ORIGINAL ARTICLE

Voluntary inspiration breath-hold for left sided breast irradiation: Heart and lung doses; Dosimetric comparison with free respiration Three-Dimensional Conformal Radiotherapy

Amr Abdelaziz, MD[1]; Azza Helal, MD[2]

(1) Clinical Oncology Department, Faculty of Medicine, Alexandria University
(2) Medical Physics Unit, Diagnostic Imaging Department, Faculty of Medicine, Alexandria University

Corresponding Author: Dr. Azza Helal, MD
Medical Physics Unit, Diagnostic Imaging Department,
Faculty of Medicine, Alexandria University, Egypt
E-mail: helals2002@yahoo.com

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Abstract

Introduction: Radiation is widely used to prevent recurrences for breast cancer and so it is quite effective to decrease breast cancer mortality. But it has shown that radiation increases the risk of heart and lung diseases so increases their mortality. This is more common in the left sided breast cancer patients. The mean cardiac dose of a left-sided breast cancer can be two or three times that for a right-sided breast cancer and the mean ipsilateral lung dose can be two or three times the mean contralateral lung dose.

Various approaches have been taken to reduce the dose to heart and lung during breast irradiation. These methods include 3D dose planning, inclusion of an electron field, proton therapy, intensity-modulated radiation therapy (IMRT), respiratory gating, and deep inspiration breath-hold. All these methods have proven to reduce the dose to the heart to relatively low levels without compromising PTV coverage.

Purpose: The aim of this study is to investigate the role of deep inspiration breath-hold to reduce heart and lung dose for left-sided breast cancer treatment using tangential fields and to compare the dose to heart and lung with free respiration technique.

Methods: A computed tomography (CT) simulation is performed for 10 patients with left sided breast cancer with the patient supine in breast board with arms above the head. Each patient will have two scans; free breathing and voluntary deep inspiration breath-hold scan. The clinical breast borders are outlined with radiopaque markers. The CT data will be transferred to CMS treatment planning system (Xio, Germany).

All required structures are contoured. They include the PTV which is defined as the breast borders excluding the first 5 mm of tissue under the skin. The heart and both lungs are contoured. The heart is contoured starting just below the branches of the pulmonary trunk to the most inferior part of the heart near the diaphragm. All CT scans will be planned, calculated and treated with a 6 MV photon beam on a Primus linear accelerator (Siemens, Germany). Optimized plans are carried out using medial & lateral wedged tangential photon fields to encompass the breast volume. The dose of 45Gy in 20 fractions is prescribed to the isocenter which is placed at the center of the PTV. The dose is normalized to a point two thirds the perpendicular distance from the skin to the posterior border of the field at mid-separation on isocenter slice. The coverage of PTV is evaluated using the dose to 95% of the planning target volume ($D_{95\%}$). Sparing of the lung and the heart are assessed using the volume of lungs that receives 20Gy (V_{20Gy}) and the volume of the heart that receives 2.5Gy, 5Gy, 10Gy and 20Gy ($V_{2.5\ Gy}$, $V_{5\ Gy}$, $V_{10\ Gy}$, $V_{20\ Gy}$). The dose to 5% of heart volume ($D_{5\%}$) and mean heart dose are also recorded for all plans. All plans during free respiration and breath hold techniques are compared and analyzed statistically. Consent was obtained from all participating patients.

Introduction

External beam radiotherapy is an essential component of breast conservation therapy in the treatment of breast cancer. It is considered as a safe and effective treatment option for women with early-stage breast cancer. After breast-conserving surgery, adjuvant radiotherapy delivered to the whole breast is known to be the current standard of care for early stage breast cancer.[1,2]

The most commonly used technique to treat the whole residual breast and to minimize radiation exposure to the heart and lung consists of two opposing tangent beams to the chest wall [1]. Randomized, retrospective and population based studies have shown that the radiotherapy of the chest wall is associated with a significantly increased risk of developing ipsilateral second lung cancer and in patients treated on the left side with a significantly increased risk of cardiac morbidity and mortality. [3,4]

The curvature of the chest wall and breast motion due to breath-related chest wall motion cause some volume of lung and heart (in left-sided breast cancers) to be included in the radiation beam. Also adding a margin to the whole residual breast to account for setup and organ motion variations and to obtain the planning target volume (PTV) is considered as an important factor for increasing the volume of lung and heart in the radiation field. [1]

The dose to normal heart depends on patient anatomy, radiation technique, the location of the tumor bed in the breast, total dose delivered and fractionation scheme.

When radiation therapy is limited to the breast itself it does not increase the risk of cardiovascular disease. However, when the chest wall or either internal mammary chain of lymph nodes is included in the radiation field, as in post-operative radiotherapy, the risk is increased. [2,5]

The dose to the heart also depends on whether right or left breast is irradiated. A number of studies suggest that left sided breast irradiation using tangential irradiation can cause cardiac injury in some patients with an increased risk of coronary artery disease and myocardial infarction compared with irradiation of the right breast. This is because for left-sided breast cancer, a larger volume of heart may be included in the tangential fields. [6,7]

The range of cardiovascular problems that can follow intense irradiation of the heart is in fact very broad. It includes pericardial disease, acute pericarditis during irradiation, pericardial effusion, constrictive pericarditis, myocardial dysfunction, diffuse myocardial fibrosis and coronary artery disease (CAD). There was some evidence that most of the deaths were due to radiation-induced damage to the small blood vessels of the heart. The addition of some chemotherapy to radiation causes an increased risk of congestive heart failure. [8]

The exact relationship between dose volume information and cardiac injury is still not clear. Although some authors suggested that the volume of the heart that receives 2.5Gy, 5Gy, 10Gy and 20Gy ($V_{2.5\ Gy}$, $V_{5\ Gy}$, $V_{10\ Gy}$, and $V_{20\ Gy}$) are predictives of coronary heart disease, others suggested that mean cardiac dose and dose to 5% of the heart volume ($D_{5\%}$) are predictors for coronary heart disease. [2] $D_{5\%}$ was also chosen because there is evidence that a small volume of heart exposed to large doses of radiation can result in significant cardiac complications. So radiotherapy techniques used for treatment of breast cancer should minimize the dose to the heart. [9-11]

To reduce the volume of heart and lung which is irradiated breast motion immobilization during inspiration can be used. Modern radiation delivery techniques can also be used to allow precise delivery of radiation to the breast away from the heart so the heart receives a minimal dose. These methods include three dimension conformal radiotherapy (3DCRT), intensity-modulated radiation therapy (IMRT), deep inspiration breath-hold and respiratory gating. [12-17]

Breathing causes parts of heart to move into and out of radiation fields however with the deep inspiration breath-hold position for treatment of breast cancer patients the distance between the heart and chest wall due to the expansion of the lungs is maximized causing reduction of the dose to the lung and heart. Also with respiratory gating technique, irradiation can be restricted only in the inspiratory phase and so the distance between heart and chest wall will be increased. As a result the dose to the heart, particularly to the anterior wall can be reduced. [18]

Aim

The aim of this study was to investigate the role of deep inspiration breath-hold to reduce heart and lung dose for left-sided breast cancer treatment using tangential fields and to compare the dose to heart and lung with free respiration technique.

Materials and Methods

A computed tomography (CT) simulation was performed for 10 left sided breast cancer patients aged from 38-59 years. The patients included in the present study treated from August 2010 to June 2011 in Ayady Almostakbal Oncology centre. CT-simulation was performed in the supine position on breast board with the arms positioned above the head. Each patient had two scans; free breathing and voluntary deep inspiration breath-hold scan. In breath-hold scan, all patients were asked to voluntary hold their breath during the scan; it took about 30 second which was not long time for holding the breath and so all patients were tolerate the scan without complain. The clinical breast borders were outlined with radio-opaque markers. Then CT data were transferred to CMS treatment planning system (Xio, Germany).

All required structures were contoured. They include the PTV which is defined as the chest wall excluding the first 5 mm of tissue under the skin. Whole heart and both lungs volumes were contoured entirely. The heart was contoured starting just below the branches of the pulmonary trunk to the most inferior part of the heart near the diaphragm. Table 1 shows the volumes of lungs, heart and PTV during free respiration and breath hold techniques.

Both scans for all patients were planned, calculated and treated on a Primus linear accelerator (Siemens, Germany). Optimized plans were carried out using medial & lateral wedged tangential photon fields. To optimize coverage of the PTV, and to reduce the dose to the lung and heart and to avoid contralateral breast irradiation beam angles, wedge angles, and beam weighting were chosen. Gantry angles ranged from 298° to 303° for the medial fields and from 121°.to 129° for the lateral fields. In some cases field in field technique was used to decrease the area of high dose and to improve the dose distribution. Collimator rotation 10^0-15^0 was done. The dose rate of the machine is 200 Mu/min & the time of delivery was 1-2min /field. The patients were treated only using free breath technique; the breath hold technique was done in this study for comparing issues.

The dose of 45Gy in 20 fractions was prescribed to the isocenter which is placed at the center of the PTV on isocenter slice.

The coverage of PTV was evaluated using the dose to 95% ($D_{95\%}$) of the planning target volume. Sparing of the lung and the heart were assessed using the percentage volume of lungs that receives 20Gy (V_{20Gy}) and the percentage volume of the heart that receives 2.5Gy, 5Gy, 10Gy and 20Gy ($V_{2.5\ Gy}$, $V_{5\ Gy}$, $V_{10\ Gy}$, $V_{20\ Gy}$). The dose to 5% of heart volume ($D_{5\%}$) and mean heart dose were also recorded for both plans. these parameters were obtained from dose-volume histograms (DVH).

Table 1 Mean volume of PTV, lungs and heart during free breath and deep inspiration breath-hold techniques. P values are from Wilcoxon Signed-Ranks test.

Volume in CC^3	Free breath mean	Deep inspiration mean	Difference	Difference %	P Value
PTV	227.54 (57-668)	239.68 (54-652)	12.14	5	0.241
Rt lung	1448 (943-2657)	1966 (1156-2698)	518	35.77	0.009
Lt lung	1313.85 (710-2556)	1744 (891-2543)	430.15	32.74	0.017
Heart	441.65 (285-593)	469.42 (291-710)	27.77	6	0.445

Statistical analysis:

This study included 10 patients, for each patient 2 planes were done one during free breath and the other during deep inspiration breath-hold technique. Then the two plans for all patients were compared using visual inspection of the dose distribution, dose volume histogram and dose volume histogram parameters. $D_{95\%}$ of the PTV, V_{20Gy} of left & right lung and all heart dose volume parameters mentioned above during free breath and breath hold techniques were listed and analyzed statistically using excel sheet and SPSS (version18). Comparison of the dosimetric parameters of the two plans for the ten patients was done by Wilcoxon signed Rank test. A P value of less than 0.05 was taken as statistically significant. (Table 2).

Results

This study compared plan parameters of opposed tangential 3DCRT using free breathing and voluntary deep inspiration breath-hold techniques for radiotherapy of the left sided chest wall for 10 breast cancer patients after mastectomy.

For all patients, the PTV, lungs and heart were contoured. For free breath and deep inspiration breath-hold techniques respectively, the mean volume of the PTV (chest wall) was 227 & 239.68cm^3, of both lungs was 1448, 1313.85cm^3 & 1966, 1744 cm^3 for right and left lung respectively and of the heart was 441.65 & 469.42 cm^3 (table1).

For all patients two scans; free breathing and voluntary deep inspiration breath-hold scans were performed. The treatment planning and dose volume histograms of all patients were reviewed, Relevant plan parameters of opposed tangential 3DCRT using free breathing and voluntary deep inspiration breath-hold techniques were listed in table 2.

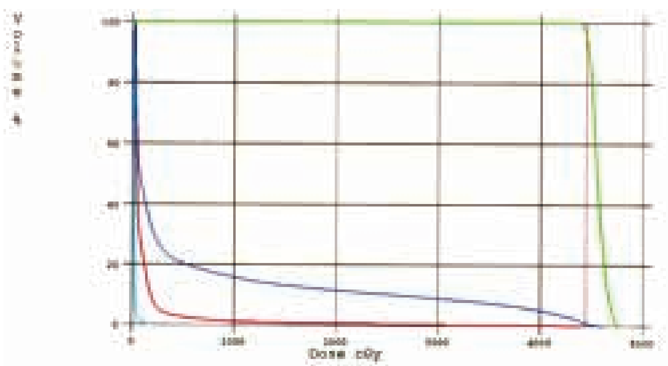
Our data show that deep inspiration breath-hold techniques of the chest wall significantly reduce the heart dose-volume parameters in patients treated on the left side chest wall compared to free breathing (figure 1). All patients planned with deep inspiration breath hold showed an average reduction of 27.8%, 51%, 59% , 65%, 38% & 31% in $V_{2.5\ Gy}$, $V_{5\ Gy}$, $V_{10\ Gy}$, $V_{20\ Gy}$, heart mean dose and $D_{5\%}$ respectively compared to free breath technique. As shown in table 2 the reduction was significant for all parameters (P values are <0.05) except for $D_{5\%}$, the reduction was not significant (p=0.093).

Regarding lungs V_{20Gy}, for both techniques the mean of the percentage volume of the left lung that received 20 Gy was equal and less than tolerance value (V_{20Gy}=9.31% for both techniques). For right lung the dose was almost negligible & there is no volume received 20Gy or more so we did not list the results. (Figure 1).

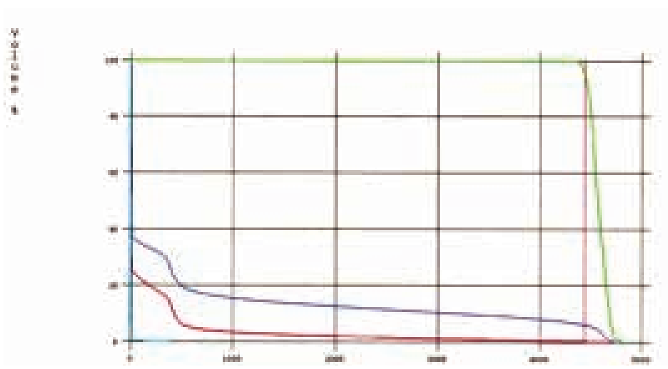
Regarding PTV coverage, the coverage was excellent and did not show any significant difference between both techniques (P=0.415), the mean of $D_{95\%}$ (the dose in Gy to 95% of target volume) is about 44Gy for both techniques. (Figure 1).

Table 2. Plan parameters for free breath versus deep inspiration breath-hold techniques used in irradiation of the chest wall in post mastectomy breast cancer patients. Mean of the volume is in %. P values are from Wilcoxon Signed-Ranks test.

Dose volume parameters	Free breath Mean	Deep inspiration Mean	Difference	Difference %	P Value
PTV $D_{95\%}$ in Gy	44.23 (44-45)	44.43 (44-45)	0.2	0.5	0.415
Left lung V_{20Gy}	9.31 (3-18)	9.31 (1-16)	0	0	0.878
Heart $V_{2.5\ Gy}$	19.17 (9-45)	13.84 (5-39)	-5.33	-27.80	0.017
Heart $V_{5\ Gy}$	5.88 (1-11)	2.88 (0-9)	-3	-51	0.007
Heart V_{10Gy}	3.51 (0-8)	1.44 (0-6)	-2.07	-59	0.007
Heart V_{20Gy}	2.18 (0-5)	.76 (0-4)	-1.42	-65	0.011
Heart $D_{5\%}$ in cGy	669.80 (91-1598)	462.08 (250-1535)	-207.72	-31	0.093
Heart Mean dose in cGy	195 (64-373)	121.50 (34-299)	-73.5	-38	0.012



(A)



(B)

Fig1: Dose volume histogram parameters in cGy for target volume in green, heart in pink, left lung in deep blue & right lung in pale blue comparing deep inspiration breath-hold technique (A) and free breath technique (B)

Discussion

Various approaches have been taken to reduce the dose to organs at risk during breast irradiation without compromising PTV coverage. These methods include 3D dose planning, proton therapy, intensity-modulated radiation therapy (IMRT), deep inspiration breath-hold, and respiratory gating. [12-17]

Many authors have demonstrated a dosimetric benefit of deep inspiration breath-hold techniques compared to free breath techniques used in irradiation of the chest wall in post mastectomy breast cancer. 3D conformal breath hold technique is a method that can be used to reduce dose to the heart and to reduce the secondary cancer risk by reducing the lung dose volume. [3,12-15]

As Taylor et al [20] suggested that the dose to different cardiac structures may be a more important predictor of cardiac morbidity and mortality than the volume of heart irradiated, so beside the volumes of heart that received different doses we also used $D_{5\%}$ in this study. $D_{5\%}$ was also chosen because there is evidence that a small volume of heart exposed to large doses of radiation can result in significant cardiac complications.

In the present study, we dosimetrically compared 3D conformal free and breath hold breast irradiation techniques for the same patients. Breath hold technique showed a significantly smaller volume of irradiated heart for all doses evaluated as well as a significant reduction in mean heart dose. $D_{5\%}$ was also reduced but the reduction was not significant. Both techniques showed excellent target coverage and low left lung $V_{20Gy,}$ (there was no significant differences between both techniques). We found that our dosimetric results are in agreement with the literatures.

In our study the mean of dose to the heart was 1Gy and $D_{5\%}$ was 4Gy. Both were far lower than cardiac tolerance investigated by Carr ZA et al [9] who found a statistically significant elevated risk of coronary heart disease for patients who received a mean heart dose of 2.8 Gy and D_5 value of 12.9 Gy.

Brosius FC et al [21] found that radiation induced heart disease have been observed in patients who received therapeutic doses of about ≥35 Gy to partial volumes of the heart. McGale et al [22] also suggested a relationship between cardiac mortality and low radiation doses in the range of ≤4 Gy. The values of the present study were lower; the volume that received 20 Gy was 0.76% and no volume received 35Gy or more & $D_{5\%}$ was 4.6Gy.

In T. A. Swanson study [23], there was a statistically significant decrease in heart, ipsilateral lung, and both lungs dosimetric parameters evaluated for each patient favoring the delivery of deep inspiration breath hold over free breath.

In Keiko Nemoto et al study [24], deep inspiration breath hold led to significant cardiac sparing effect compared with free breath. The median lung volume receiving 20 Gy or more was 5.0% for free breath, and 4.3% for deep inspiration breath hold. There were no significant differences between each respiratory phase. We achieved also reductions in all heart parameters but for lungs, For both techniques the value was lower than tolerance, left lung V_{20Gy} for both plans was equal 9% and there was no significant difference between both plans as found by keiko et al.

Zsuzsanna Kahán et al [25] found a significant positive associations between the development of lung abnormalities (pneumonitis or fibrosis) 3 months or 1 year after the radiotherapy and the age of the patient, the ipsilateral mean lung dose (MLD>15Gy), the radiation dose to 25% of the ipsilateral lung (D25%>26Gy) and the volume of the ipsilateral lung receiving 20 Gy (V20 Gy>30%). In our study we achieved a significant lower left lung V_{20Gy} (9%) than achieved by Zsuzsanna Kahán et al [25] for both plans.

Lind PA et al [26] found an association between pulmonary complications and increasing age and irradiated lung volume (V20), the cut-off level for pulmonary complications (mild or moderate) was V20 Gy =29% (ipsilateral lung volume).

Remouchamps et al [13]. achieved a reduction in heart V30 Gy and lung dose in patients with left-sided breast cancer for moderate deep inspiration breath hold during adjuvant whole breast radiotherapy in left-sided breast cancer patients. Our dosimetric results are also in agreement with the this study.

In the study done by Sixel et al [14]. Deep inspiration showed a significant dose-volume histogram improvement with decreases in the heart volume receiving 25 Gy of more than 40 cc and a relative reduction of 31.4% for V30Gy lung and 91.0% for V30Gy heart was recorded.

Conclusions

As breath hold technique significantly reduces the dose-volume parameters of the heart with significant sparing of cardiac tissue and relatively similar low lung dose volume parameters and excellent PTV coverage compared with free respiration so it should be used as the main technique for radiotherapy of the left sided chest wall of postmastectomy breast cancer patients.

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