



Deep inspiration breath hold in post-operative radiotherapy for right breast cancer: a retrospective analysis

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ABSTRACT

Background: The aim of our study is to determine whether deep inspiration breath hold (DIBH) is effective for reducing exposure of the heart, left coronary artery (LAD) and both lungs in right breast radiotherapy.

Materials and methods: We have analyzed 10 consecutive patients with right-sided breast cancer (BC), simulated during free breathing (FB) and in DIBH modality. For all patients we contoured breast PTV and organs at risk (right and left lungs, heart, LAD) on both CT scans (FB and DIBH). Finally, 5 patients were treated with IMRT and 5 with VMAT techniques.

Results: All patients were able to end the treatments in DIBH modalities regardless of the longer treatment time in comparison to FB. The maximum and mean dose to the heart are lower in the DIBH modality. The mean values of the heart mean dose were 1.76 Gy in DIBH and 2.19 Gy in FB. The mean heart maximum dose in DIBH and FB were, respectively, 9.3 Gy and 11 Gy. Likewise, the maximum dose to the LAD is lower in DIBH; 2.57 Gy versus 3.56 Gy in FB. Noteworthy, 3 patients with hepatomegaly treated with the DIBH technique showed a higher ipsilateral lung dose than FB, but a decrease of liver dose.

Conclusion: We report that the use of DIBH for right-sided BC allows the dose to the heart, LAD and to the liver to be reduced in case of hepatomegaly. This technique is well tolerated by patients, when adequately trained, and could be considered effective even in right sided BC.

Key words: right breast cancer; deep inspiration breath-hold; radiotherapy; left coronary artery; heart

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Introduction

Locoregional radiotherapy (RT) following breast conserving surgery is the standard adjuvant treatment for women with early stage breast cancer. RT has been shown to reduce the risk of breast cancer local recurrence in several large, prospective, randomized trials [1-4]. In addition, meta-analyses have also shown its benefits in terms of improving breast cancer survival [5]. However improvements in treatment outcome must always

be balanced with the potential risk of long-term toxicity. Associations between the use of adjuvant radiation therapy for left-sided breast cancer and increased risk of cardiac morbidity have been described with older RT techniques [6, 7]. In recent years, a large effort has been made to develop techniques to reduce the dose to organs at risks (OAR), especially the heart and lung, for patients receiving postoperative RT for breast cancer.

Deep inspiration breath hold (DIBH) is a well-established respiratory modality which has

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been shown to reduce cardiac and pulmonary dose in left-sided breast cancer patients [8–11].

Despite the widespread implementation of DIBH for left-breast RT, few studies have investigated its benefit in right-breast cancer.

Early data suggest cardiac and pulmonary benefits also for right-breast cancer patients, particularly when regional nodes are included in the irradiated volume. Liver-sparing is also reported, however data remains limited [12, 13].

The aim of our study is to determine whether DIBH is effective for reducing exposure of heart, left coronary artery (LAD) and both lungs in right breast RT compared to free breathing (FB) modality.

Materials and methods

Between October 2020 and November 2020 ten patients diagnosed with right-breast cancer underwent FB and DIBH computed tomography (CT) scans. All patients were planned on DIBH CT for the RT treatment to the whole right breast and retrospectively planned on FB CT. No extra imaging was required for the study.

CT (Philips Big Bore) scans were performed with patients in a supine position with arms raised over head and using a Posirest™ breast board (CIVCO Radiotherapy) with a slice thickness of 3 mm in FB. A second CT scan with DIBH was performed immediately after FB TC. The DIBH technique was performed using the surface-based Catalyst™/Sentinel™ system during CT simulation and treatment delivery. The system, through a continuous optical surface scanning, generates a reference surface image during the CT scan simulation and records the deep inspiration amplitude. The gating window was set to 3 mm at the level of stable and reproducible deep inspiration.

CT scans were imported into the Eclipse™ (Varian) planning system for volume delineation and treatment planning.

Treatment planning was performed by Varian Eclipse system (TPS, version 16.1) and delivered by Truebeam® (Varian Inc., Palo Alto, CA) Linac equipped with a 120 leaves Millennium Multileaf Collimator of 0.5 mm. Five patients were treated with VMAT plans and five patients with IMRT plans. Prescription dose was 50 Gy in 25 fractions. The plan technique was an optimized RapidArc® with algorithm Acuros XB 15.3 and treatments

were delivered with 6 MV photon beams for VMAT plans, while for IMRT photon beams of 6 MV or a combination of 6 and 10 MV were used.

All the plans approved must have the 95% isodose covering more than 95% of PTV. The following dose-volume objectives for the lungs and heart are in use in our department: homolateral lung V20Gy < 25% and mean dose < 18 Gy, heart V5 Gy < 40% and mean dose < 5 Gy, the maximum dose to the LAD < 20 Gy, the contralateral left breast 5 Gy < 15%.

Verification and adjustment of patients' setup has been performed using Electronic Portal Imaging Device (EPID) with 5 mm limit in each direction.

Plan evaluation and statistical analysis

Dose-volume histograms (DVHs) were evaluated for target volumes and OARs on the FB and DIBH plans. We recorded the following dose-volume parameters: ipsilateral lung (mean dose, volume receiving 20 Gy), heart (mean dose and volume receiving 5 Gy), LAD (maximum dose) and contralateral breast (volume receiving 5 Gy).

Wilcoxon signed-rank tests were used to examine differences in the dose-volume constraints between the FB and DIBH plans. Statistical analysis was performed using the software SYSTAT version 11.0 (SPSS, Chicago, IL, USA). Two-tailed $p < 0.05$ was considered statistically significant.

Results

We compared data between the FB and DIBH plans from 10 consecutive patients. Comparison of OAR dose-volume parameters in DIBH and FB plans are reported in Table 1.

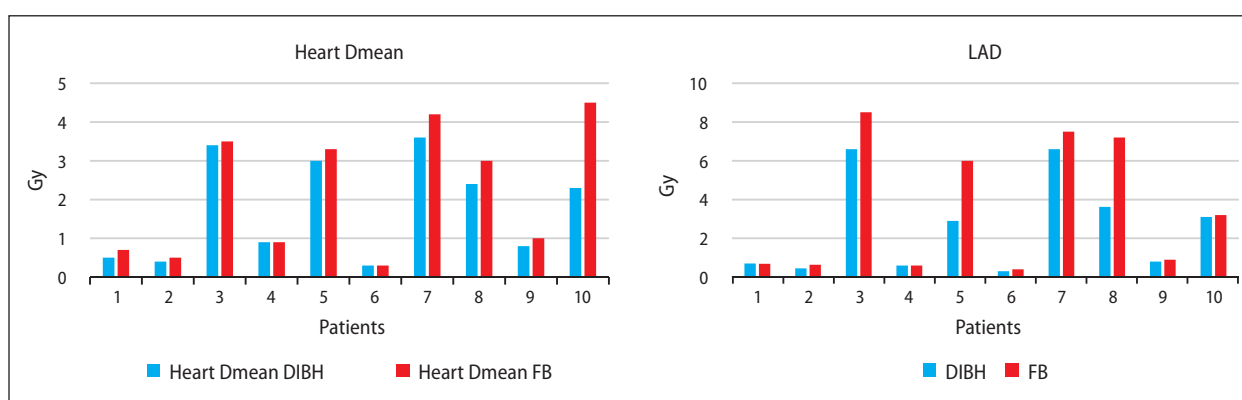
There was no difference in plan quality between DIBH and FB in terms of target coverage.

As expected in DIBH technique, our data show that D_{mean} and V_5 for the heart are below our constraints, while for FB two patients were slightly out of tolerance in terms of D_{mean} . Although VMAT plans were expected to give higher dose, our data show only a modest increase of 1 Gy for D_{mean} respect to IMRT. We register for a patient a relevant decrease of 2.2 Gy for heart D_{mean} between DIBH and FB, and V_5 follows the same pathway, decreasing of 25.2% (from 32.2 to 7%) in DIBH plan. We report a lower heart D_{max} in DIBH, 9.2 ± 4.7 Gy, than FB plans, 11.2 ± 5.7 Gy ($p = 0.01$)

Table 1. Organs at risk (OARs) dose-volume parameters for whether deep inspiration breath hold (DIBH) and free breathing (FB) modalities

Dosimetric endpoints	DIBH	FB	p-value
Mean heart [Gy]	1.8 ± 1.3	2.2 ± 1.6	0.01
Heart V5 (%)	6.6 ± 8.5	10.6 ± 12.4	0.03
Maximum dose LAD [Gy]	2.6 ± 2.4	3.6 ± 3.3	0.01
Mean right lung [Gy]	8.8 ± 3.1	9.5 ± 1.8	0.6
Lung V20 (%)	14.9 ± 5	15.2 ± 3.4	0.6
Left breast V5 (%)	4.9 ± 5.8	10 ± 17.3	0.5

LAD — left coronary artery

**Figure 1.** Histogram showing maximal dose (Dmax) values for left coronary artery (LAD) and mean dose (Dmean) values for heart in deep inspiration breath hold (DIBH) (blue) and free breathing (FB) (red) of the 10 patients analysed

Comparing D_{\max} of LAD for DIBH vs FB plans highlights the same results (Fig. 1). Regardless of the technique, VMAT or IMRT, all patients register a mean D_{\max} below 20 Gy and the higher reduction of maximum dose to LAD was 3.2 Gy for a patient undergoing a VMAT treatment.

There was a similar increase in total lung volume for both modalities. Lung volumes increased from $1458.7 \pm 285 \text{ cm}^3$, in the FB set up, to $2466.6 \pm 260.3 \text{ cm}^3$ in DIBH ($p = 0.005$). DIBH is associated with pulmonary sparing. The mean V_{20} of the ipsilateral lung for DIBH treatments is $14.9 \pm 5\%$ showing a decrease respect in to FB plans, $15.2 \pm 3.4\%$. We observe the same behaviour for D_{mean} , $8.8 \pm 3.1 \text{ Gy}$ for DIBH vs. $9.5 \pm 1.8 \text{ Gy}$ in FB plans. All patients met the criteria of $V_{20} < 25\%$ for both the ipsilateral and both lungs, but for 3 patients we observed V_{20} and mean ipsilateral lung dose of DIBH plans higher than in FB. This is due to the liver position in the field of view for FB treatments as shown in Figure 2.

As an example in this patient, the calculation highlighted a lower dose for the liver in

the DIBH plan with a V_{20} of 0.1% vs. 5.7% for FB and D_{\max} decreased from 49.7 Gy in the FB plan to 22.1 Gy of the DIBH plan. DVH comparison of this patient for the FB and DIBH technique is shown in Figure 3.

For contralateral breast, $V_5 < 15\%$ was respected in all DIBH plans with a mean value of $4.9 \pm 5.8\%$. The mean value for FB plans was $10 \pm 17.3\%$, but 2 patients didn't meet the constraint because of small lung volume. Conversely, in these two patients the constraints were respected in the DIBH modality.

We observed only a slight increase in the time of beam delivery: from 42.4 sec/arc FB to 63.6 sec/arc in DIBH for VMAT plans, and from 25 sec/field for FB plans to 36.2 sec/arc IMRT for DIBH plans.

Our analysis highlights a chest wall excursion of $1.05 \pm 0.44 \text{ cm}$ in DIBH, ranging from 0.33 to 1.89 cm.

Discussion

DIBH is a well-established modality that reduces cardiac and other surrounding organ doses during

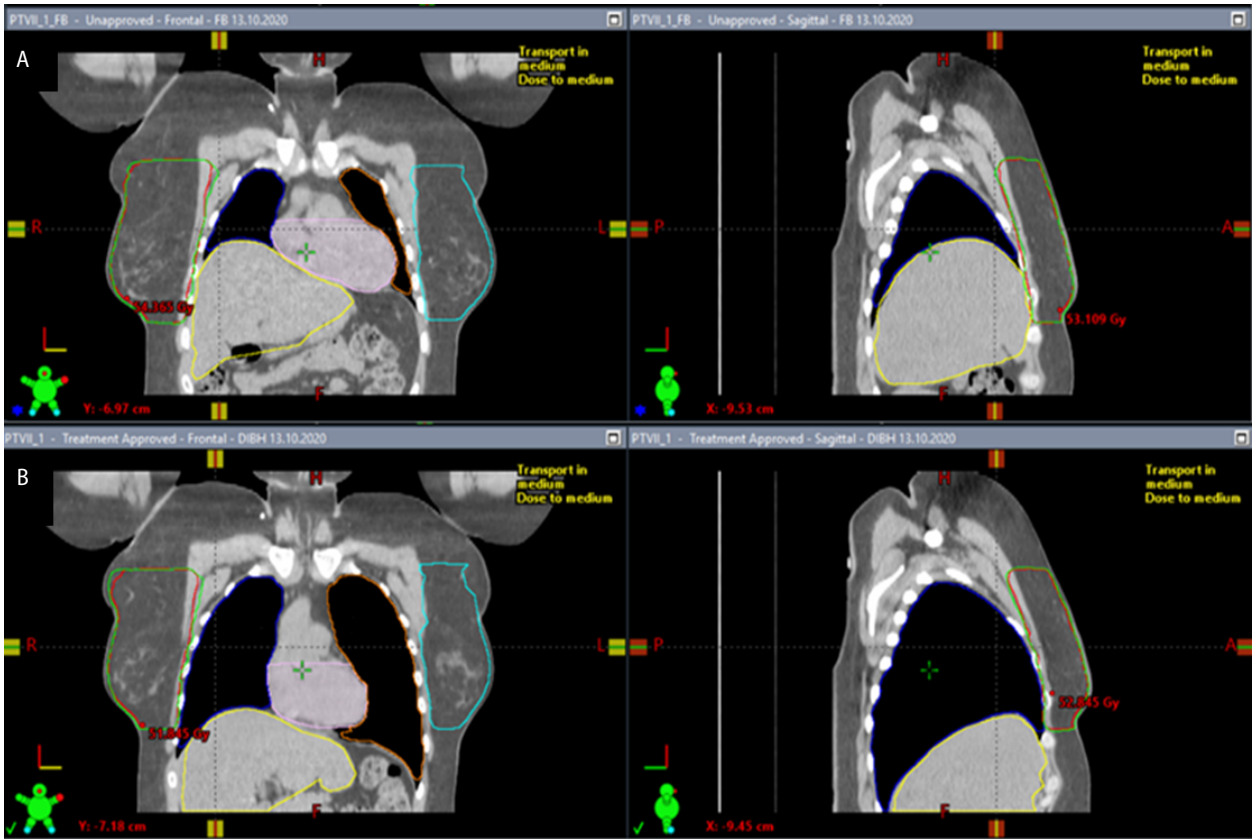


Figure 2. Coronal and sagittal computed tomography (CT) in deep inspiration breath hold (DIBH) (A) and free breathing (FB) (B) demonstrating the liver displacement (yellow arrow). Green line represents 95% isodose

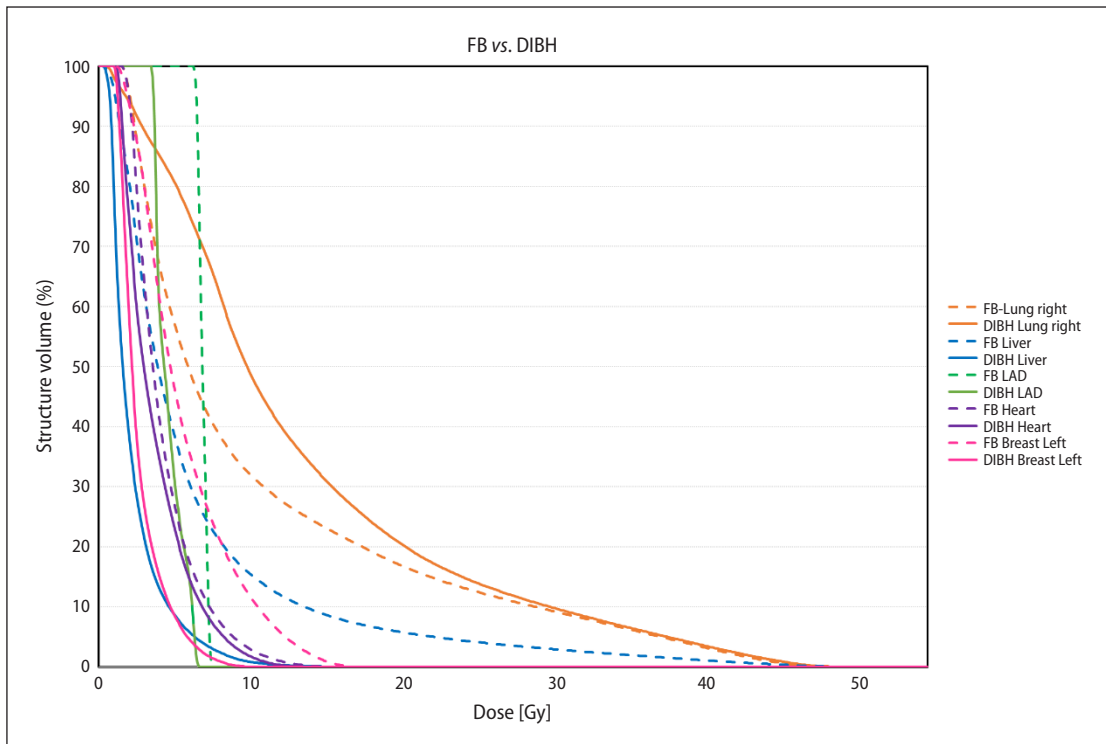


Figure 3. Dose-volume histogram (DVH) for organs at risk (OARs) in deep inspiration breath hold (DIBH) and free breathing (FB) (dotted lines) in a patient with hepatomegaly

left breast cancer RT. To our knowledge, few studies have investigated its benefit in right-breast cancer treatment.

The importance of limiting cardiac dose has been highlighted by several studies. Darby et al. [7] previously demonstrated that the risk of major coronary events increases linearly with mean heart dose at a rate of 7.4% per Gy, with no threshold dose. Consequently, every effort should be made to obtain the highest cardiac protection even if cardiac dose is already low in case of right breast RT.

Although cardiac-sparing is most relevant to left breast radiotherapy, our data demonstrate that DIBH is effective in reducing the maximum and mean heart dose, compared to FB even for the right side. Our results confirm those of a previous paper [12] in which the authors concluded that DIBH reduces heart exposure in right breast irradiation. In addition, Pedersen et al. [14], although only in 8 patients, confirmed that DIBH could exclude the heart from irradiated volume in nearly all patients. On the other hand, Essers et al. [15] reported that DIBH in right breast patients did not result in a significant dose reduction to the heart.

We observed that DIBH decreased heart dose in all patients, even if we were able to respect dose constraints with free breathing modality, too.

Our data show a reduction of the maximum dose to the LAD with DIBH. While there is limited data on the effects of radiation on the LAD, a recent study by Patel et al. [16] suggests that high doses to the proximal LAD could predispose patients to coronary artery disease and LAD stenosis.

Another major toxicity of breast radiotherapy is that of the lung. We are aware that increasing pulmonary dose is associated with a higher rate and severity of radiation-induced pneumonitis [17].

We registered an ipsilateral lung dose reduction in patients treated with the DIBH technique because it reduces mean percentage of lung volume receiving ≥ 20 Gy (V20 Gy) compared with FB. These data are in line with previous studies [12, 15]. Noteworthy, DIBH not only reduces the percentage volume of lung receiving 20 Gy, but also reduces lung tissue density [18] which could further contribute to lowering normal tissue complication probability [19]. One of the potentially considerable findings of our study is the significant

reduction in hepatic dose with DIBH, particularly in patients with hepatomegaly, counterbalanced by an increased lung dose.

Radiation-induced liver damage is not commonly associated with breast radiotherapy, but rather with treatments involving the abdomen, lower lobe of the right lung, or distal oesophagus. The clinical impact of high hepatic dose during right-breast radiotherapy remains to be established. We are aware that these results, due to the small number of patients examined, deserves to be confirmed by other studies with more patients and adequate follow-up.

The longer duration of RT treatment is another critical point of this technique. The addition of DIBH can be expected to extend treatment time by three to five minutes.

Another issue, in our experience, is the need to perform 2 planning CTs: one in FB and the other in DIBH modality, given an extra dose to the patient.

Therefore, its real usefulness must be carefully evaluated. The patient's ability to comply with breath-hold requirements is another feature to carefully consider before RT beginning.

Conclusions

Techniques to minimize dose to adjacent OARs need to be improved, due to longer survival in breast cancer patients. We report that the use of DIBH for right-sided BC decreases maximum and mean dose to the heart and maximum dose to the LAD. It decreases V20Gy to the ipsilateral lung too, except in 3 patients with hepatomegaly even if in these cases we registered lower dose to the liver. Therefore, we recommend this modality in case of patients with hepatomegaly as reported by other authors.

This technique is well tolerated by patients and all of them have been able to conclude the RT treatment with this modality. Because of this experience, we strongly recommend careful selection and training of candidates during the planning CT. We only propose DIBH treatment in cooperating patients, to avoid delays during a daily session of RT.

Irrespective of the technique (IMRT or VMAT), the average treatment time was longer with the DIBH mode but this did not compel us to reduce the number of daily treatments.

After this preliminary results, we are treating all breast cancer patients with respiratory gating, regardless of side, with the aim of reducing cardiac, pulmonary and hepatic toxicity.

Finally, this was a planning analysis study with a relatively small number of patients in each group. Future prospective studies, with larger cohorts, should be designed to more robustly determine the dosimetric benefits of adding DIBH to right-breast RT. Long-term follow-up of toxicity and clinical outcomes will be essential in establishing the true value of DIBH in the context of right-sided breast radiotherapy.

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Ethics approval

Ethical approval was not necessary for the preparation of this article.

Contributors

All authors have approved the final article.

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