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Deep inspiration breath hold in left sided tangential breast radiotherapy: Degree of lung inflation needed to compansate for cardiac motion

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► ***Original article***

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ABSTRACT

Background: To determine the degree of lung inflation sufficient to compensate for cardiac motion in patients receiving standard tangential left-breast radiotherapy during deep inspiration breath hold (DIBH). ***Materials and Methods***: Computed tomography (CT) scans were performed in 20 patients with left-sided early breast cancer during free breathing (FB) and DIBH. Standard tangential field plans were generated in both CT sets. Doses to the organs at risk were assessed. The margin between the left anterior descending artery (LAD) and posterior field edge was measured from the closest point. ***Results***: The DIBH plans showed equal coverage of the breasts, so it was possible to obtain lower cardiac doses with DIBH. The median increase in the left-lung volume with DIBH was 53% (range 12.6% - 108%). A LAD safety distance ≥ 5mm from field edges was not obtained in any of the patients during FB, whereas in 60% of the patients during DIBH the safety distance was obtained. The lung inflation rate and cardiac safety distance were strongly correlated. The mean distance between the LAD and tangential field posterior edge increased significantly from 0.23 cm to 0.64 cm (p=0.041) in the patients who inflated their ipsilateral lung > 1.5 times. ***Conclusion***: Lung inflation of ≥50% compensated for cardiac motion during treatment using DIBH. The lung inflation capacity should be considered in choosing the irradiation technique in left-sided breast cancer patients.

INTRODUCTION

Standard treatment for early breast cancer consist of postoperative whole breast irradiation following breast- conserving surgery. Prospective randomized trials have proven that postoperative radiotherapy improves locoregional control and overall survival in both post-lumpectomy and post-mastectomy settings [1,2]. Radiotherapy before the 1980s led to heart diseases due to the use of old radiotherapy techniques, mostly targeting of internal mammary lymph nodes; therefore, an increase in overall survival could not be demonstrated [3,4]. Additionally, therapeutic agents, such as anthracyclines and trastuzumab, which improves overall survival in breast cancer but have cardiotoxic side effects, are also frequently used at present [5,6]. In patients with left-sided breast cancer treated with potentially cardiotoxic chemotherapeutic agents, radiation exposures to the heart should be eliminated modern radiotherapy techniques. For every 1 Gy of radiation, a woman's risk of subsequent heart disease increases by 7.4% starting within 5 years after radiotherapy treatment and continuing for 30 years [7]. Similarly, increased risks have been noted in women with or without cardiovascular risk factors during irradiation. The absolute increase in radiotherapy risk is greater in women with pre-existing cardiac risk factors than other women. Correa *et al.* reported a significantly higher prevalence of left-sided breast abnormalities in irradiated breast cancer patients, with 70% occuring in the left anterior descending artery (LAD) region than in right-sided irradiated breast cancer patients at a median follow-up of 12 years [8]. In a study with long-term follow-up, 50% - 70% of patients treated with left-sided tangents exhibited persistent myocardial perfusion defects 3 to 6 years after irradiation [9]. Intensity-modulated radiotherapy (IMRT) is an alternative method for reducing cardiac doses, but low and moderate cardiac doses as well as contralateral pulmonary and contralateral breast doses are increased with IMRT. Standard tangential fields is a safe method in early breast irradiation, and is recommended by the 2018 ASTRO evidence-based guidelines [10]. Previous studies have shown that treatment with standard tangential fields with deep inspiratory breath holding (DIBH) reduced cardiac structure doses relative to those for free breathing (FB) [11]. Lungs inflated by DIBH push the diaphragm down and move the heart caudally from the chest wall. Presently, despite contemporary radiotherapy techniques with respiratory control part of the cardiac apex or ventricle wall and the remain in the tangential during

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treatment it is possible for a person to hold their breath, but the heart continues to beat.

The focus of earlier studies on respiratory gating in breast cancer radiotherapy has been to decrease cardiac and lung doses, but new studies have examined the movement of the LAD. A study from MD Anderson Cancer Center showed that the LAD should be at a distance of 5 mm from the posterior edge of the planned tangential field to eliminate heartbeat-related movement in treatment with DIBH [12]. A French study that used cardiac-gated CT scans with an intravenous contrast agent to evaluate the three-dimensional (3D) diameter and heartbeat-related LAD movement showed that the average LAD displacement in the 3D axis was approximately 5 mm for all patients [13].

The study aim was to determine the degree of lung inflation sufficient to compensate for cardiac motion in patients receiving standard tangential left-breast radiotherapy during DIBH.

MATERIALS AND METHODS

In this study, patients were prospectively accrued with the approval of the Istanbul Bilim University Research Ethics Committee in March 2014 (44140529/2014-17). Twenty consecutive patients with left-sided early breast cancer after breast-conserving surgery were enrolled in the study after providing written informed consent. For all partients, current international guidelines were used for treatment selections made by a multidisciplinary tumor board. None of patients received neoadjuvant treatment. Chemotherapy was initiated in 13 patients prior to initiation of radiotherapy and mostly consisted of an anthracycline and cyclophosphamide-containing schedule.

Three patients with HER2 positivity also received trastuzumab. Patient information such as age, height, weight, body mass index (BMI), and smoking history was obtained and recorded. None of the patients had a history of chronic lung disease or previous lung surgery, congestive heart failure, or psychiatric diseae. The BMI was classified according to the World Health Organization categories as "Underweight" (<18.5 kg/m2), "Normal weight" (18.5 kg/m2 to <25.0 kg/m2), "Pre-obese" (25.0 kg/m2 to <30.0 kg/m2) and "Obese" (>30.0 kg/m2). According to the normal upper limit of the BMI, the patients were assigned to one of two groups: the ≤25 kg/m2 group and >25 kg/m2 group.

CT simulation

Before computed tomography (CT) scanning; a standardized respiratory training session was given to each patient individually. Patients were supine on the breast board (Civco indexed carbon fiber MT-IL4101; Civco, Kalona, IA, USA) with both arms elevated. Radio-opaque wires were clinically placed to delineate the breast. The CT bore size was 80 cm (GE, Optima CT580). The CT scans were performed during FB and DIBH by using the Real-time Position Management (RPM)™ system (Varian Medical Systems, Palo Alto, CA, USA). Patients were scanned from the mandible to the upper abdomen, including the whole breasts. The slice thickness was 2.5 mm. The RPM™ system was used to measure motion. An infrared reflecting marker was placed over the xiphoid process, and an infrared camera registered~~s~~ the anterioposterior motion of the marker due to respiration. The CT images were transferred to a Varian Eclipse treatment planning Workstation (version 10.0.28, Varian Medical Systems).

Contouring

The contralateral breast, heart, LAD and ipsilateral lung are considered organs at risk (OARs). Body and lung contours were created by dosimetrists using an automatic contouring feature. For consistency, delineation of other structures was performed by the same radiation oncologist (G.A.) according to the Radiation Therapy Oncology Group breast-contouring guidelines [14]. Left breast was drawn as the breast clinical target volume (CTV) following the radio-opaque-wire and 5 mm from the skin surface was removed. LAD contours were drawn from the origin of~~f~~ the main coronary artery to the apex under supervision from a radiologist (M.B.) on all scans. The heart contour began just inferior to the pulmonary artery, inclusive of all major cardiac and vascular structures with the pericardium at that level, and ended when the left and right ventricles were no longer discernible. Lung volumes inside the tangential beams were contoured after treatment plans were ~~done~~ completed following the customized multi-leaf collimator (MLC) blocks.

Treatment planning

Tangents were used with a using 6-MV photon half-beam, and plans were determined to expose 50 Gy in 2-Gy fractions. The field in field (FiF) technique has been used in breast cancer treatment in our clinic since 2009 [15]. The heart was blocked by using customized MLCs without compromising breast CTV in every segment. The calculation algorithm was Eclipse Analytical Anisotropic Algorithm (Version 10.0.28). The grid size in the dose calculation matrix was 0.25 cm. To evaluate the target coverage, 95% of the breast CTV received ≥98% of the prescribed dose. The mean, minimum and maximum doses and volume sizes were obtained from the dose-volume histogram (DVH) statistics. The target conformity index (CI) was calculated by using the formula (V95/ Vbreast CTV), and the homogeneity index for breast CTV was defined as (D2% - D98% / D50%). Central lung distances (CLD) were measured in beam's-eye view. Lung volumes inside the tangential field with

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MLCs were contoured after treatment planning for each plan. The ratio of the lung volume inside the tangential field to the whole ipsilateral lung volume was calculated for each patient. The safety margin between the LAD and posterior field edge was measured from the closest point (figure 1A and -B). Lung volumes were compared between patients with and without ideal LAD safety distance.

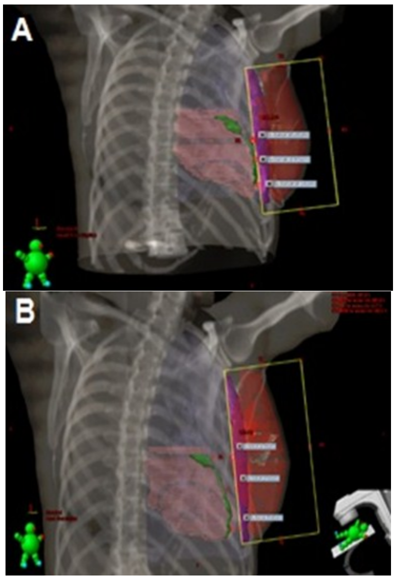

Figure 1. A; Distances between tangential field posterior border and left anterior descending artery during free-breathing. **B;** Distances between tangential field posterior border and left anterior descending artery during deep-inspiration breath hold.

Statistical analysis

SPSS- 22 (Statistical Packages for Social Sciences-version 22) was used for statistical analysis. Dose analysis and volume comparisons of the heart, LAD, ipsilateral lung and contralateral breast in two breathing techniques were assessed by paired samples *t* test. The independent samples *t* test was used to assess the association between ipsilateral lung inflation volume and the LAD safety distance from the field edge. Spearman's rank correlation coefficient was used for correlational analysis. Data were considered statistically significant for p < 0.05.

RESULTS

The median age was 56 (range: 30–79) years. The mean BMI in this study was 27.25 kg/m2 (range, 21–34 kg/m2), and 35% of the patients had a BMI ≤ 25.0 kg/m2. Only three patients had a smoking history. The mean volumes of breast CTV and OARs, and the dosimetric parameters for all 20 patients are shown in table 1. For FiF plans, a median of four segments (range: 3- 4 segments) was used. No significant difference in size was found for the breast CTV between plans. The comparison of DVH parameters for breast CTV were quite similar in both FB and DIBH plans without a significant change in CI and HI.

The percent volumes (7.6% vs 6.8%, p = 0.148) of the ipsilateral lung within the tangential fields were also not significantly different between the two plans. The mean and maximum doses and V5 through V30 values of the heart and LAD significantly decreased with DIBH.

The mean volume of the ipsilateral lung increased significantly during DIBH from 1172 cc (range: 722–1494 cc) to 1810 cc (range: 988–2559 cc) (p < 0.001). The median ipsilateral lung inflation volume was 677 cc (range: 182.3–1154.3 cc), and the median ipsilateral lung inflation ratio was 53.3% (range: 12.6%–108%) for DIBH. Looking at the results another way shows that the ipsilateral lung volume increased from initiation by a median 1.5 (range: 1.12 –2.08) times with DIBH. Only five (25%) patients were able to inflate their lungs >1.8 times.

The LAD was closest to the posterior field edge in the middle 1/3 region. In FB, despite cardiac blocking; a ≥ 5 mm safety margin between the LAD and posterior field edge was not achieved in any of the 20 patients, and the LAD was inside of field in 18 of the 20 patients. Using DIBH technique with customized cardiac blocking, a ≥ 5 mm safety margin to compensate ~~the~~ for cardiac motion was obtained in 60% of (n=12) our study's cohort. Lung inflation significantly correlated with distance between the LAD and posterior field edge. Ten of the 20 patients had <677 cc lung inflation and the total margin from the LAD to posterior field edge was 0.23 cm, whereas the remaining 10 patients had >677 -cc lung inflation and a total margin from the LAD to the posterior field edge of 0.64 cm (p=0.041). In other words, the mean LAD and posterior field edge distances increased significantly from 0.23 cm to 0.64 cm (p=0.041) for the half of our cohort who could inflate their ipsilateral lung by >50% with DIBH.

There was no correlation between the smoking history and ratio of ipsilateral lung inflation since only three patients were smokers, which is probably insufficient for analysis. Age and BMI distribution were more balanced, the BMI median value was found to be 27 (range: 21–34), 40% of the cases were underweight or normal, and 60% were overweight or obese. However, in the correlation analysis, there was no correlation between the patient-spesific factors (age, BMI, smoking) and neither ipsilateral lung inflation rate and nor the LAD distance from field posterior edge.

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Table 1. Comparison of dosimetric results.

	FB mean	DIBH mean	Paired sample *t* test (p value)
Conformity index	0.983	0.939	0.343
Homogeneity index	0.075	0.067	0.184
Breast CTV			
V95 (Gy)	48.88	48.83	0.663
%	97.78	98.15	0.082
Max	107.4	107.4	0.957
Min	45.53	54.07	0.228
Mean	102.3	102.3	0.516
Heart			
Mean (Gy)	1.57	1.02	**<0.001**
Max	46.52	25.47	**<0.001**
V5	3.4	1.31	**<0.001**
V10	1.8	0.36	**<0.001**
V20	1.12	0.1	**<0.001**
V25	0.83	0.04	**<0.001**
V30	0.73	0.02	**<0.001**
LAD coronary artery			
mean	9.44	3.91	**0.001**
Max	36.88	17.95	**<0.001**
V5	42.35	18.97	**<0.001**
V10	23.63	3.61	**<0.001**
V15	18	1.8	**0.002**
V20	14.97	1.07	**0.005**
V25	12.63	0.71	**0.009**
V30	10.53	0.5	**0.014**
Ipsilateral lung			
Volume total (cc)	1172 (722-1494)	1810 (988-2559)	**<0.001**
Volume inside of field (%)	7.6	6.9	0.148
Mean (Gy)	5.6	5.3	0.178
V5	18.8	18.7	0.868
V10	12.6	11.8	0.232
V20	9.3	8.3	0.110
V30	7.6	6.8	0.125
Contralateral breast			
Max	4.43	1.61	0.195
Mean	0.16	0.13	0.285
CLD (cm)	1.82	1.86	>0.05

DISCUSSION

Due to concerns about potential cardiotoxicity, methods to maximize heart protection in breast radiotherapy are being actively investigated. LAD doses cannot be reset in left-breast irradiation due to the proximity of the cardiac apex to the chest wall. Although millimeter-specific treatments can be performed with today's precision technology, all measures should be taken to reduce LAD doses. In this study, we showed that not every patient can fulfill the breath-holding conditions necessary for DIBH. In our study, we could only achieve successful lung inflation that could eliminate cardiac motion in 12 (60%) of the 20 patients, and the LAD moved 0.5–1.3 cm away from the posterior margin in their plans. Dosimetric parameters of the ipsilateral whole lung and the percent ipsilateral lung volume in the tangential field and contralateral breast were not changed with DIBH (table 1).

It was previously shown that greater lung inflation resulteds lower doses to the heart and LAD [16-23]. Some selected studies are summarized in table 2. Compared with those studies, our study obtained the lowest doses to OAR, which may be because cardiac blocking is performed with an MLC in the tangential field without compromising target coverage.

The patients' characteristics have an important role in their inspiration hold capacity. The anatomical variations and racial characteristics of the body, age, obesity, exercise habits, smoking history, comorbidities (such as chronic obstructive pulmonary disease), educational level and treatment anxiety may affect breath-holding performance.

Two studies from Denmark reported that lung volumes almost doubled with DIBH [17, 19]. In the cohort of a study by Register et al. DIBH resulted in a relative increase of 75% in the absolute left-lung volume [24]. Similarly, in a Japanese study the mean volume of the lungs during DIBH increased by ~ 160% relative to that during FB [25]. Tanguturi et al. also showed that greater inspiratory lung volumes benefit from DIBH for cardiac dosimetry in left-sided breast cancer patients [26]. Chang *et al.* [27] obtained results similar to those for our study cohort, and they suggested that the difference in ipsilateral lung volume between DIBH and FB of 1.8 [lung volume in DIBH (cm^3) / lung volume in FB (cm^3)] indicated that the patients obtained more benefit from the DIBH technique with IMRT. Although we individually trained each patient in our cohort for ≥15 minutes with standardized respiratory training, only 25% of the patients were able to inflate their ipsilateral lungs >1.8 times. In our study, ipsilateral lung volumes increased by a median of 1.5 times with DIBH. The threshold value for lung inflation was also given in cc units in previous studies, and ranged from 730 – 1000 cc versus approximately 700 cc found in our study [17,19,24,25].

Consistent with our findings, Schönecker *et al.* revealed that the heart completely moved out of the treatment field during DIBH in six of nine patients in their cohort, in another study from Canada; in 13 of 20 patients, the LAD was completely excluded from the tangential field when using DIBH, and the ratio was similar to that in our study, but they did not investigate the LAD field distance [22,28].

There are conflicting findings in previous studies regarding the relationship between patient-specific factors and effective deep breath holding [18, 25, 26, 29]. In a Japanese cohort, they found that a relative reduction in the mean heart dose correlated with inspiratory volume [25]. The mean BMI was 21.9 kg/m2, and only a few patients were categorized as overweight or obese, which means that their cohort included many underweight patients. In our Turkish cohort, the median BMI was 27 kg/m^2 (range, 21–34 kg/m^2), none of the patients were underweight, 65% of the patients were overweight, and BMI was not

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correlated with inspiratory volume change. Our results concur with Wang *et al.* [28], who stated that desired and feasible cardiac protection could not be achieved with DIBH in all patients with the same BMI profile. As it is not easy to predict which patient can achieve the ideal benefit in DIBH, some centers simulate patients with left-sided breast cancer by using both DIBH and FB scans [26]. Better pre-treatment training procedures can also be developed to reduce patients' anxiety. A new study demonstrated the advantage of educating patients with online materials, such as training videos, that increase their knowledge of radiation treatment [30].

Table 2. Published doses of heart, left anterior descending artery and ipsilateral lung with breathing adapted radiotherapy.

Authors and date	Patient number	Target volume prescribed dose and energy	Technique	Mean heart dose FB	Mean heart dose DIBH	Mean LAD dose FB	Mean LAD dose DIBH	Mean left lung dose FB	Mean left lung dose DIBH
Stranzl *et al.*, 2008 [16]	22	Breast CTV 50Gy 6MV	3D-CRT RPM	2.3Gy	1.3Gy	Not reported		Not reported	
Vikström *et al.*, 2011 [17]	17	Breast PTV 50Gy 6-15MV	V95 > 98% Audiovisual guidance 3D-CRT RPM	3.7Gy	1.7Gy	18.1Gy	6.4Gy	6.9Gy	5.9Gy
Jarvis *et al.*, 2012 [18]	11	Breast CTV or chest wall 50.4Gy	Max ≤ 110% 3D-CRT RPM	(LV*) 2.31-2.38Gy	1.24Gy	8.98-11.32Gy	3.5 Gy	Not reported	
Hjelstuen *et al.*, 2012 [19]	17	Breast PTV and lymphatics 50Gy 6-15MV	3D-CRT RPM	6.2Gy	3.1Gy	25Gy	10.9Gy	21.7Gy	16.4Gy
Swanson *et al.*, 2013 [20]	87	Breast CTV 45Gy	IMRT (step&shoot) ABC	4.23Gy	2.54Gy	Not reported		9.1Gy	7.9Gy
Bolukbasi *et al.*, 2014 [21]	10	Breast PTV 50Gy 6 - 18MV	V95> %98 Forward IMRT Inverse IMRT RPM	1.7Gy 4.9Gy	0.66Gy 3.7Gy	1.7Gy 5Gy	0.8Gy 4Gy	Not reported	
Schönecker *et al.*, 2016 [22]	9	50Gy	Catalysts surface	2.73Gy	1.31Gy	18.9Gy	4.2Gy	8Gy	6.45Gy
Oeschner *et al.*, 2019 [23]	31	Breast PTV 50Gy	3D-FinF RPM	4Gy	1.7Gy	Not reported		10Gy	8.1Gy
Current study	20	Breast CTV 50Gy 6MV	3D-FinF RPM (heart blocked with MLC)	1.57Gy	1.02Gy	9.44Gy	3.91Gy	5.63Gy	5.3Gy

CONCLUSION

In conclusion we demonstrated that irradiated heart and LAD volumes could be significantly reduced in left-sided breast cancer patients by using the DIBH technique without any change in ipsilateral lung and contralateral breast doses. In our study, despite cardiac blocking in FB; none of our patients with a ≥ 5-mm safety margin between the LAD and posterior field edge was achieved. Using the DIBH technique with cardiac MLC blocking a ≥5mm safety margin ~~to~~ that eliminated cardiac motion was obtained when the lung was inflated ≥1.5 times more than in FB. Although DIBH has widespread use, cardiac gating is uncommon, and there is no evidence showing that it is feasible. Therefore, we emphasize that it is best to ignore cardiac motion with an appropriate increase in lung volume. Patient performance to breathe effectively is the primary condition necessary for achieving an ideal left-breast treatment plan with DIBH and the best way to protect patients from the long-term cardiovascular effects of left-lateral breast irradiation.

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Conflicts of Interests: None to declare

Ethical considerations: This study was approved by the Istanbul Bilim University Research Ethics Committee in March 2014 (44140529/2014-17) and was performed in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Patients were enrolled in the study after providing written informed consent.

Authors' Contributions: GA designed the study, radiotherapy plans done by TE, MB made contribution in delineating the LAD volume, GA, SI, SO and MD drafted the manuscript. All authors contributed the interpretation of data; read and approved the final manuscript.

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REFERENCES

1. No authors listed (2000) Early Breast Cancer Trialists' Collaborative Group: Favorable and unfavorable effects on long term survival of radiotherapy for early breast cancer: An overview of the randomised trials. *Lancet, **355**: 1757-1770.*
2. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans V, *et al.* (2005) Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15 year survival: an overview of the randomised trials. *Lancet, **366**: 2087-106.*

[DOI: 10.52547/ijrr.20.2.11]

3. Cuzick J, Stewart H, Rutqvist L, Houghton J, Edwards R, Redmond C, *et al.* (1994) Cause-spesific mortality in long term survivors of breast cancer who participated in trials of radiotherapy. *J Clin Oncol, **12**: 447-453*.
4. Rutqvist LE and Johansson H (1990) Mortality by laterality of the primary tumour among 55,000 breast cancer patients from the Swedish cancer registry. *Br J Cancer, **61**: 866-868*.
5. Jensen BV (2006) Cardiotoxic consequences of anthracycline-containing therapy in patients with breast cancer. *Semin Oncol, **33(3 Suppl 8)**: S15-21*.
6. Telli ML, Hunt SA, Carlson RW, Guardino AE (2007) Trastuzumab related cardiotoxicity: Calling into question the concept of reversibility. *J Clin Oncol, **25**: 3525-3533*.
7. Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Brønnum D, *et al.* (2013) Risk of ıschemic heart disease in women after radiotherapy for breast cancer. *N Engl J Med, **368**: 988-998*.
8. Correa CR, Litt HI, Hwang W-T, Ferrari VA, Solin LJ, Harris EE (2007) Coronary artery findings after left-sided compared with right-sided radiation treatment for early-stage breast cancer. *J Clin Oncol, **25**: 3031–7*.
9. Prosnitz RG, Hubbs JL, Evans ES, Zhou SM, Yu X, Blazing MA, *et al.* (2007) Prospective assessment of radiotherapy-associated cardiac toxicity in breast cancer patients: Analysis of data 3 to 6 years after treatment. *Cancer, **110**: 1840-1850*.
10. Smith BD, Bellon JR, Blitzblau R, Freedman G, Haffty B, Hahn C, *et al.* (2018) Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. *Pract Radiat Oncol, **8(3)**: 145-152*.
11. Bergom C, Currey A, Desai N, Tai A, Strauss JB (2018) Deep ınspiration breath hold: Techniques and advantages for cardiac sparing during breast cancer ırradiation. *Front Oncol, **4(8)**: 87*.
12. Wang X, Pan T, Pinnix C, Zhang SX, Salehpour M, Sun TL, *et al.* (2012) Cardiac motion during deep-inspiration breath-hold: implications for breast cancer radiotherapy. *Int J Radiat Oncol Biol Phys, **82(2)**: 708-14*.
13. Nicolas E, Khalifa N, Laporte C, Bouhroum S, Kirova Y (2021) Safety Margins for the Delineation of the Left Anterior Descending Artery in Patients Treated for Breast Cancer. *Int J Radiat Oncol Biol Phys, **109(1)**: 267-272*.
14. https://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx.
15. Ercan T, Igdem S, Alco G, Zengin F, Atilla S, Dinçer M, *et al.* (2010) Dosimetric comparison of field in field intensity-modulated radiotherapy technique with conformal radiotherapy techniques in breast cancer. *Jpn J Radiol, **28 (4)**: 283-289*.
16. Stranzl H and Zurl B (2008) Postoperative irradiation of left-sided breast cancer patients and cardiac toxicity: Does deep inspiration breart hold technique protect the heart? *Strahlentherapie und Onkologie, **??**: 354-358*.
17. Vikström J, Hjelstuen MH, Mjaaland I, *et al.* (2011) Cardiac and pulmonary dose reduction for tangentially irradiated breast cancer, utilising deep inspiration breath-hold with audio-visual guidance, without compromising target coverage. *Acta Oncol, **50**: 42-50*.
18. Jarvis LA, Maxim PG, Horst KC (2012) Deep inspiration breath hold reduces dose to the left ventricle and proximal left anterior descending artery during radiotherapy for left- sided breast cancers. J of Cancer Therapy, **3**: 673-679.
19. Hjelstuen MHB, Mjaaland I, Vikström J , Dybvik KI (2012) Radiation during deep inspiration allows loco-regional treatment of left breast and axillary-, supraclavicular- and internal mammary lymph nodes without compromising target coverage or dose restrictions to organs at risk. *Acta Oncologica, **51**(3): 333-344*.
20. Swanson T, Grills IS, Ye H *et al.* (2013) 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. *Am J Clin Oncol, **36(1)**: 24-30*.
21. Bolukbasi Y, Saglam Y, Selek U, *et al.* (2014) Reproducible deep-inspiration breath-hold irradiation with forward intensity-modulated radiotherapy for left-sided breast cancer significantly reduces cardiac radiation exposure compared to inverse intensity -modulated radiotherapy. *Tumori, **100**: 169–178*.
22. Schönecker S, Walter F, Freislederer P, *et al.* (2016) Treatment planning and evaluation of gated radiotherapy in left-sided breast cancer patients using the CatalystTM/SentinelTM system for deep inspiration breath-hold (DIBH). *Radiat Oncol, **11**: 143*.
23. Oechsner M, Düsberg M, Borm KJ, *et al.* (2019) Deep inspiration breath-hold for left sided breast irradiation: Analysis of dose-mass histograms and the impact of lung expansion. Radiat Oncol, 14, 109.
24. Register S, Takita C, Reis I, Zhao W, Amestoy W, Wright J (2015) Deep inspiration breath-hold technique for left-sided breast cancer: An analysis of predictors for organ-at-risk sparing. *Med Dosim, **40(1)**: 89-95*.
25. Yamauchi R, Mizuno N, Itazawa T, Saitoh H, Kawamori J (2020) Dosimetric evaluation of deep inspiration breath hold for left-sided breast cancer: analysis of patient-specific parameters related to heart dose reduction. *J Radiat Res, **61(3)**: 447-456*.
26. Tanguturi SK, Lyatskaya Y, Chen Y, Catalano PJ, Chen MH, Yeo WP, *et al.* (2015) Prospective assessment of deep inspiration breath-hold using 3-dimensional surface tracking for irradiation of left-sided breast cancer. *Pract Radiat Oncol, **5(6)**: 358-65*.
27. Chang CS, Chen CH, Liu KC, Ho CS, Chen MF (2020) Selection of patients with left breast cancer for IMRT with deep inspiration breath-hold technique. *J Radiat Res, **61(3)**: 431-439*.
28. Wang W, Purdie TG, Rahman M, Marshall A, Liu FF, Fyles A (2012) Rapid automated treatment planning process to select breast cancer patients for active breathing control to achieve cardiac dose reduction. *Int J Radiat Oncol Biol Phys, **82(1)**: 386-93*.
29. Mkanna A, Mohamad O, Ramia P, Thebian R, Makki M, Tamim H, *et al.* (2018) Predictors of Cardiac Sparing in Deep Inspiration Breath-Hold for Patients With Left Sided Breast Cancer. *Front Oncol, **27(8)**: 564*.
30. Kumar KA, Balazy KE, Gutkin PM, Jacobson CE, Chen JJ, Karl JJ, *et al.* (2021) Association Between Patient Education Videos and Knowledge of Radiation Treatment. *Int J Radiat Oncol Biol Phys, **109(5)**:1165-1175*.

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