	FB		DIBH		*p* value
	Mean	SD	Mean	SD	
Left Lung (%)					
V_{5Gy}	22.06	5.09	19.55	3.33	0.08
V_{10Gy}	16.64	5.13	14.18	2.92	0.11
V_{20Gy}	13.11	4.07	10.33	2.66	0.01
V_{30Gy}	9.06	4.15	7.12	2.47	0.10
Heart D_{mean} (Gy)	2.51	0.92	1.42	0.69	<0.01

DIBH: deep inspiration breath hold, FB: free breathing, SD: standard deviation

Paired Student t-test used for statistical mean comparisons

FB in-field heart volume was associated significantly with absolute reduction of mean heart dose using correlation test (r = 0.36, $p = 0.03$). Mean measured FB-CCDax was 6.21cm whereby mean measured FB-CCDps was 4.44 cm. There was a significant positive correlation between FB-CCDax/FB-CCDps and mean heart dose reduction, (r = 0.38, $p = 0.02$) and (r = 0.43, $p = 0.01$) respectively. The magnitude of mean heart dose reduction is higher with longer FB-CCDax and FB-CCDps, whereas mean LAD dose reduction only showed significant positive correlation with FB-CCDps (r = 0.47, $p = 0.003$), but not with FB-CCDax (r = 0.16, $p = 0.34$) and FB in-field heart volume (r = 0.10, $p = 0.57$).

Linear regression analysis showed weak positive correlation between FB-CCDax and mean heart dose for both FB and DIBH scans as shown in Figure 3(A). Only a small number of changes in mean heart dose could be attributed to changes in FB-CCDax, R^2 was 0.114 for FB scan and 0.020 for DIBH scan respectively. For FB-CCDps as demonstrated in Figure 3(B), a meaningful positive correlation was observed and the difference was more marked beyond the cutoff length of 2cm. A 0.54 Gy increase in FB mean heart dose could be expected for every additional 1cm increase in FB-CCDps. The regression lines of FB and DIBH mean heart dose intersected when FB-CCDps was more than 2cm. After intersection, the separation of the two regression lines continued and appeared to become wider with longer FB-CCDps.

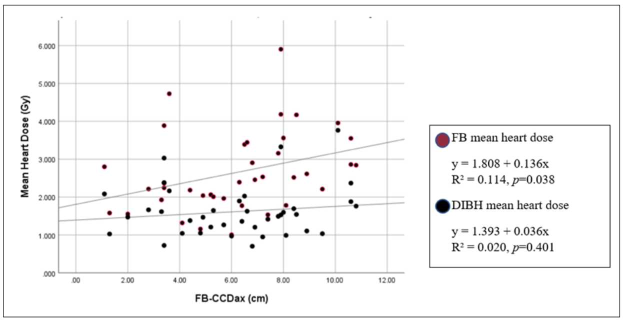

Figure 3(A): Correlation and linear regression analysis between mean heart dose and FB-CCDax for FB (red) and DIBH (black)

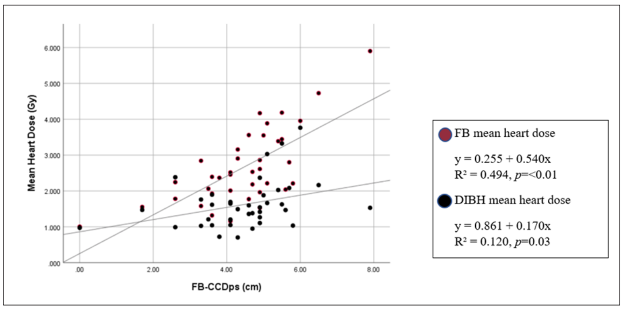

Figure 3(B): Correlation and linear regression analysis between mean heart dose and FB-CCDps for FB (red) and DIBH (black)

Discussion

DIBH in radiotherapy for left-sided breast cancer has been evaluated by several studies but these were mostly retrospective in nature with small sample sizes. To the best of our knowledge, there has been one prospective dosimetric analysis of DIBH in left-sided breast cancer radiotherapy by a single institutional study in India (15). Our study conducted prospective data collection and analysed DIBH in left-sided breast/chest wall radiotherapy. In our cohort, the dosimetric data showed consistent results with other published data, demonstrating a significant reduction in both heart and lung doses by utilising DIBH.

DIBH Heart D_{mean} is 1.62 Gy as compared to 2.65 Gy in FB Heart D_{mean}, with absolute reduction of 1.03 Gy. Although the difference is not big numerically, Darby et al. (2013) has shown that there is no apparent safe threshold for mean heart dose, in relation to the rates of major coronary events (4). To date, it is still uncertain which anatomical structure of the heart is the main contributor to cardiac morbidity and mortality. The heart parameters that have been evaluated include mean heart dose, coronary arteries namely left anterior descending artery and left ventricles. The mean heart dose may not be the most suitable parameter for evaluating cardiac morbidity, nonetheless it is the most consistently reported parameter in most studies and provides a benchmark for comparison.

Long term data on cardiac risks of radiotherapy come from long term survivors of Hodgkin lymphoma. In a recent publication, the predicted absolute excess radiation related incidence of heart disease was about 3% at 30 years, if the mean heart dose was between 1 to 5 Gy. The absolute risk reduced to 0.70% with mean heart doses <1 Gy (16). Therefore, for the large majority of our breast patients with expected long-term survival, it is imperative that we try to reduce the dose to the heart as low as possibly achievable. Carlson et al. (2021) had conducted a population-based study to evaluate the risk of radiation-associated coronary artery disease (CAD) comparing women with breast cancer treated with left-sided radiation therapy (RT) versus right-sided RT. The study found that young women who received left-sided RT had over twice the risk of CAD compared when with women treated with right-sided RT (17). Therefore, DIBH is deemed beneficial for the treatment of left-sided breast radiotherapy regardless of the magnitude of mean heart dose reduction. The absolute reduction of 1.03 Gy in mean heart dose by utilisation of DIBH in our cohort is expected to bring clinically meaningful long term outcome for patients.

Our baseline FB Heart D_{mean} is 2.65 Gy, lower than other reported series. Inter-trial comparisons are difficult to make as reported heart doses vary across different regions. This could be attributed to differences in patient anatomy, radiotherapy technique, target volume, and delineation of the heart. For example, in the large Danish and American series, Heart D_{mean} was reduced from 5.2 Gy to 2.7 Gy and 4.23 Gy to 2.54 Gy respectively (18, 19).

Other than assessing the dose to the whole heart, few studies have pointed out the importance of considering LAD as an independent OAR to assess potential cardiac risk in the future, because it is often exposed to high doses in left-sided breast radiotherapy (20, 21). Our study has demonstrated significantly lower LAD D_{mean} in DIBH (6.81 Gy) compared to FB (11.57 Gy). LAD D_{max} in DIBH (22.66 Gy) was also significantly lower compared to FB (31.93 Gy). However, caution needs to be applied when interpreting these results as delineation of the LAD artery has large inter-observer variability, and the threshold dose for LAD remains unknown.

Planning studies have shown variable results regarding the impact of DIBH on lung dose-volume relationships. Some authors have reported that DIBH significantly reduced lung dose while others showed no difference (22 - 24). In the current study, DIBH recorded significantly less volume of left lung receiving 5 Gy, to 30 Gy, as opposed to FB for those receiving nodal irradiation, and reached significance for V_{20Gy} in those undergoing breast or chest wall irradiation only.

One of the major limitations in implementation of DIBH is the extra time and resources required for coaching and treatment. This has a significant impact on a busy department with a large number of patients and long waiting queues. Thus, the selection of patients who might benefit the most from DIBH technique remains crucial but challenging (25, 26). Studies have shown that anatomic metrics, FB-CCDax and FB-CCDps, are reproducible and are potentially helpful in selecting patients who would benefit most from DIBH. FB-CCDps is plausible as a good tool to identify patients with unfavourable cardiac anatomy (12, 27). In our study, we found a significant correlation of an increase in both FB-CCDax and FB-CCDps with more mean heart dose reduction. Hiatt et al. (2006) has defined unfavourable cardiac anatomy as cases with a FB-CCDax beyond the cutoff length of 5cm and a FB-CCDps beyond the cutoff length of 2cm but this is not validated in prospective studies (27). There was no meaningful association between FB-CCDax and Heart D_{mean} demonstrated from regression analysis in this study. But we found that FB-CCDps beyond the cutoff length of 2cm could be a potential parameter to help us in patient selection. A significant positive correlation was observed between FB-CCDps and Heart D_{mean} especially beyond the cutoff length of 2cm when the regression lines of FB and DIBH Heart D_{mean} intersected. After intersection, we observed that a wider separation of two regression lines continued with longer FB-CCDps. This coincides with the definition of unfavourable cardiac anatomy as cases with a FB-CCDps beyond the cutoff length of 2cm as proposed by Hiatt el al. (2006) (27). However, the small sample size of our study has limited us to validate an optimal cutoff value of FB-CCDps, but FB-CCDps appears to be a promising parameter to select patients most likely to benefit from DIBH in future studies.

In our cohort, further reduction in mean heart dose was observed when there was more in-field heart volume in FB scan. This is consistent with an Indian prospective analysis which found that when differences of in-field heart volume between FB and DIBH scans were bigger, a reduction in mean heart dose was more likely (15). Other studies including one by the Australian group, reported that maximum heart in the field of greater than 0.7 cm in FB scan could be a potential factor to identify patients who may benefit most from DIBH (28). Another useful parameter for DIBH patient selection is body mass index (BMI) as published by Yamauchi R et al. (2020). The authors concluded that the degree of benefit from DIBH varied with each patient, and the patients with low BMI benefited more from DIBH (29).

There are studies looking at whether those who receive regional nodal irradiation would benefit more from DIBH. Few published studies have evaluated differences in heart or lung dose reductions between patients receiving breast/chest wall radiotherapy alone and those requiring additional regional nodal irradiation (23, 24, 30, 31). In our study Heart D_{mean} was significantly lower in DIBH compared to FB with or without regional nodal radiotherapy. This is likely due to the fact that there were no internal mammary nodes treated in our cohort of patients and that none of our patients were treated with intensity-modulated radiation therapy (IMRT). When left lung dosimetry was analysed in patients who had received nodal irradiation (n=23), the results consistently showed that all the volume parameters of V_{5Gy} to V_{30Gy} for DIBH were significantly lower than that of FB. But in patients who did not receive nodal irradiation (n=15), the benefit of left lung dosimetry was less with only V_{20Gy} showing a significant reduction. The magnitude of the benefit will likely be larger when IMRT is used.

With the constant growth in demand for DIBH and the resource intensive nature of the technique, knowledge of factors that could identify breast cancer patients who may benefit most from DIBH would help department policymakers provide treatment that makes the most impact whilst balancing the service demands of a busy department. Currently. it is not clear from the available data what these factors are. In our study, it would appear that all patients derived benefit from DIBH. This is the first prospective dosimetry data collection on DIBH in radiotherapy for left-sided breast cancer in Southeast Asia. To overcome the limitation of this study, future studies should aim for a bigger sample size to validate the cutoff value of FB-CCDps. We also aim to continue collecting long term data to report on the late toxicities of radiotherapy.

Conclusion

Our prospective observational study has confirmed the benefit of DIBH in reducing mean heart and lung dose in left-sided breast/chest wall radiotherapy. FB-CCDps is a potentially reliable parameter to guide us in selecting patients who would benefit most from DIBH. More prospective data collection is needed to validate the cutoff value of FB-CCDps and future studies should continue to identify robust parameters for DIBH patient selection. As the prospective dosimetry data analysis of DIBH has shown significant benefit, DIBH should continue to be adopted as a routine practice for left sided breast radiotherapy in the future.

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Ethical Clearance

The study obtained ethical approval from University Malaya Medical Centre Medical Research Ethics Committee (MREC

ID NO: 201937-7208). Informed consent was obtained from all patients in this observational study.

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Competing Interests

The authors declare that they have no conflicts of interest to disclose.

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