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Scientific Article

Continuous Positive Airway Pressure−Assisted Breathing With Supine Tangential Left Breast Radiation Therapy When Deep Inspiration Breath-Hold Radiation Therapy Was Ineffective or Unsuitable: Clinical Implications for an Affordable Heart-Sparing Breast Radiation Therapy to Reduce the Health Care Disparities in Low-Resource Settings

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Purpose: To report continuous positive airway pressure (CPAP)-assisted breathing with supine tangential left breast radiation therapy (CPAP-RT) when deep inspiration breath-hold RT (DIBH-RT) was ineffective or unsuitable.
Methods and Materials: Ten patients with left breast cancer underwent computed tomography simulation scan (CT-sim) under DIBH followed by CPAP-assisted breathing (15 cm H_2O) to create CPAP-RT plans in authors' institute. Reasons for CPAP-RT include inability to reproduce DIBH (n = 5), DIBH-RT plan exceeded dose limits to the heart (n = 2), and unable to proceed with planned DIBH-RT due to mechanical issues (n = 3). Radiation target volumes and organs at risk were contoured according to published atlas data. For dosimetric comparison, supine tangential fields for breast only RT (Breast-RT) and wide-tangential fields for breast + internal mammary nodal RT (Breast + IMN-RT) were used with prescription of 40 Gy in 15 fractions on each patients' CT-sim with free-breathing (FB), DIBH, and CPAP-assisted breathing, respectively.
Results: Planning target volume (PTV) coverage was acceptable and comparable in all RT plans. Compared with FB, both DIBH and CPAP-assisted breathing inflated the thorax and increased left lung volume on average by 46% and 51%, respectively (FB: 1230 vs DIBH: 1802 vs CPAP-assisted breathing:1860 cc, $P < .01$), and increased the shortest distance between PTVeval-Breast to the heart by 5.6 ± 3.0 and 11.9 ± 3.6 mm ($P < .01$) and to LAD by 4.9 ± 2.9 and 10.8 ± 4.3 mm, respectively ($P < .01$). Compared with FB, both DIBH and CPAP significantly reduced radiation dose to the heart and LAD. A mean dose to the heart ($Heart_{Dmean}$) was FB: 2.3 ± 0.9, DIBH: 1.2 ± 0.7, and CPAP: 0.9 ± 0.4 Gy in Breast-RT ($P < .01$); FB: 3.2 ± 1.7, DIBH: 1.7 ± 0.8, and CPAP: 1.3 ± 0.5 Gy in

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Data are stored in an institutional repository and will be shared upon request to the corresponding author and approval from an institutional authority.

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Breast + IMN-RT ($P < .01$). LAD_{Dmean} was FB: 11 ± 4.5, DIBH: 5.4 ± 3.2, and CPAP: 2.4 ± 0.9 Gy in Breast-RT ($P < .01$); FB: 15.5 ± 7.8, DIBH: 7.4 ± 4.1, and CPAP: 3.5 ± 1.4 Gy in Breast + IMN-RT ($P < .01$). A maximum dose to LAD (LAD_{Dmax}) was FB: 35.8 ± 8.7, DIBH: 22.4 ± 15.4, and CPAP: 7.8 ± 5.3 Gy in Breast-RT ($P < .01$); FB: 38.7 ± 5.0, DIBH: 25.3 ± 15.2, and CPAP: 10.2 ± 6.8 Gy in Breast + IMN-RT ($P < .01$). All patients successfully completed CPAP-RT.

Conclusions: CPAP-RT provides efficient and practical heart and LAD sparing RT using simple supine tangential fields for Breast-RT or wide-tangential fields for Breast + IMN-RT when DIBH-RT was ineffective or unsuitable. With its easy accessibility and low infrastructural requirement, CPAP-RT can provide affordable heart-sparing left breast RT to reduce the health care disparities in low-resource settings.

Introduction

Deep inspiration breath-hold (DIBH) is a well-established and commonly adopted technique in radiation centers that offer heart-sparing radiation therapy (RT) to patients with left-sided breast cancer. These heart-sparing effects with DIBH come from intrathoracic changes such as increased thorax inflation and heart displacement away from the chest wall compared with free-breathing (FB). To accomplish DIBH, however, patients are required to physically coordinate and mentally attend to complex procedures and instructions. Although a majority of patients tolerate DIBH, a fair number of patients are reportedly unable to take advantage of heart-sparing effects from DIBH due to individual physical and/or psychological factors.[1,2]

Alternate heart-sparing left breast RT modalities include prone-position RT, volumetric arc therapy (VMAT), and proton therapy (PT). However, the prone position is usually limited to breast-only radiation therapy (Breast-RT), not for postmastectomy radiation therapy, and may not be suitable for patients requiring regional nodal stations including internal mammary node RT (Breast + IMN-RT).[3-5] VMAT with DIBH (VMAT-DIBH) usually requires 2 to 3 times the monitor units of a 3-dimentional conformal RT (3DCRT), which results in increased treatment time and corresponding increased integral dose. With increased treatment time for daily VMAT-DIBH, some patients need multiple pauses and repeating DIBH, which can trigger physical and mental fatigue and further elongate daily treatment time. Additional physics time for quality assurance and analysis of VMAT plan and the mechanical stress associated with delivering a VMAT compared with 3DCRT are also notable. More advanced RT techniques (VMAT, PT) would require more infrastructural resources and increase financial toxicity for both patients and radiation centers than a simple 3DCRT technique such as the supine tangential RT.[6]

Continuous positive airway pressure (CPAP) is an established medical device for patients with obstructive sleep apnea. Like DIBH, CPAP inflates the thorax and displaces the heart away from the chest wall.[7-11] As a safe home-use device, CPAP can be easily implemented in radiation centers and assist patients to take deep inspiration and inflate the thorax during RT without adding a large treatment-related burden on both patients and radiation centers. Therefore, integrating CPAP-assisted breathing with RT can be an affordable and efficient heart-sparing left breast RT technique when patients cannot achieve heart-sparing benefits from DIBH-RT.

Herein, authors report experiences of CPAP-assisted breathing radiation therapy (CPAP-RT) for patients with left-sided breast cancer when their DIBH-RT was ineffective or unsuitable.

Methods and Materials

Patients

Between January 2022 and August 2023, 10 patients with left-sided breast cancer could not proceed with DIBH-RT in our institute (6 Breast-RT and 4 Breast + IMN-RT). Of the 10 patients, 5 patients tolerated DIBH during computed tomography simulation (CT-sim) but couldn't reproduce suitable DIBH during RT; 2 patients' DIBH-RT plan exceeded a mean dose to the heart ($Heart_{Dmean}$) per our institutional protocol (<2 Gy in Breast-RT and <4 Gy in Breast + IMN-RT); and 3 patients could not receive planned DIBH-RT due to mechanical issues at the time. Initial DIBH-RT plans were created using a respiratory gating for scanners system (RGSC, Varian Medical System, Palo Alto, CA) with the audio−video coaching device. The median age of patients was 59 years old (range, 36∼71 years). All 10 patients agreed to try CT-sim under CPAP-assisted breathing for planning CPAP-RT before considering VMAT or PT for heart-sparing RT. The institutional review boards waived a board review on this case series. All patients provided signed consent for using CPAP and reporting the results of their cases.

CPAP-assisted breathing during CT-simulation

Before CT-sim, the individual maximum tolerable air pressure was determined for each patient by gradually ramping up the air pressure to 15 cmH_2O with 0.21 of fraction of inspired oxygen with the use of an individual mask interface. Radiation therapists and/or nurses set up and measure the individual maximum tolerable air pressure for the patients according to the institutional pulmonology clinic guidelines. After 15 minutes of CPAP-assisted breathing, patients underwent CT-sim in the same supine position using the same Vac-lok bag on a breast board for CT-sim with both FB and DIBH.

RT planning

Clinical target volumes for breast and regional nodal stations and organs at risk (OARs) were contoured on all CT-sims according to the RTOG 1304 protocol and published guidelines.[12,13] The left anterior descending coronary artery (LAD) was defined as beginning from the end of the left main coronary artery passing anteriorly behind the pulmonary artery to the interventricular groove on noncontrast CT-simulation scans.[12] A 0.7-cm isometric expansion from clinical target volume for breast was applied for planning target volumes (PTVs). PTV-breast was edited anteriorly to 3 to 5 mm under the skin and excluded sternum and intrathoracic structures (lung, heart) to create the PTV evaluation (PTV*eval*). For dosimetric comparison, prescription of 40 Gy in 15 fractions without boost was given to PTVs for all RT plans in this report. Eclipse RT planning system, version 15.6 (Varian Medical Systems) was used with a Varian Trilogy or Edge linear accelerator using 6-MV photons. In plan evaluation, we aimed to achieve the planning objectives set forth in the institutional protocol (Appendix E1). For Breast-RT, 2 tangential fields covering the PTV-breast were used. Two wide tangential fields covering PTV-breast and IMN and anterior−posterior fields covering PTV-supraclavicular were used for Breast + IMN-RT. The beam's-eye view was used to shape multileaf collimators to block the heart, LAD, lung, and other OARs. Field-in-field techniques were used to maximize dose homogeneity. RT planning aimed to reduce dose to OARs without compromising the coverage of the PTVs.

Daily CPAP-assisted breathing RT

After RT plan evaluations and comparisons, all patients received CPAP-assisted breathing RT. On each treatment day, patients started CPAP-assisted breathing in the waiting area for 15 minutes and continued CPAP-assisted breathing while they were escorted to the treatment room and throughout the daily treatment. The institutional sleep clinic policy was followed to manage and clean CPAP devices.

Statistics

Statistical analysis of dosimetric comparison between RT plans was done using a Student *t* test. Data are presented as mean ± standard deviation. A probability level of a P value < .05 was considered significant.

Results

Intrathoracic changes with CPAP-assisted breathing

All patients tolerated CPAP-assisted breathing with an air pressure of 15 cmH_2O. Intrathoracic changes with DIBH and CPAP-assisted breathing are shown in Table 1 and Fig. 1. Compared with FB, both DIBH and CPAP-assisted breathing significantly inflated the thorax and increased left lung volume on average by 572 cc and 630 cc (46% and 51% increase, respectively, $P < .01$). Both DIBH and CPAP-assisted breath also displaced the heart more caudally and posteriorly than with FB (Fig. 1), which increased the closest distance from PTV*eval* to the heart by 5.6 ± 3.0 and 11.9 ± 3.6 mm, respectively ($P <$ .01) and to LAD by 4.9 ± 2.9 and 10.8 ± 4.3 mm, respectively ($P < .01$), in comparison with FB.

RT plan evaluations

All RT plans with FB, DIBH, and CPAP-assisted breathing demonstrated acceptable PTV and/or PTV*eval* structure coverage per our institutional protocol: ≥95% receives 40 Gy, except ≥90% receives 40 Gy for PTV-IMN.

Radiation dose to OARs with CPAP-assisted breathing RT

A dosimetric comparison of RT plans with FB, DIBH, and CPAP-assisted breathing is shown in Table 1. Increased distances from PTV-breast to the heart and LAD with both DIBH and CPAP-assisted breathing significantly decreased radiation dose to the heart and LAD in both DIBH-RT and CPAP-RT in comparison with FB-RT. Compared with FB, $Heart_{Dmean}$ was decreased on average by1.0 Gy (46% reduction) with DIBH and 1.4 Gy (58% reduction) with CPAP-assisted breathing in Breast-RT plans ($P < .01$); 1.4 Gy (43% reduction) and 1.8 Gy (55% reduction) in Breast + IMN-RT plans ($P < .01$).

An LAD_{Dmean} was significantly decreased by both DIBH and CPAP-assisted breathing than its status with FB: average 5.5 Gy (52%) and 8.5 Gy (75%) of reduction with DIBH and CPAP-assisted breathing, respectively, in

Table 1 **Dosimetric comparison of RT plans with FB, DIBH, and CPAP-assisted breathing**

	Breast-RT (tangential fields)				Breast + IMN-RT (wide-tangential fields)			
	FB	DIBH	CPAP	*P* value	FB	DIBH	CPAP	*P* value
Heart								
to PTV*eval*, mm	2.6	8.1	14.4	**<.01**	2.6	8.1	14.4	**<.01**
D_{mean}, Gy	2.3	1.2	0.9	**<.01**	3.2	1.7	1.3	**<.01**
LAD								
to PTV*eval*, mm	6.7	11.6	17.5	**<.01**	6.7	11.6	17.5	**<.01**
D_{mean}, Gy	11.0	5.4	2.4	**<.01**	15.5	7.3	3.5	**<.01**
D_{max}, Gy	35.8	22.4	7.8	**<.01**	38.7	25.3	10.2	**<.01**
Left lung								
Volume, cc	1230	1802	1860	**<.01**	1230	1802	1860	**<.01**
D_{mean}, Gy	6.7	6.3	5.5	NS	14.5	12.5	11.8	**<.01**
V20, %	13.4	12.5	11.3	NS	32.1	27.5	25.2	**<.01**

Abbreviations: CPAP = continuous positive airway pressure—assisted breathing; D_{max} = maximum dose; D_{mean} = mean dose; DIBH = deep inspiration breath hold; FB = free-breathing; IMN = internal mammary nodal station; LAD = left anterior descending artery; RT = radiation therapy; to PTV*eval* = average shortest distance from heart or LAD to PTV*eval*; V20 = volume receiving equal or greater than 20 Gy.
Values in boldface indicate the significantly different comparison results.

Breast-RT plans ($P < .01$); 8.2 Gy (53%) and 12 Gy (76%) of reduction in Breast + IMN-RT plans ($P < .01$). Maximum dose to LAD (LAD_{Dmax}) was lowered on average by 13.4 Gy (42% reduction) with DIBH and 28 Gy (79% reduction) with CPAP-assisted breathing than its status with FB in Breast-RT plans ($P < .01$); by 13.4 Gy (37% reduction) and 28.5 Gy (75% reduction) in Breast + IMN-RT plans ($P < .01$).

Increased left lung volume with both DIBH and CPAP-assisted breathing resulted in a trend of less radiation dose (but not statistically significant) to the left lung in Breast-RT plans compared with FB. However, in Breast + IMN-RT plans, both D_{mean} and V20 to the left lung were significantly decreased on average by 2 Gy (13.8% reduction) with DIBH and 2.7 Gy (18.6% reduction) with CPAP-assisted breathing (all $P < .01$).

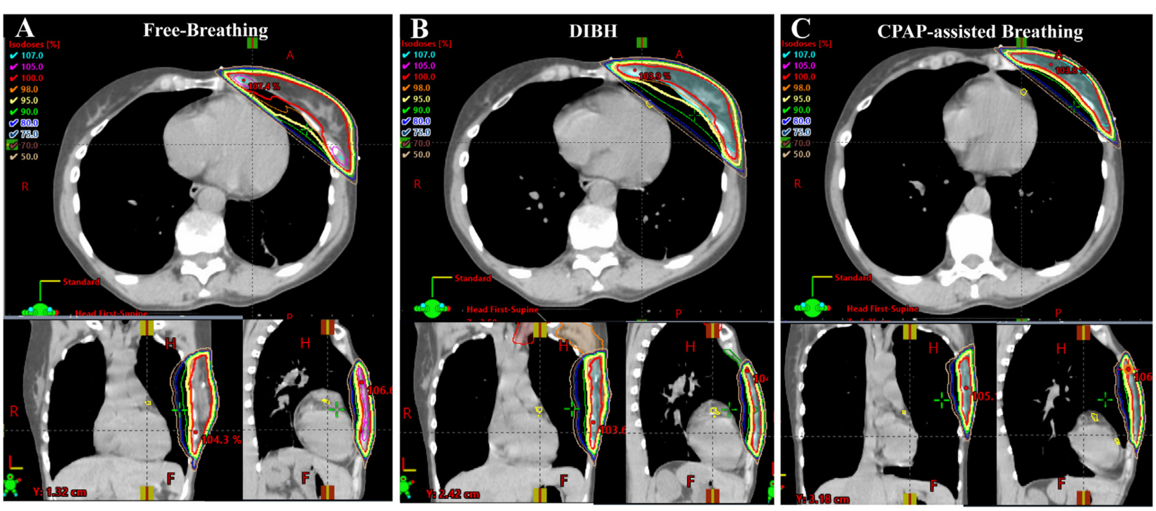

Figure 1 Digitally reconstructed images from computed tomography (CT)-simulation scans representative intrathoracic changes and radiation dose distribution in left breast only radiation therapy plan under free-breathing (A), deep-inspiration breath hold (DIBH) (B), and continuous positive airway pressure (CPAP)-assisted breathing (C) at the same axial, coronal, and sagittal level in same patient. Patient starts CPAP-assisted breathing in the patients waiting area at least 15 minutes before CT-simulation and scheduled daily treatment and continues CPAP-assisted breathing during treatment.

Discussion

The risk of cardiac toxicity after left breast RT is well documented. Darby et al[14] reported that rates of major coronary events increased linearly without threshold by 7.4% per 1 Gy of $Heart_{Dmean}$ among patients who received breast RT in the mid-to-late 1990s. Their analysis, however, was made from a case−control study using reconstructed $Heart_{Dmean}$ from 2-dimentional RT data. Data from modern RT techniques and CT-based planning have shown an association of increased cardiac events and increase radiation dose to the heart and its substructures.[15,16] Among cardiac substructure, the LAD is located along the anterior interventricular groove and ended near the apex of the heart. As such, LAD can be within or close to the supine tangential RT fields, which is a commonly used RT technique to treat breast cancer. In retrospective analysis of women who received left breast RT from 2012 to 2018, it has been reported a correlation between radiation dose to LAD_{Dmean}, LAD_{Dmax}, and the $Heart_{Dmean}$ with cardiac events and suggested a threshold for major cardiac events of $Heart_{Dmean}$ 1.3 Gy and LAD_{Dmean} 3.0 Gy.[15,17]

Radiation dose to the heart and LAD is inversely proportional to the square distance from PTV*eval* on chest wall. Since the chest wall can be vertically elevated away from the heart during inspiration, advanced respiration management techniques such as DIBH have been widely adopted in radiation centers to detect and deliver RT only when patients are in the deep inspiration phase of their breathing cycle. With increased distance between the heart and chest wall, DIBH-RT for left breast cancer has markedly decreased radiation dose to the heart and LAD compared with RT with FB.[1,2,18-20] In our clinic, patients who successfully underwent moderately hypofractionated DIBH-RT for left breast cancer had an average $Heart_{Dmean}$ of 1.0 Gy and lung volume of 1906 cc with $Lung_{Dmean}$ of 6.0 Gy and V20 of 11.1% in Breast-RT plans. Breast-IMN-RT plans produced 1.8 Gy, 1799 cc, 11.5 Gy and 24.4% in Breast-IMN-RT plans, respectively.

Although there are dosimetric advantages from intrathoracic changes with DIBH over FB, it has been reported that 20% to 30% of patients with left breast cancer were unable to follow DIBH maneuvers.[1,2,15] Of note, data also suggest that the heart-sparing effects from DIBH can vary among the patients who tolerated DIBH procedures, as 12% to 26% of patients with left breast cancer did not demonstrate dosimetric benefits from DIBH.[18,19,21] Individual physical factors such as breathing characteristics, smoking history, decreased thoracic tissue flexibility with age, pre-existing lung and/or heart disease, variation of intrathoracic anatomy, and psychological factors such as anxiety, depression, and level of understanding of DIBH maneuvers can hinder patients accomplishing successful heart-sparing benefits from DIBH-RT.

Compared with DIBH maneuvers, CPAP-assisted breathing is a more intuitive and less patient-dependent procedure. All patients in this report including 5 patients who couldn't reproduce suitable DIBH had successfully completed CPAP-RT with significant heart-sparing benefits over FB-RT (Table 1) regardless of age or intrathoracic anatomy. Interestingly, the shortest distance from PTV*eval* to the heart and LAD was increased with CPAP-assisted breathing (heart: 14.4 ± 4.8 and LAD: 17.5 ± 4.7 mm) in comparison with DIBH (heart: 8.1 ± 4.9 and LAD: 11.6 ± 3.7 mm). As such, 2 patients in this report whose breast-only DIBH-RT exceeded our institutional dose limits to the heart ($Heart_{Dmean}$ greater than 2.0 Gy: 2.8 and 2.1 Gy, respectively) were able to achieve $Heart_{Dmean}$ less than 2.0 Gy (1.9 and 1.3 Gy, respectively) without compromising PTV coverage using a simple tangential RT under CPAP-assisted breathing. For other 3 patients who accomplished successful DIBH for Breast + IMN-RT but underwent CPAP-RT due to mechanical issues at that time, CPAP-RT further lowered radiation dose to the heart and LAD compared with DIBH: average absolute reduction by 0.5 Gy on $Heart_{Dmean}$ and by 4.7 Gy on LAD_{Dmean}. More favorable intrathoracic changes such as further posterior−inferior displacement of the heart (Fig. 1) and vertically elevated chest wall with an increased lung volume (Table 1) under CPAP-assisted breathing compared with DIBH can explain aforementioned further dosimetric benefits in CPAP-RT in those patients. Such heart-sparing benefits from CPAP-assisted breathing has been also reported in postmastectomy radiation therapy case as well.[8] Moreover, Breast + INM-RT plans using wide-tangential field under CPAP-assisted breathing in this report showed average $Heart_{Dmean}$ to 1.3 Gy and LAD_{Dmean} to 3.5 Gy, which are comparable with those using VMAT and to the proposed threshold dose ($Heart_{Dmean}$ 1.3 Gy and LAD_{Dmean} 3.0 Gy) for major cardiac events.[9,15,17]

Although CPAP-RT data in this report demonstrated favorable dosimetric benefits comparable with DIBH-RT, reproducibility of heart-sparing effects during daily CPAP-RT would be of concern before implementing this technique. In their retrospective analysis of 4D CT under CPAP in 20 female patients with lung cancer, Choi et al[9] reported the average intrafractional breast movement less than 5 mm (2.5 ± 2.0 mm, 1.8 ± 1.4 mm, and 0.5 ± 0.5 mm in the craniocaudal, anteroposterior, and mediolateral directions, respectively). Using daily cone-beam CT (CBCT) data, they also reported the interfractional absolute average heart movement of 2 ± 2 mm under CPAP. In a healthy volunteer study, Liang et al[22] reported that CPAP resulted less interfractional lung volume variation compared with those with FB. Likewise, analysis of 40 daily CBCT images under CPAP-assisted breathing in 2 patients in our institute also demonstrated an interfractional absolute average heart movement of less than 4 mm. Altogether, CPAP-assisted breathing has demonstrated high compliance, efficient heart-sparing effect, and good reproducibility in daily supine tangential RT for patients with left breast cancer.

As with any treatment, careful evaluation of patients before considering CPAP-RT is important. Although CPAP-assisted breathing under an air pressure of 15 cmH_2O is a well-tolerated procedure, certain patients with history of pneumothorax, interstitial pulmonary diseases, pulmonary blebs, or any risks of pulmonary barotrauma would need pulmonology evaluations to determine availability of CPAP-assisted breathing and/or to set appropriate individual air pressure. In such cases, VMAT or other advanced heart-sparing RT techniques would be more appropriate than CPAP-RT. Patient's preference on respiration management techniques is also an important consideration before applying CPAP.

Nonetheless, our experiences using CPAP-RT in a community radiation center well corroborate published data[7-11,22] and suggest CPAP-RT can be considered as an efficient heart-sparing left breast RT for those who failed to achieve heart-sparing benefits from DIBH.

Conclusions

CPAP-RT is a simple and efficient heart-sparing technique for patients with left-sided breast cancer when their DIBH is ineffective or unsuitable. In addition, with its easy accessibility and low infrastructural requirement compared with other heart-sparing RT techniques, CPAP can be easily implemented in radiation centers to provide an affordable and practical heart-sparing left breast RT technique to reduce the health care disparities in low-resource settings.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2024.101472.

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