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Challenges and benefits of implementing DIBH for breast cancer radiotherapy: Experiences from Guangzhou Concord Cancer Center

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Abstract – Radiation therapy is used for breast cancer treatments to improve local control and overall survival but may also lead to unwanted complications such as cardiac toxicity and pneumonitis. Deep inspirational breath hold (DIBH) has been used to reduce doses to the heart and other organs near the treatment target to lower the risk of radiation-induced complications. In this study, we present our experience on the clinical implementation and application of DIBH for breast cancer patients, its dosimetric benefits in heart and other organ sparing based on comparisons with free breathing plans, effects on the treatment efficiency as represented by treatment imaging, and beam delivery times, as well as challenges during implementation and clinical application at our center.

Key words: DIBH, Breast cancer, Heart, LAD, Radiotherapy.

Introduction

Breast cancer is the most commonly diagnosed cancer worldwide. It is also the leading cause of mortality among women in the world [1] and the 5th in China [2]. Radiation therapy is one of the main modalities in the management of breast cancer, in addition to surgery, chemotherapy, and endocrine therapy. Radiation therapy is typically prescribed post-breast surgery to improve local control and prolong survival time for non-metastatic breast cancer and is used for palliative treatment of metastatic breast cancer [3].

With the advancement of early cancer detection and better cancer treatment, more breast cancer patients become long survivors, thus it is important to minimize the complications associated with radiation therapy. Cardiac morbidity and mortality are long-term complications of breast radiation therapy, increasing by 1.76-fold in death due to cardiac disease and 1.33-fold in death due to vascular disease over an average of 28 years of follow-up compared to patients who did not receive radiotherapy [4]. The risk of major coronary events induced by radiation was reported to increase linearly with the mean heart dose by 7.4% per gray with no threshold dose [5]. Clarke et al. reported that radiation therapy increased the mortality rate from heart diseases by 1.27-fold compared to patients without radiation therapy [6].

Various techniques have been developed to reduce heart dose for breast cancer radiation treatments, such as deep inspiration breath hold (DIBH). The use of DIBH during breast cancer radiotherapy would move the heart further away from the treatment volume, leading to less heart volume in the radiation field and a consequentially reduced dose to the heart [7, 8]. DIBH has been increasingly used for left breast cancer treatment and its benefit for heart dose sparing and resulting reduction of cardiac toxicities has been reported in numerous studies. Doležel et al. showed that using DIBH would decrease heart dose from 3.22 Gy with free breathing to 1.21 Gy on average for 100 left-sided breast cancer patients [9]. Vikström et al. reported an average dose reduction of mean heart dose from 3.7 to 1.7 Gy using 3D conformal radiotherapy (3D-CRT) [10], and Sakka et al. showed that mean heart dose was reduced from 3.71 to 2.96 Gy for intensity-modulated radiotherapy (IMRT) treatments, and from 5.30 to 4.03 Gy for volumetric modulated arc therapy (VMAT) [11]. Several studies showed that the use of DIBH would lower the dose for other OARs

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such as the left anterior descending artery (LAD) and ipsilateral lung [12–14]. Recently, several studies reported that DIBH could also be used for right-sided breast cancer treatments and reduced doses to heart and LAD, although its clinical benefit is to be determined [15–17].

The DIBH technique was clinically implemented at Guangzhou Concord Cancer Center in 2021 and has been applied to most left breast cancer patients. In this article, we present our experience on the clinical implementation and application of DIBH for breast cancer patients, its dosimetric benefits in heart and other organ sparing, as well as challenges during implementation and clinical application at our center.

Material and methods

Patient selection

All patients with left-sided breast cancer were evaluated for DIBH treatments at our center. All patients with right-sided breast cancer were treated with free breathing. For left-sided breast cancer, only those patients who can reliably hold their breath for sufficient time (20 s or longer) were selected to undergo DIBH treatment. In total, 313 breast cancer patients had been treated with radiotherapy at our center from July 2021 to June 2023, including 309 females and 4 males, with 168 left-sided, 142 right-sided, and 3 bilateral. Patients were aged from 22 to 84 years old with a median age of 46. The majority of patients were of stage I (38.5%) or II (37.8%), with very few of stage IV (4.7%) and the rest of stage III (19.0%).

Immobilization and simulation

A discovery RT CT scanner (GE, Wisconsin, USA) was used for CT simulation. During the initial consultation before the CT simulation, patients were shown how to perform DIBH, and given an education pamphlet with instructions to practice DIBH at home. During CT simulation, the patient was set up in a supine position with hands up in a vacuum bag indexed to a slant breast board, and further immobilized using a head thermoplastic mask with chin slightly turned to the contralateral side of the breast with tumor, as shown in Figure 1. A reflective marker box with reflective dots was placed on the patient, typically at the xiphoid process area, as a surrogate to measure the respiratory motion of the patient chest during the DIBH process. A camera was located on the inferior side of the CT table, with a video coaching device (VCD, Varian Medical Systems) on the superior side near the patient's head to show the respiratory signal. A free-breathing patient CT scan was performed first. After free breathing CT, the patient was instructed to hold breathing several times, with radiation therapists inspecting the patient's breathing pattern for DIBH acceptability. Another CT scan was subsequently acquired with the patient performing DIBH. The same CT scanning protocol was used for both free breathing and DIBH CTs, with a helical scan mode, a slice thickness of 3.75 mm, and a large scanning field of view (SFOV). A typical workflow for breast cancer treatment with DIBH technique including patient consultation, immobilization and simulation, treatment planning, and treatment delivery is shown in Video 1.

Video 1. Typical workflow for breast cancer radiotherapy with deep inspiration breast holding (DIBH) technique. https://vcm.edp-sciences.org/10.1051/vcm/2023005#V1.

Treatment planning

The eclipse treatment planning system (TPS) (v15.6, Varian Medical Systems) was used for the contouring of tumor targets and other organs and the generation of treatment plans. 3D-CRT, IMRT, and VMAT techniques were used in breast cancer treatment planning. Thirty five patients treated with DIBH radiotherapy were selected in the dose comparison study between DIBH and free-breathing, including 16 patients planned with 3D-CRT, 14 with IMRT, and 5 with VMAT. All patients were treated post-lumpectomy and without breast implants. No internal mammary nodes were involved except for 8 IMRT/VMAT cases. The prescription was 40.05 Gy in 15 fractions for 3D-CRT cases, and 50.40 Gy as initial treatment plus a simultaneous integrated boost (SIB) of 59.4 Gy for the tumor bed in 28 fractions for VMAT/IMRT cases. Structures such as the patient body (external contour), target volume, organs at risk (OAR) such as ipsilateral lung, heart, and LAD were contoured on the DIBH CT, then copied to the free-breathing CT based on deformable registration using the Velocity system (v4.0, Varian Medical Systems). Field in-field technique was used for 3D-CRT planning, 5–7 fields were used for IMRT planning, and 2 partial arc beams were used for VMAT planning. Planning goals were to maintain 95% of the isodose curve coverage for at least 95% of the PTV, minimize high dose areas outside treatment target volume, and minimize dose to OARs such as heart and lung according to institutional guidelines. Optimized treatment plans were created on free-breathing CTs using the same treatment delivery techniques, and the dose volume histogram for both target and OARs was compared. The Anisotropic Analytical Algorithm (AAA) was used for dose calculation in all plans.

Treatment delivery

A linear accelerator (TrueBeam, Varian Medical Systems) was used to deliver radiation doses to patients. A real-time position management (RPM) system (Varian Medical Systems) was used to monitor patient respiratory motion, and a VCD identical to the one used for CT simulation was used to provide

Figure 1. Patient setup during CT simulation for a left breast cancer patient. The patient lies on a vacuum bag with both hands up. A marker box (block) is placed on xiphoid process as a surrogate for patient chest motion. Patient can monitor her own breathing pattern on the visual coaching device (VCD) and perform breath hold accordingly...

visual feedback of respiratory signals to patients. CBCT and/or orthogonal X-rays were used to match patient positioning accurately between treatments and CT simulation and guide beam delivery to the tumor target according to the treatment plan. Patients were instructed to perform DIBH during both imaging and beam delivery for DIBH treatments.

Time study

In this study, we analyzed the imaging time and treatment delivery time during each treatment fraction for 30 patients, including 10 with free breathing treatment, 10 with DIBH treatment with VCD, and 10 with DIBH treatment without VCD. For each group, the same mixes of treatment techniques were selected, including 4 3D-CRT cases, 1 IMRT case, and 5 VMAT cases. The imaging time was calculated as the duration from the start of imaging to the start of the first treatment field for each treatment fraction, the treatment time was calculated as the time from the start of the first treatment field to the end of the last treatment field, and the total fraction time was the sum of both imaging and treatment time.

Statistical analysis

Dosimetry and time study results were summarized using descriptive statistics, with quantitative variables expressed as mean ± standard deviation. A paired *t*-test (2 variables) was used to compare patient-related dosimetry data between free breathing and DIBH and compare the time between any two of the three breathing techniques (the free-breathing, DIBH with VCD, and DIBH without VCD) over all fractions.

Results

Dosimetric comparison

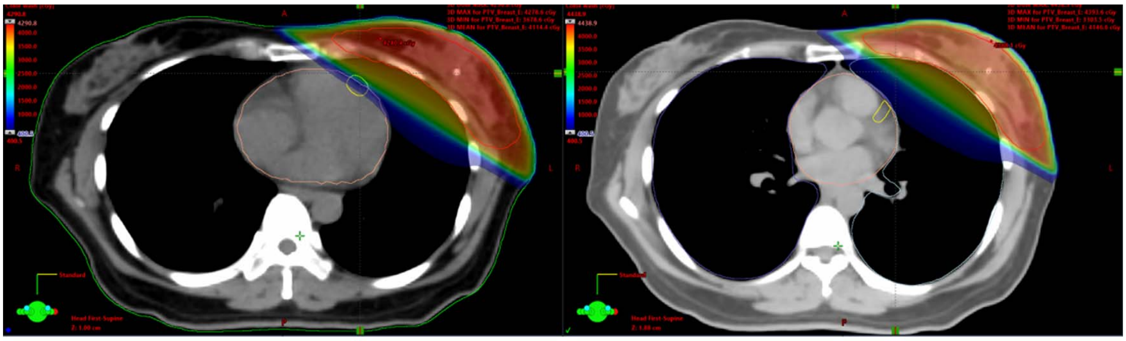
Treatment plans for the selected 35 patients with the DIBH technique were compared to the corresponding plans on the free-breathing CTs. As shown in Figure 2, for a sample left cancer patient, the heart was clearly further away from the tumor target and the radiation field in a DIBH plan (Figure 2a) than in a free-breathing plan (Figure 2b), leading to less mean and max heart dose for DIBH treatment (Figure 2c). As demonstrated in Figure 2c, the use of DIBH not only led to lower heart dose but also reduced dose to other OARs such as LAD and ipsilateral lung, while maintaining similar target coverage.

On average, as shown in Table 1, the target coverage was almost the same between plans on DIBH and free-breathing CTs and met the clinical goals. The use of DIBH reduced the mean heart dose from 2.66 to 1.11 Gy for 3D-CRT plans ($p < 0.001$), and from 4.59 to 3.72 Gy for IMRT/VMAT plans ($p = 0.013$). The max LAD dose (defined as the dose received by 0.1 cc of volume) was reduced from 39.48 to 29.97 Gy ($p = 0.007$) for 3D-CRT and from 39.36 to 22.64 Gy ($p < 0.001$) for IMRT/VMAT. There was a slight reduction in lung dose, with a p-value < 0.05 for IMRT cases, but it was not significant for 3D-CRT cases. The difference in the right breast dose for DIBH plans was similar compared to free breathing plans.

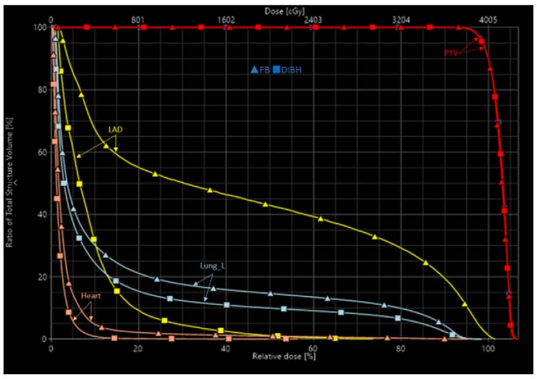
Time comparison

The average imaging time, treatment time, and total session time for patient treatments with various breathing modes as a function of treatment fraction number are shown in Figure 3. Both imaging and treatment times were the longest or close to the longest at the first fraction, then fluctuated in the rest of the fractions. As expected, the shortest time was observed for treatments with free breathing, DIBH treatments without the use of VCD was the longest, and DIBH with the use of VCD were in between.

Averaged over all fractions for all patients, the imaging time was 240, 369, and 439 s, the treatment time was 126, 174, 301 s, and the total session time was 375, 578, and 774 s, for free breathing, DIBH with use of VCD, and DIBH without



a) Free breathing b) DIBH



c) DVH comparison

Figure 2. Screenshots of dose distribution and DVH comparison of treatment plans for a left-sided breast cancer patient between DIBH and free breathing CTs which were deformably registered based on the treatment breast volume. (a) Dose distribution for free breathing plan, (b) dose distribution 3 for DIBH plan and (c) DVH comparison of both plans.

Table 1. Dosimetric comparison between treatment plans planned on DIBH CT and free breathing CT. If the *p*-value was over 0.05, it was considered non-significant (N.S.).

Technique	Dosimetric endpoint	Free-breathing	DIBH	p
3D-CRT	PTV V_{95} (%)	99.43 ± 0.59	99.28 ± 0.49	N.S.
	Heart D_{mean} (Gy)	2.66 ± 0.85	1.11 ± 0.24	<0.001
	LAD $D_{0.1CC}$ (Gy)	39.48 ± 1.52	29.97 ± 4.37	0.007
	Left lung V_{4Gy} (%)*	29.9 ± 6.55	28.43 ± 5.19	N.S.
	Left lung V_{16Gy} (%)*	15.43 ± 4.74	13.31 ± 3.02	N.S.
	Left lung D_{mean} (Gy)	6.95 ± 1.74	6.24 ± 1.17	N.S.
	Right breast D_{mean} (Gy)	0.19 ± 0.09	0.23 ± 0.11	N.S.
VMAT&IMRT	PTV V_{95} (%)	99.01 ± 1.1	99.31 ± 0.99	N.S.
	Heart D_{mean} (Gy)	4.59 ± 1.23	3.72 ± 0.79	0.013
	LAD $D_{0.1CC}$ (Gy)	39.36 ± 7.94	22.64 ± 11.95	<0.001
	Left lung V_{5Gy} (%)	63.4 ± 6.69	59.79 ± 3.45	0.044
	Left lung V_{20GY} (%)	25.66 ± 3.49	22.67 ± 3.36	0.011
	Left lung D_{mean} (Gy)	13.84 ± 1.46	12.88 ± 110	0.028
	Right breast D_{mean} (Gy)	3.76 ± 0.79	3.24 ± 0.95	N.S.

* Lung dose constraints V4 and V16 for 3D-CRT treatments with 40.05 Gy prescription were scaled down from V5 and V20 for IMRT/VMAT with 50 Gy prescription.

VCD respectively, as shown in Table 2. The *p*-value was less than 0.001 for comparison between any two of the three breathing techniques. Roughly speaking, patients performing DIBH with the use of VCD took about 3–4 min longer during each fraction compared to free breathing, and about 3–4 min less than DIBH without the use of VCD. As expected, both imaging and treatment time were longer for IMRT/VMAT compared to 3D-CRT, but the time comparison among free breathing, DIBH with VCD, and DIBH without VCD shows a similar pattern between 3D-CRT and IMRT/VMAT.

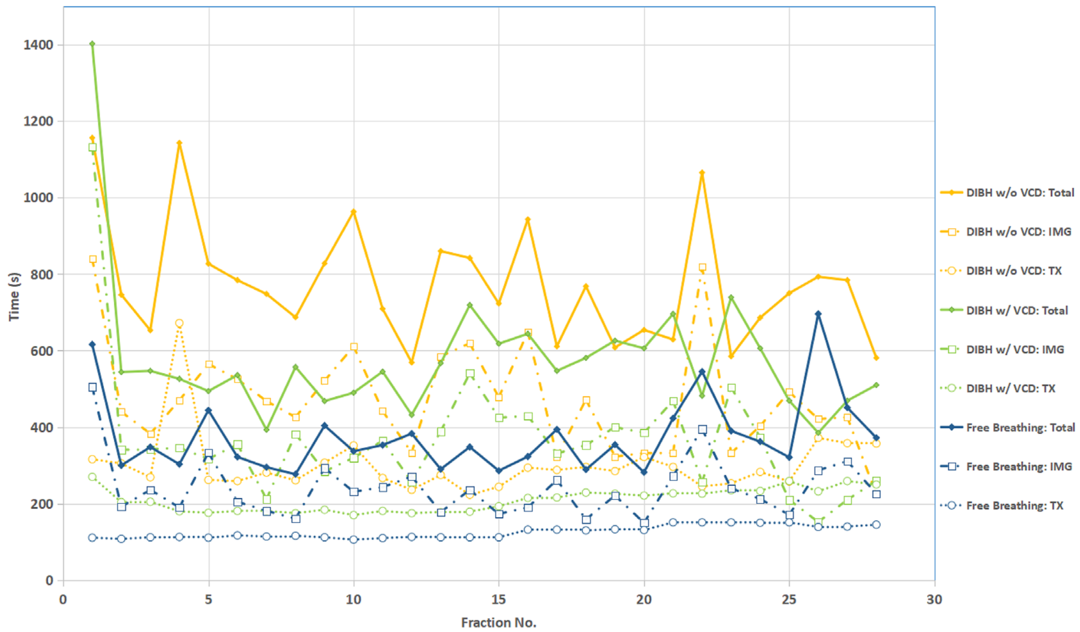


Figure 3. Imaging (IMG), treatment (TX), and the total fraction (Total) time as a function of fraction number for breast cancer patients treated with free breathing, DIBH with VCD, and DIBH without VCD.

Table 2. Comparison of imaging, treatment, and total time averaged for all fractions for patients with free breathing, DIBH without VCD, and DIBH with VCD for different treatment planning techniques.

Technique	Session	Time (s)		
		Free breathing	DIBH w/ VCD	DIBH w/o VCD
3D CRT	Imaging	198 ± 34	337 ± 107	474 ± 139
	Treatment	63 ± 5	101 ± 12	150 ± 24
	Total	261 ± 35	438 ± 109	623 ± 133
IMRT/VMAT	Imaging	238 ± 66	392 ± 102	439 ± 142
	Treatment	136 ± 8	241 ± 14	321 ± 57
	Total	384 ± 93	633 ± 101	798 ± 184
Average	Imaging	240 ± 59	369 ± 92	439 ± 127
	Treatment	126 ± 16	174 ± 28	301 ± 84
	Total	375 ± 91	578 ± 90	774 ± 144

Discussions

Our study shows the use of DIBH during radiation therapy led to a significant reduction of mean heart dose for left breast cancer patients, about 1.6 Gy and 1 Gy reduction for 3D-CRT and IMRT/VMAT, respectively. Our results are similar to what have been reported in previous studies [9–14]. It should be noted that the amount of dose reduction depends on patient selection, treatment technique, and institutional planning and treatment protocols. However, it is clear that the dose reduction of heart and its substructure LAD was substantial in all known studies [18–20], which could result in less cardiac toxicity, better quality of life, and increased survival rate post-radiation [5, 21]. The main reason for dose reduction to heart and LAD during DIBH is due to the displacement of the heart and LAD further away from the left breast treatment volume compared to free breathing, as shown in our study and other studies [7, 8]. In addition, the magnitude of breast motion would also be reduced during DIBH compared to free breathing, thus less planning target margin can be used, leading to further dose reduction for OARS near treatment targets such as heart, LAD, right breast, and ipsilateral lung [22, 23]. At our center, the same margin was currently used for both patients with and without the use of DIBH, but a smaller margin is being evaluated and could be applied in future clinic practice.

Our study shows a slight reduction of the mean dose and V20 for IMRT/VMAT (V16 for 3D-CRT) on the ipsilateral lung with the use of DIBH compared to free breathing, while the difference on V5 for IMRT/VMAT (V4 for 3D-CRT) seems minimal between the two techniques. Our results are consistent with other studies as summarized by Lu et al. [20]. The lower dose in the lung would lead to potentially less radiation-induced lung toxicity such as pneumonitis [24].

Our time study shows that a longer time was needed for patients treated with DIBH compared to free breathing, about 3 and half minutes of extra time for DIBH treatments with the use of VCD, and about 7 min more for DIBH without VCD. This was expected because when we were targeting the cancer with greater precision using DIBH, more time was needed for multiple breath holds and consequent breathing recovery intervals, especially for patients who may have difficulty in complying with DIBH requirements. With the aid of VCD and better training, both imaging and treatment time were reduced compared with DIBH without VCD. It should be noted that the imaging time was longer than the treatment time as it was calculated from the start of the imaging to the start of treatment delivery, which included time spent on image review and potential patient re-setup.

Many challenges exist in the implementation and application of DIBH treatment. First, an experienced clinic team with a good quality assurance program is critical to ensure the DIBH technique is properly implemented. Procedures and guidelines for all aspects of the clinical application from CT simulation to treatment delivery need to be established, such as patient training, breathing pattern (chest breathing or abdomen breathing), minimum breath hold length, planning and setup margin, imaging technique and frequency, gating window during DIBH and so on. For example, Literature research and staff training including site visits to clinics with existing DIBH programs would be of great help. Quality assurance is to be performed for equipment related to breath holding and gated beam delivery as well as patient compliance such as breath hold length and reproducibility.

Second, patient cooperation and compliance with DIBH treatments are very important but extremely challenging. Not all cancer patients might be able to hold their breath long enough and perform DIBH reproducibly during CT simulation or treatments. In our center, about 16.7% of left-sided breast cancer patients were determined not suitable for treatments with DIBH. Challenges in applying DIBH technique for these patients included: (1) inability to hold breath long enough due to poor lung functionality or weak performance, (2) inability to comply with training during CT simulation, (3) inability to hold breath reproducibly during treatment, and (4) no dosimetric advantages for DIBH over free breathing treatment planning. For these patients, 4D gated treatment delivery may be a viable option, although its accuracy, reproducibility, and impact on treatment delivery efficiency remain to be comprehensively evaluated [25].

There are also technical challenges in DIBH implementation. For example, many breast cancer patients require an electron beam boost after photon treatment of the primary target volume. However, currently, the gating capability is not available for the Truebeam linac to deliver an electron beam during DIBH treatment. Therefore, we used free-breathing for electron beam boost instead of DIBH, which would require separate contouring and planning on the free-breathing CT, leading to more time and effort on planning and challenges on dose summation and evaluation. In addition, a typical CBCT imaging would take about 1 min or more, and require patients to hold breaths more than once to complete. This would lead to not only longer patient setup time but also could compromise the image quality of CBCT if patients hold breaths inconsistently during the acquisition of CBCT images.

Finally, the longer imaging and treatment time when DIBH is used would pose a big challenge for a busy clinic. Proper training of patients and the use of audio/visual feedback such as the VCD we used have been proven to be helpful in both patient compliance and treatment efficiency [26, 27]. In addition, investigations have been conducted to screen patients for DIBH use by predicting whether a patient might benefit from the use of DIBH based on the tumor size, location, and type as well as patient tolerance [28–30].

Conclusions

The use of DIBH reduces the dose in the heart, LAD, and ipsilateral lung for left breast cancer radiotherapy, leading to potentially less cardiac morbidity and mortality, better survival rate, and improved quality of life post-radiation therapy. Many challenges exist during the implementation and application of DIBH treatments, and proper quality assurance and staff and patient training are needed to ensure safe and effective DIBH breast treatment.

Conflicts of interest

None.

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