Research Article

A Feasibility and Dosimetric Observational Analysis of Cardiac Dose with or without Active Breath Coordinator using Deep Inspiratory Breath Hold in Left Sided Breast Cancer Radiotherapy – A Tier II City Case Series.

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Abstract

***Background and Aim**: Cardiac toxicity is a major concern in locoregional radiation therapy for left-sided breast cancer. Cardiac volume and amount of doses to heart leads to late lethal cardiotoxicity. Moderate deep inspiration breath-hold (mDIBH) during radiation treatment delivery helps in reducing the cardiac dose. This small observational study compares dosimetric parameters of heart with and without active breath coordinator (ABC) mDIBH during tangential field breast cancer radiation.*

***Study Type**: This is a dosimetric comparative study.*

***Materials and Methods**: Five consecutive patients with left-sided breast cancer who underwent breast cancer surgery and adjuvant tangential field radiotherapy with ABC mDIBH between August 2019 and January 2020 in Onco-Life Cancer Centre, Satara, Maharashtra, India, a peripheral tier II city center, were analyzed. The ABC device was used for respiratory control and patients who could hold their breath for 20–30 s were considered for radiation with ABC mDIBH. Simulation scans of both free-breathing (FB) and ABC mDIBH were done. Tangent field treatment plans with a dose prescription of 40 Gy/ 15# were generated for each patient, in both scans after standard contouring. Target coverage and dose to the heart and lung were documented with dose-volume histograms.*

***Results**: SPSS, version 25 software, was used for analysis and the level of significance was set at P < 0.05. Mean V30 of heart was 857 cGy with FB and 502 cGy with ABC (P < 0.0001). Mean percentage reduction in cardiac dose was 59 % while there were no significant differences in lung parameters. Target coverage was equal in both the plans.*

***Conclusion**: We report that the use of ABC mDIBH technique resulted in a significant reduction in cardiac dose and hence can be considered as a promising tool for cardiac sparing and may be promoted wherever feasible including remote tier II city centres like ours.*

***KEYWORDS:** ABC, moderate deep inspiration breath-hold, cardiac dose, radiotherapy, tangent field*

Abbreviation

ABC - active breath coordinator,

mDIBH - moderate deep inspiration breath hold,

FB - free breathing,

s – seconds,

#- fraction,

BCS - Breast Conservation Surgery,

MRM – Modified Radical Mastectomy,

RT - Radiation therapy,

CT - computed tomography,

CTV - clinical target volume,

RTOG - Radiation Therapy Oncology Group,

IMRT – Intensity Modulated Radiation Therapy,

LAD artery – Left Anterior Descending artery,

TLV - Total lung volume,

MHD - maximum heart distance,

DVHs - Dose-volume histograms,

MLD - mean lung dose,

cGy - centigray

Introduction

Breast cancer comprises the most common type of cancer in females worldwide with 1,78,361 new cases and 90,408 deaths in India alone. **[**1,2**]** Radiation therapy (RT) is an integral part of breast cancer management after breast conservation surgery (BCS) and after mastectomy, if risk factors are present.**[**3**]**

According to the most recent Early Breast Cancer Trialists' Collaborative Group meta-analyses, adjuvant RT after BCS reduces the rate of breast cancer mortality compared to surgery alone.[4] However, as survival improves for breast cancer patients, the long-term morbidity of RT becomes a concern.[5] Comprehensive RT for breast cancer targets the breast, chest wall, and lymph nodes when indicated. The proximity of these targets to critical structures can cause radiation-induced toxicity. The common late side effects of RT include fibrosis, telangiectasia, pigmentation of the skin, and lymphedema. Rare but serious problems are cardiac and lung morbidity. Many studies had shown increased cardiac mortality and morbidity after breast radiotherapy and any dose to heart is significant [5-12] Left-sided breast radiotherapy is associated with increased risk of coronary artery disease [10,12,13] Moreover, cardiotoxicity of RT in breast cancer patients may further be enhanced by the use of some chemotherapeutic agents such as anthracyclines.

Cardiac dose-volume parameters should be thoroughly optimized in breast cancer RT to avoid potential cardiac toxicities of treatment. Improvements in techniques of RT have helped decrease cardiac doses over the years. Besides 3D-based planning and intensity modulation, nowadays, respiratory management strategies are also being used to reduce cardiac dose in breast cancer RT. The active breath coordinator (ABC) system, first developed by Wong et al., offers an effective respiratory management strategy that can be used to improve cardiac sparing in breast cancer RT with the advantages of separating heart and target by changing the internal anatomy with moderate deep inspiration breath-hold (mDIBH).[14] However, the availability of such high-end accessories is still scarce especially in remote and peripheral parts of the country and such patients can hardly avail its benefits. Centers choose not to invest in such higher techniques mainly considering the cost issues. So also training for ABC is again a challenge due to the limited literacy rate in such regions thus posing an overall added challenge in using the same. The benefit with different techniques largely depends on the individual patient anatomy and so also on various socio-economic parameters. As of date there is very limited real-world data from peripheral parts of the country. Hence, to analyze the proposed benefit with mDIBH, in a limited study population at our center, we have compared the dosimetric parameters with and without using ABC-mDIBH technique in the left-sided breast cancer tangential field irradiation.

Materials and Methods

Inclusion criteria

From August 2019 and January 2020, 5 consecutive patients with left-sided breast cancer after BCS or with MRM, who underwent tangential RT with ABC-mDIBH technique were included in this analysis. Inclusion criteria included age ≤70 years, Eastern Cooperative Oncology Group performance score 0–1, no previous RT to the breast, no history of any cardiac and lung disease, and patients with a comfortable breath-hold duration of 20–30 s.

Radiation treatment workflow

Pretreatment patient education

All the patients were explained about ABC mDIBH procedure right since the OPD visit if they were deemed fit by the physician. Detailed and repeated counseling was the key. Before the simulation computed tomography (CT) scan, all patients were given training for at least 3 days with the ABC (Elekta) device to enhance patient compliance and to determine individual (mDIBH) levels, which was set at 75% of maximum inspiratory capacity.

Simulation and treatment planning

All patients were simulated in a supine position with both arms above head, using a breast board. Palpable breast tissue and visible surgical scar were marked with radiopaque copper wires. After acquiring a steady breathing pattern, two sets of CT images were acquired for each patient with a slice thickness of 5 mm, one with mDIBH with ABC system and the other with free-breathing (FB). Breath-hold duration was documented. The gross tumor volume, clinical target volume (CTV), and organ at risk were delineated on the Monaco contouring station on both the scans as per the Radiation Therapy Oncology Group (RTOG) breast contouring guidelines for breast cancer. Treatment Planning was done using a treatment planning system (MONACO Ver 5.11) **[**Figures 1 and 2**]**. To maintain uniformity, the same physician performed all contouring procedures and the same physicist performed the treatment planning procedures. Although our CT image resolution is optimal owing to a detector size of 0.5 mm, the patient's breathing and cardiac kinetics are likely to produce image blurring that renders the visualization of the artery difficult. So also owing to a large variety of breast RT techniques, including the use of mixed photon/electron fields, large tangents, electron/photon IMRT, or arc therapy, doses received by the heart vessels as reported in the literature are pretty heterogeneous **[**15-18**]**. Hence, LAD artery dose was not taken into consideration in this particular study. All the patients were planned to receive a whole breast/chest wall dose of 40 Gy in 15 fractions as in START B trial protocol **[**19**]** using 6 MV photons.

Dose-volume parameters

Total lung volume (TLV), total cardiac volume, and maximum heart distance (MHD) were all documented in both scans for each patient. Dose-volume histograms (DVHs) were generated for all delineated structures in both plans. For the heart, mean dose (Dmean), maximum dose (Dmax), and percentage volumes receiving doses ≥5 Gy (V5), 10 Gy (V10), 15 Gy (V15), 20 Gy (V20), 25 Gy (V25), 30 Gy (V30), 35 Gy (V35), and 40 Gy (V40) were recorded. MHD is defined as the maximum perpendicular distance from the posterior border of the tangential field to the cardiac border. For the ipsilateral lung, Dmean, Dmax, and percentage volumes receiving doses ≥5 Gy (V5), 10 Gy (V10), 15 Gy (V15), 20 Gy (V20), 25 Gy (V25), 30 Gy (V30), 35 Gy (V35), and 40 Gy (V40) were recorded. V20, mean lung dose (MLD), and TLV were calculated for both right and left lungs.

Statistical analysis

The Kolmogorov–Smirnov test was used to detect whether the variables were normally distributed or not. After the assessment of all variables for normal distribution, variables with normal distribution were analyzed using paired t-test while variables with nonnormal distributions were analyzed using Wilcoxon signed-rank test. In descriptive statistics, mean and standard deviation was used for normally distributed variables which were analyzed using the paired t-test. Statistical Package for the Social Sciences, version 25 software (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corporation), was used for analysis and the level of significance was set at $P < 0.05$.

Ethical approval

This study was approved by the Institutional Review Board. All procedures performed involving human participants were in accordance with the ethical standards of the institutional and/or the National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This is only a dosimetric comparison with no intervention in the actual treatment delivered, and patient identity was not revealed.

Results

All the 5 patient's data with 10 CT scans were analyzed. The median age was 50.4 years (42–62 years). Three patients had Stage III (60%), and two patients had Stage II (40%) disease. The mean breath-hold duration was 29 s. CT scans using mDIBH showed a significantly larger TLV. The mean increase in the TLV was 22.00 %. Smaller MHD was observed in mDIBH scan when compared with scans performed in FB. The mean MHD in FB and mDIBH scans was 2.56 cm and 2.05 cm, respectively. The dose-volume parameters of the heart, left lung, both lungs, and CTV volume was compared for each patient using DVH generated for FB and mDIBH scans as shown in Tables 1-3. The mDIBH with ABC technique significantly reduced Dmean and Dmax heart dose compared to FB. There was also a significant reduction in all the heart dose-volume parameters. The average mean heart dose (Dmean) was reduced from 857 cGy with FB to 502 cGy with ABC (P < 0.0001). The relative reduction in average mean heart dose was 59 % while the average relative reduction in average Dmax heart dose was non-significantly just 1%. MLD with mDIBH was 293 cGy, 14 % higher than with FB which was 252 cGy. The difference in the rest of the lung dose-volume parameters was not significant. There were no significant difference in the breast CTV target dose parameters in both plans. Refer to Figures 1-5 for planning images with and without ABC.

PLAN	HEART										
	V5 (%)	V10 (%)	V15 (%)	V20 (%)	V25 (%)	V30 (%)	V35 (%)	V40 (%)	Dmean (CGy)	Dmax (CGy)	MHD (cm)
FB	21.64	17.72	15.76	14.30	12.96	11.54	9.55	0	685.2	3990.7	2.8
DIBH	18.07	14.62	1293	11.72	10.58	9.41	7.76	0	585.1	3995	2.6
FB	14.01	10.47	8.81	7.54	6.46	5.38	4.07	0.38	429.9	4060	1.9
DIBH	11.32	7.89	6.30	5.24	4.33	3.46	2.52	0.87	342.3	4115.7	1.46
FB	17.02	13.61	11.94	10.62	9.37	7.96	5.57	0	527.8	3884.8	2.5
DIBH	10.49	7.90	6.65	5.72	4.90	4.03	2.85	0	342.8	3937.9	2
FB	23.85	19.40	17.34	15.69	14.19	12.48	10.01	0.13	758.3	4055.6	3
DIBH	23.65	17.74	14.66	11.87	8.45	4.31	2.04	0	616.7	3952.8	2.35
FB	18.33	13.27	10.79	8.94	7.28	5.50	2.96	0	515.4	3828.1	2.64
DIBH	13.85	9.51	7.54	6.26	5.10	3.93	2.27	0	412.7	3753.6	1.88

Table – 1 – Cardiac DVH parameters

PLAN	LEFT LUNG									
	V5 (%)	V10 (%)	V15 (%)	V20 (%)	V25 (%)	V30 (%)	V35 (%)	V40 (%)	Dmean (CGy)	Dmax (CGy)
FB	22.33	17.36	15.23	13.71	12.30	10.64	7.26	0.08	635.7	4094.5
DIBH	22.66	17.40	15.12	13.48	11.96	10.15	6.41	0.10	627.7	4087
FB	22.34	17.66	15.38	13.70	12.14	10.33	7.30	0.24	627.3	4091.2
DIBH	20.14	14.79	12.36	10.65	9.08	7.31	4.35	0.16	520.1	4171.1
FB	12.06	8.77	7.30	6.21	5.22	4.11	2.48	0	333.2	3909.8
DIBH	13.31	10.08	8.57	7.47	6.43	5.29	3.55	0	379.6	4005.5
FB	19.74	15.02	12.95	11.44	9.99	8.28	5.25	0.12	569.5	4107.1
DIBH	27.17	21.07	18.29	16.05	13.66	10.72	5.18	0	723.7	3967.1
FB	11.82	7.71	6.00	4.81	3.77	2.70	1.14	0	318.8	3871.1
DIBH	22.58	16.55	13.90	12.02	10.25	8.02	3.65	0	518.6	3994

Table – 2 – Ipsilateral (left) lung DVH parameters

PLAN	BOTH LUNG		
	V20 (%)	Total Volume(cc)	MLD (cGy)
FB	6.59	3211.29	323.5
DIBH	6.47	3595.35	319.4
FB	6.58	2166.86	322.1
DIBH	5.14	3419.63	269.8
FB	2.86	2486.42	169.2
DIBH	3.62	2790.44	199.4
FB	5.18	1844.8	278.8
DIBH	7.86	2688.35	374.6
FB	2.20	1817.66	167.4
DIBH	5.92	3251.85	305.9

Table – 3 – Whole lung DVH parameters

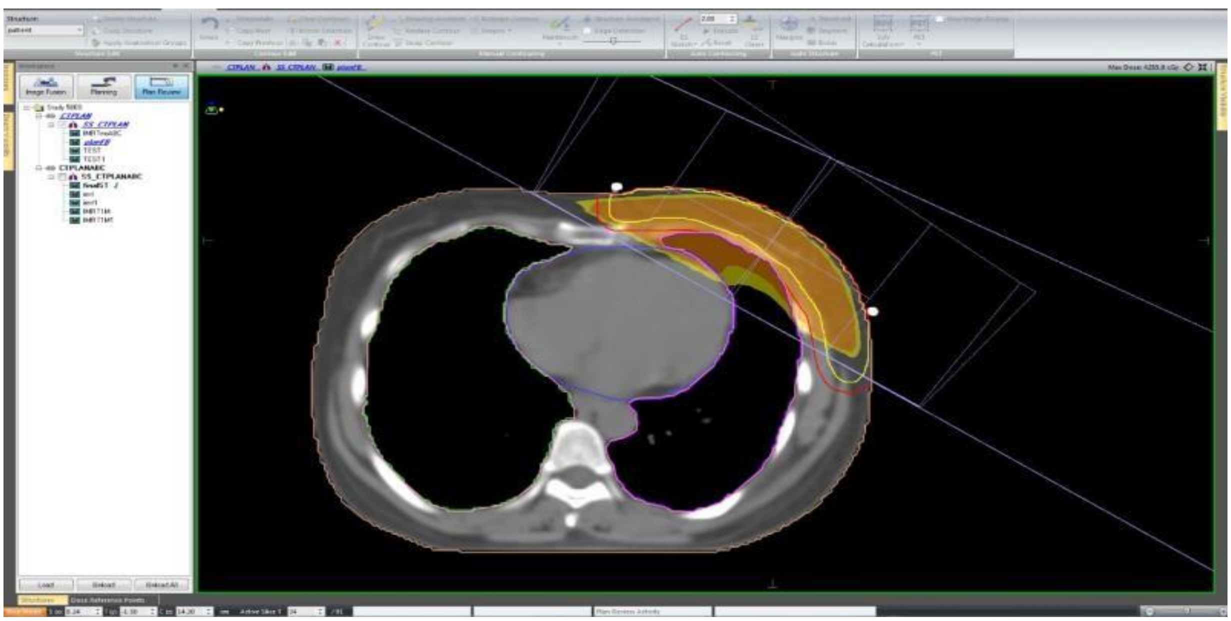

Figure 1 - Isodose distribution with FB in one particular patient

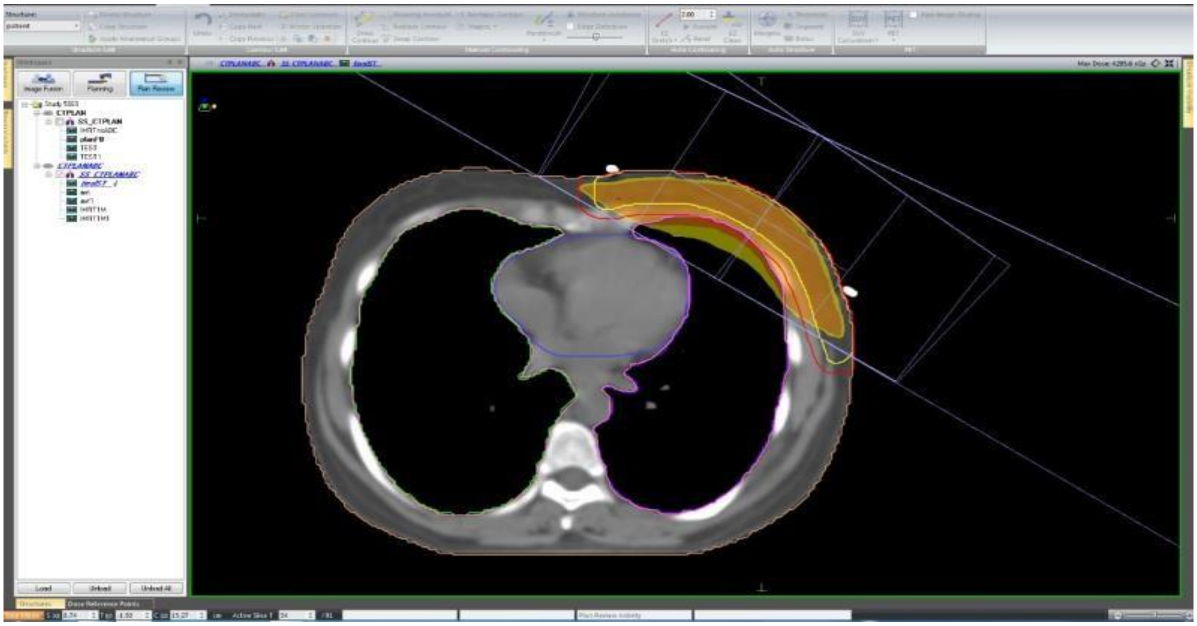

Figure 2 - Isodose distribution with ABC mDIBH in one particular patient

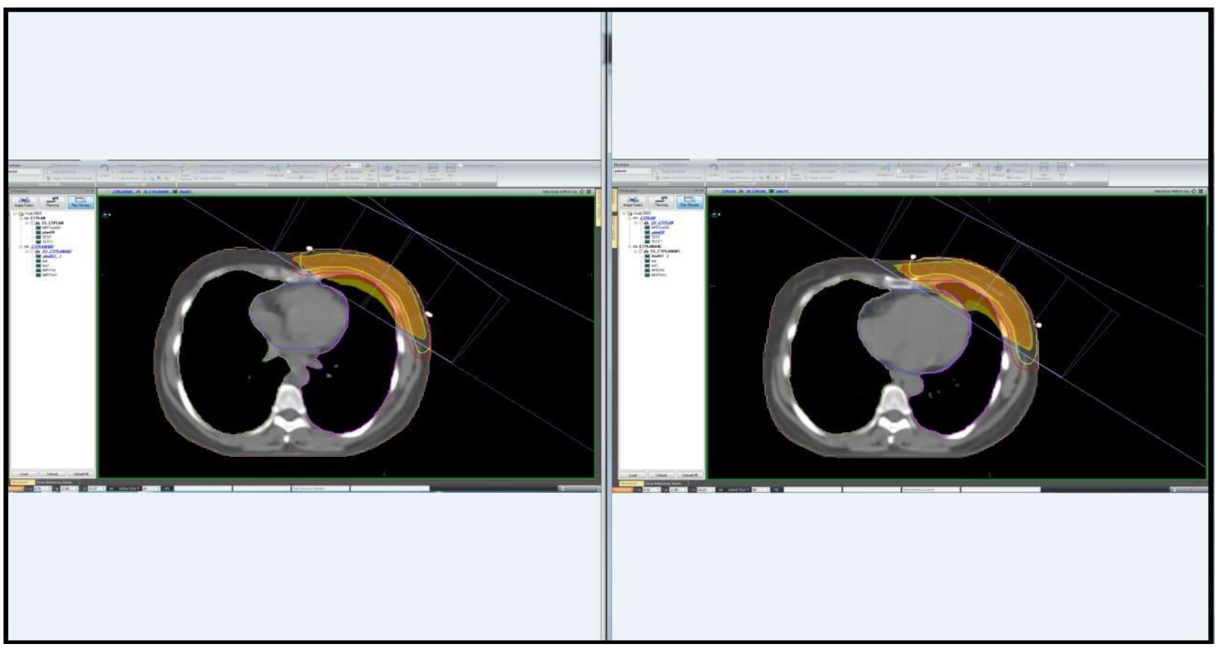

Figure 3 – Comparision of isodose distribution with and without (FB) use of ABC mDIBH in one particular patient

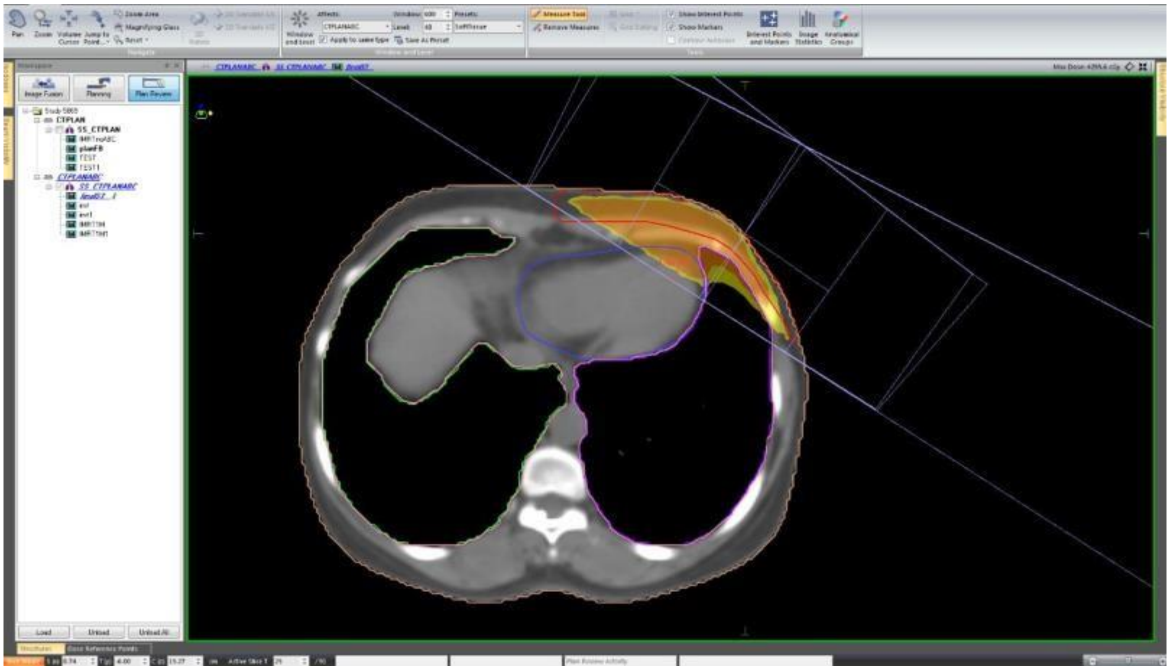

Figure 4 – Maximum Heart Distance (MHD) with ABC in one particular patient

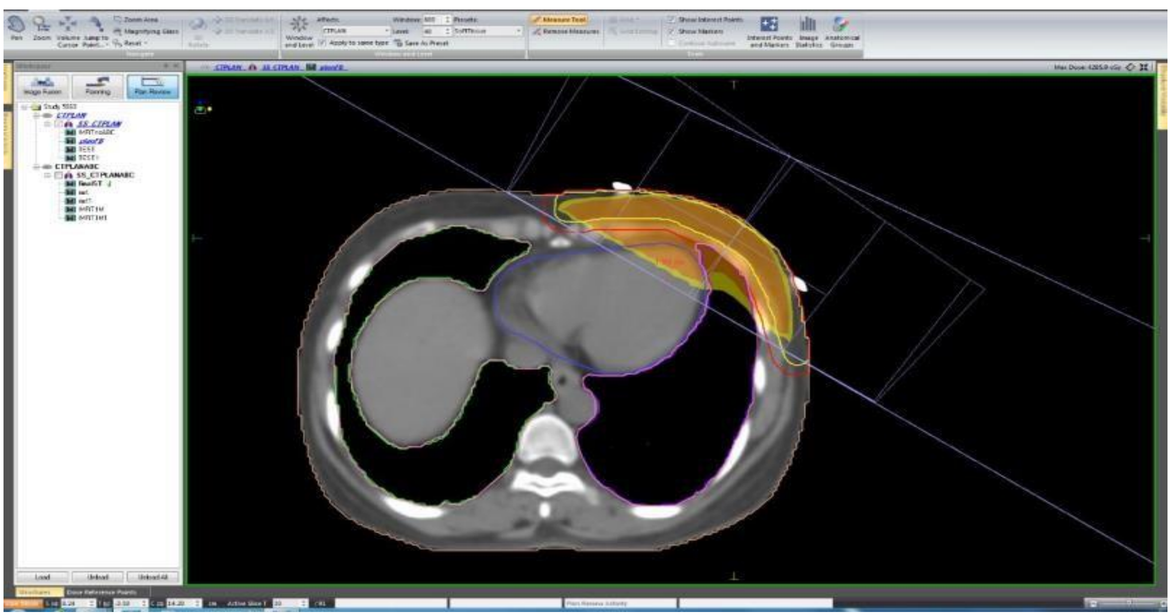

Figure 5 – Maximum Heart Distance (MHD) with FB in same (above) patient

Discussion

Late cardiac morbidity is a serious concern for left-sided breast cancer patients who receive tangential RT, especially in the younger age group. Darby et al. from Oxford after a retrospective study concluded that rate of the coronary event increases by 7.4% for an increase of every 1 Gy to the heart[20,21] and NSABP 51 study recommended a mean cardiac dose of <4 Gy for left-sided breast irradiation, and both emphasize the need for cardiac dose reduction in breast cancer radiotherapy. Hence, the integration of respiratory motion management to reduce the cardiac dose has been widely studied in the past few years. Lu et al. had shown that mDIBH could reduce the volume of heart by increasing the intrathoracic pressure, thereby increasing the distance between the heart and chest wall.[22] Vikström et al. in their study with 17 patients had shown that respiratory gating with deep inspiration breath-hold (DIBH) significantly reduces cardiac and pulmonary doses for tangentially treated left-sided breast cancer patients. The mean heart dose was reduced from 3.7 Gy to 1.7 Gy. The study also showed a reduction in pulmonary doses from 12% to 10% [23]. It has been suggested that if 5% of the heart receives 40 Gy, the risk of cardiac mortality exceeds 2%. Lee et al. showed a statistically significant reduction in mean heart dose and LAD. The mean heart doses with DIBH and FB were 2.52 Gy and 4.53 Gy, respectively. However, the mean left lung doses with DIBH and FB were 7.53 Gy and 8.03 Gy, respectively, which were not different significantly compared with FB.[24] Limitations of most of these earlier studies were small sample size and most of the authors commented that the absolute benefit in an individual patient is decided by the patients' chest wall and cardiac relationship. Published literature in this regard from our part of the country is sparse and hence this limited sample size dosimetric comparison was aimed to quantify the proposed benefit and feasibility in our set of patients wherein literacy rate, logistics and socio-financial parameters still play a vital role in selection of optimal choice of therapy.

In our study, we have analyzed 5 patient's dosimetric data. The patients in our study were relatively young with a median age of 50.4 years. The volume of the heart was smaller with mDIBH when compared to FB. There was a significant reduction in the mean heart dose with mDIBH (59%) when compared to FB. There was a 22% increase in mean TLV with mDIBH when compared to FB. However, there was no significant difference in the lung dose-volume parameters. Our study is observational compared to other studies and despite its small sample size suggests that mDIBH with ABC is feasible and effective even in our set population. Respiratory management for breast cancer patients is relatively easy to implement in clinical practice once the patient has been trained adequately compared to other novel techniques such as intensity-modulated radiation therapy (IMRT) which has been favored as another alternative method in reducing cardiac doses. Low-dose spill to critical normal structures in IMRT can also be avoided using respiratory gating with mDIBH technique. Since it is a dosimetric study, clinical endpoints in terms of cardiac morbidity and survival were not evaluated. Correlation of clinical outcome with cardiac dose-volume parameters in the future may enable to predict the dose reduction needed to reduce the cardiac morbidity and mortality in adjuvant left-sided breast cancer RT.

Conclusion

From this small sample of dosimetric comparison, we may suggest that mDIBH with ABC technique has a great impact on dose-volume parameters of heart. The mean heart dose showed a significant reduction of 59% with ABC mDIBH technique. These reductions achieved are likely to result in reduced long-term cardiac morbidity and mortality. Therefore, respiratory management strategy is a promising tool that can be routinely implemented for the tangential field radiation treatment of patients with left-sided breast cancer even in remote tier II city centres like ours.

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