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Comparison of Radiotherapy Techniques in Breast Cancer with Inclusion of Internal Mammary Nodes through Thermoluminescent Dosimetry in a RANDO Phantom

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ABSTRACT

Introduction: In various radiotherapy techniques for breast cancer, the inclusion of internal mammary nodes (IMNs) in the target volume is important for selecting the most appropriate technique. This study aimed to compare three radiotherapy techniques with the inclusion of IMNs regarding the dose homogeneity index (DHI) of regional lymph nodes and the chest wall, besides the dose received by the heart and the left lung.
Material and Methods: Three radiotherapy techniques were planned for CT imaging of the RANDO phantom, including the wide tangent (WT); oblique parasternal photon (OPP); and oblique parasternal electron (OPE) techniques. The doses reaching the contoured organs were compared between the three techniques, using the data gathered from the thermoluminescent dosimetry and treatment planning system.
Results: The OPE technique produced a lower absorbed dose for the left IMNs, compared to the other two techniques. In the OPP technique, the dose received by the left lung was higher than its tolerance, while the lung dose in the OPE technique was slightly lower than the WT technique. The absorbed dose by the heart was the lowest in the WT technique; also, the DHI value was better for this technique than the other two techniques.
Conclusion: The WT technique showed better results regarding the dose homogeneity distribution of IMNs and the chest wall, as well as protection of organs at risk.

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Introduction

Breast cancer is one of the most common malignancies in women. The prevalence of this cancer is growing rapidly around the world, and reports show that its incidence and mortality rates are on the rise [1]. The most common treatment methods for breast cancer include surgery (breast conservation and mastectomy), radiotherapy, chemotherapy, hormone therapy, and targeted therapy, although further research is required to improve these methods [2]. Breast cancer patients may experience a local/regional recurrence in the chest wall, internal mammary nodes (IMNs), axillary lymph nodes, and supraclavicular lymph nodes [3]. However, a combination of surgery and radiotherapy can significantly reduce the risk of local recurrence and decrease the rate of breast cancer mortality in the long term [4].

Radiotherapy increases the risk of cardiotoxicity, especially in women with left breast cancer and patients with pneumonia. Various methods have been evaluated to protect the heart and the lungs in breast cancer radiotherapy. Some of these methods include the tangent technique using electron beams, intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), tomotherapy, deep inspiration breath hold (DIBH), and prone positioning in patients undergoing breast-conserving surgeries [5-7]. In all of these methods, the presence of IMNs in the target volume increases the risk of cardiac and ipsilateral lung toxicity [8]; therefore, one of the controversial issues in breast cancer radiotherapy is the IMN irradiation [9].

Several studies have investigated the effect and the necessity of IMN irradiation in breast cancer radiotherapy [9-13]. Whelan et al. conducted a retrospective study on 1832 patients in two nodal irradiation and control groups [14]. They concluded that extra radiation of local nodes in breast irradiation did not improve the overall survival after a ten-year follow-up, while it reduced the recurrence rate of

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breast cancer. Poortmans et al. also investigated the effect of regional nodal irradiation on the survival of women with early-stage breast cancer [15]. Their results showed that after a median follow-up of 10.9 years, there was no significant difference between the two groups concerning the overall survival; nonetheless, breast cancer mortality was reduced in the nodal irradiation group. Their findings revealed that attention to the irradiation of lymph nodes during breast external beam radiation is advantageous.

Considering the anatomical variations and the inclusion of IMNs in the planning target volume (PTV), different radiotherapy techniques can be used for breast cancer irradiation [16]. In some developing countries, there is no advanced radiotherapy equipment, such as IMRT or VMAT; therefore, use of conventional techniques is common. Nonetheless, these techniques must be compared to identify the optimal technique, which can provide a homogenous dose distribution in PTV, while reducing the dose received by the organs at risk (OARs).

In this study, we aimed to compare three different breast cancer radiotherapy techniques, including the wide tangent (WT), oblique parasternal photon (OPP), and oblique parasternal electron (OPE) techniques in terms of the dose homogeneity index (DHI) of the left supraclavicular, axillary, and internal mammary lymph nodes and the left chest wall, as well as the dose received by the heart and the left lung. These techniques were also compared in terms of the dose received by the chest wall, lymph nodes, and OARs. The results of our comparisons could indicate which technique delivers the most homogeneous dose distribution to the target volume, while delivering the lowest dose to the heart and the lungs. Therefore, based on the results of this study, we can select the optimal technique to reduce the dose delivered to the OARs, which is essential for improving radiotherapy for breast cancer patients.

Materials and Methods

An Alderson-RANDO adult male phantom (Phantom Laboratory, NY, USA) was used in this study as a mastectomy patient. This phantom consists of 33 slices, with a thickness of 2.5 cm; the slices are numbered from the top to the bottom of the phantom. All slices contain holes, where the thermoluminescent dosimeters (TLDs) can be positioned. In this study, the TLDs were placed within slices 10 to 16 inside the phantom, including the chest, supraclavicular, and axillary regions.

TLD calibration

Dose measurements were carried out, using lithium fluoride TLDs, including TLD-100 (Harshaw-Bicron, Cleveland, OH, USA) and TLD-700 (ProRaD, Germany) with dimensions of 3×3×0.9 mm^3. TLD-100 and TLD-700 were used for photon and electron dosimetry, respectively. The annealing procedure continued for one hour at 400°C, and then, for ten minutes at room temperature, and finally, for two hours at 100°C. For dosimeter calibration, the TLD-100 and TLD-700 chips were exposed by a Primus Plus linear accelerator (Siemens AG, Erlangen, Germany). As build-up materials, Perspex slabs, with thickness of 1.5 and 2.5 cm, were used for TLD-100 and TLD-700, which were irradiated with 6-MV photon beams and 15-MeV electron beams, respectively. Also, a 30×30×20 cm^3 Perspex phantom was placed beneath the exposed TLDs to eliminate the backscattering beams. The dosimeters were read using the Harshaw 3500 reader.

The TLDs were exposed to a calibration dose of 0.5 Gy to determine the element correction coefficients (ECCs) and also the reader calibration factor (RCF). Next, these values were used to plot the dose-response curve. For this purpose, 18 TLD-100 chips were divided into six groups, and each group was exposed to a certain amount of photon dose in the range of 1.5-2.5 Gy (1.5, 1.6, 1.8, 2.0, 2.2, and 2.5 Gy). Also, 24 TLD-700 chips were divided into eight groups, and each group was exposed to a certain amount of electron dose within the range of 1.1-2.5 Gy in 0.2 Gy increments.

Simulation and treatment planning

Computed tomography (CT) images were acquired from the phantom in the supine position by a Somatom Emotion Duo CT Scanner (Siemens Co., Germany) with a slice thickness of 5 mm. The CT images of the phantom were transported to a Prowess Panther treatment planning system (TPS) version 5.2. Next, the left supraclavicular, axillary, and internal mammary lymph nodes, the left chest wall, the heart, and the left lung were contoured on each slice of CT images by an experienced oncologist. The field arrangements in all three treatment plans included a 15-MV anterior supraclavicular field and a 15-MV posterior axillary field. Also, in the WT technique, two opposed 6-MV tangential photon beams (medial and lateral views are shown in Figure 1) and two 6-MV segmented fields were used.

The WT plan included parasternal lymph nodes, and a multileaf collimator was used to protect the OARs. In the OPP and OPE techniques, two opposed 6-MV tangential photon beams were used in a similar manner. A 6-MV anterior oblique photon field and a 15-MeV anterior oblique electron field were added to two tangential beams in the OPP and OPE techniques, respectively. The prescribed dose for all three techniques was 50 Gy in 25 daily fractions of 2 Gy. A transverse view of the field arrangement in each technique is depicted in Figure 1. The dose-volume histograms (DVHs) of the countered organs were obtained and compared between the three techniques.

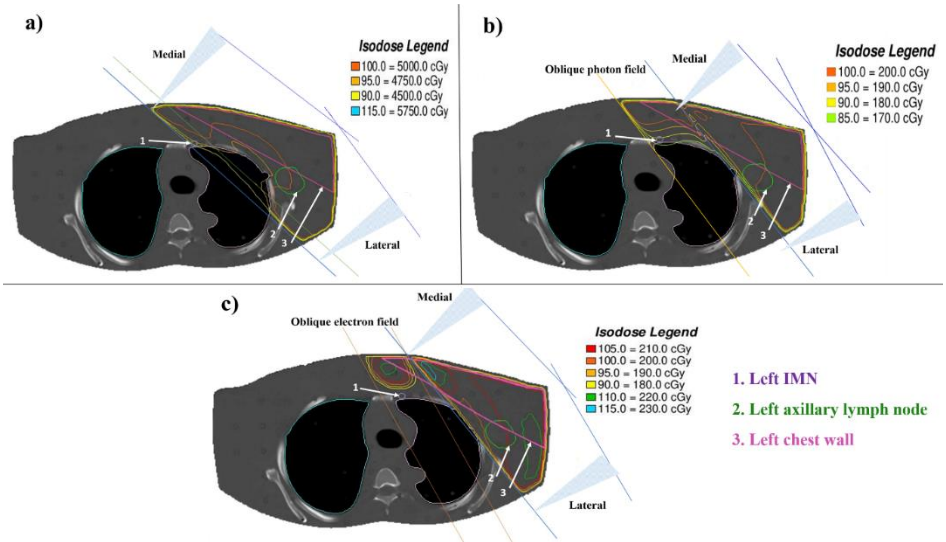

Figure 1. The transverse view of the field arrangement in a) the WT technique, b) the OPP technique, and c) the OPE technique

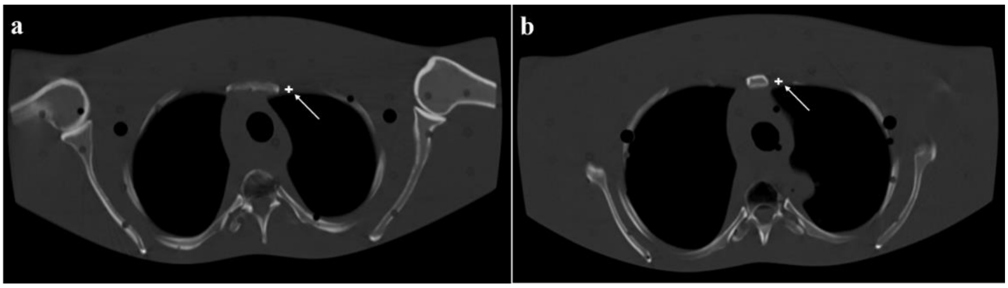

Figure 2. The TLD locations for IMN dose measurements in the slice number a) 13 and b) 14 of the phantom.

Dose measurements in the phantom

For the WT and OPP techniques, an Artiste linear accelerator (Siemens AG, Erlangen, Germany) was used. The OPE technique was performed, using the Primus Plus linear accelerator (Siemens AG, Erlangen, Germany). Three TLD chips were used for the left supraclavicular and axillary lymph nodes. Also, six TLD chips were considered for the left chest wall, while 14 and five TLD chips were used for the left lung and the heart, respectively. Considering the fixed location of the prefabricated holes in the phantom, the dosimetry of small contoured volumes, such as the IMNs in this study, may not be possible. Therefore, besides the standard grid of holes in the phantom to accommodate TLDs, custom plates with special holes for inserting the chips into the IMNs were designed. Two TLDs were placed using the mentioned approach in the phantom slices (No. 13 and 14) for the IMN dose measurements. The phantom CT images, indicating the TLD locations, are shown in Figure 2.

In both WT and OPP techniques, TLD-100 chips were positioned in proper locations in the slices of RANDO phantom. Next, the phantom was irradiated, based on the assigned treatment plan. The abovementioned procedure was repeated four times for each technique to increase the accuracy of dosimetry; then, the measured values were averaged for each point. The OPE technique was performed in two steps to consider the electron scattering effect, caused by the electron field. In the first step, all photon fields were irradiated simultaneously, based on the related treatment plan, while all TLDs were planted in small holes prepared in the phantom. Therefore, the adsorbed doses by TLDs related to the other beams were considered.

In the second step, the TLD-700 chips were positioned in the parasternal region of the phantom and the surrounding areas. Next, the phantom was exposed by the 15-MeV anterior oblique electron field. Finally, the total dose received by each point was calculated by adding the measured values in the two previous steps. This procedure was repeated four times for each step, and the measured values were averaged for each point.

Statistical analysis

SPSS was used to analyze the collected data, and the Explore procedure was performed to determine the data distribution in each contoured organ. One-way analysis of variance and Tukey’s test were then performed to compare the data related to various techniques in the left supraclavicular, axillary, and internal mammary lymph nodes, as well as the left chest wall. On the other hand, for the heart and left lung measurements, non-parametric Mann-Whitney U test was utilized.

Results

The dose-response values, read by TLD-100 and TLD-700 dosimeters, are presented in Figure 3. The best-fitted graphs were plotted as dose-response curves, and the resulting equation was considered for the TLD measurements in the non-linear range of higher doses.

The results of TLD measurements for the left chest wall, left lung, heart, and lymph nodes are shown in Table 1. These values are the means and standard deviations (SDs) of four measurements, multiplied by 25 (25 sessions of 2 Gy daily fractions) after a complete treatment course (50 Gy).

The P-values for the comparison of the three techniques, based on Tukey's and Mann-Whitney U tests, are shown in Table 2. The results indicated that the mean doses received by the left supraclavicular and axillary lymph nodes and the left chest wall were the same, and no significant differences were found in any of the three techniques (P>0.05). However, in the OPE technique, the mean absorbed dose of the IMNs was lower than the other two techniques; nevertheless, no significant differences were found between the OPE and the other two techniques (P>0.05), considering the large SD of the OPE technique.

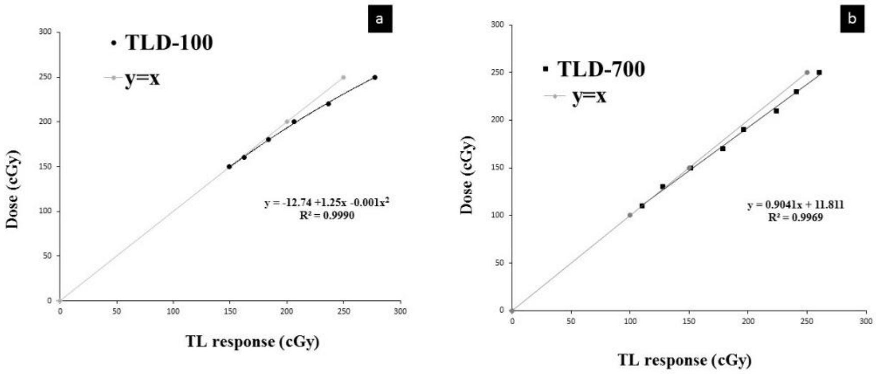

Figure 3. The TLD dose-response curves: a) TLD-100 (black circles) and b) TLD-700 (black squares). The grey lines (plotted by grey circles) depict the y=x line as the expected linear response of TLDs at low doses, and the black lines de

Table 1. The average absorbed dose and SD of the contoured lymph nodes, chest wall, and critical normal organs in the three irradiation techniques, based on the TLD measurements in the phantom

	Mean±SD dose (Gy)		
	WT technique	OPP technique	OPE technique
Left supraclavicular nodes	48.10±1.60	48.15±3.21	49.47±2.05
Left axillary nodes	49.63±3.51	48.88±3.22	47.31±3.64
Left IMNs	47.93±4.06	47.69±4.25	39.87±16.24
Left chest wall	51.56±2.32	50.80±2.47	48.26±3.91
Left lung	26.78±20.05	39.36±6.68	19.95±18.52
Heart	1.64±0.41	18.03±18.28	5.48±4.43

SD= Standard deviation; WT= Wide tangent; OPP= Oblique parasternal photon; OPE= Oblique parasternal electron; TLD= Thermoluminescent dosimeter.

Table 2. Multiple comparisons of the three radiotherapy techniques regarding the measured TLD doses

	P-value		
	WT vs. OPP	WT vs. OPE	OPP vs. OPE
Left supraclavicular nodes	0.99	0.33	0.39
Left axillary nodes	0.90	0.26	0.64
Left IMNs	0.99	0.26	0.28
Left chest wall	0.88	0.11	0.24
Left lung	0.09	0.35	0.00
Heart	0.00	0.00	0.01

WT= Wide tangent; OPP= Oblique parasternal photon; OPE= Oblique parasternal electron; TLD= Thermoluminescent dosimeter.

As summarized in Table 2, the mean absorbed dose by the left lung in the OPP technique was significantly higher than that of the OPE technique (P<0.05). According to a study by Emami, the mean doses of 7, 13, 20, 24, and 27 Gy for the lung lead to pneumonia, with probabilities of 5%, 10%, 20%, 30%, and 40%, respectively [17]. In the present study, the mean absorbed dose by the left lung was within the tolerance level in the WT and OPE techniques, while in the OPP technique, it was higher than the tolerance level (Table 1).

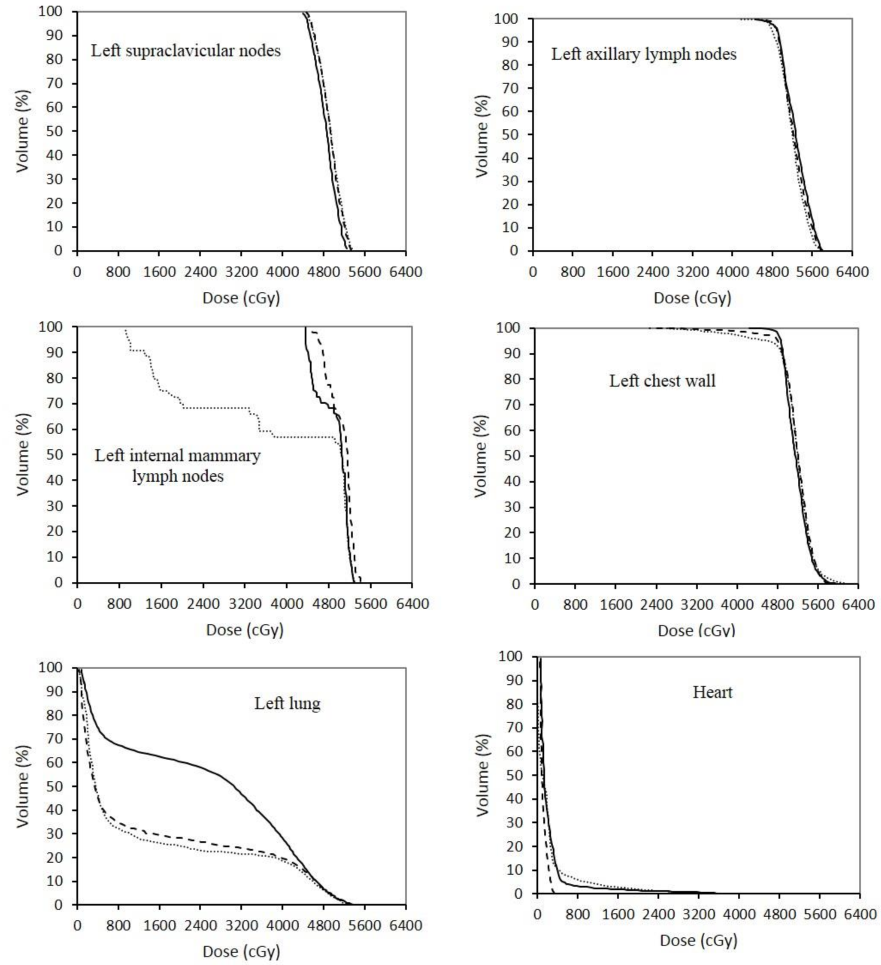

Figure 4. A comparison of DVHs for the contoured organs using the three radiotherapy techniques. The dashed curves represent the WT technique, the solid curves represent the OPP technique, and the dotted curves represent the OPE technique

Table 3. The DHI values of the left chest wall and the investigated lymph nodes in the radiotherapy techniques

	DHI		
	WT technique	OPP technique	OPE technique
Left supraclavicular nodes	0.90	0.89	0.89
Left axillary nodes	0.89	0.89	0.88
Left IMNs	0.90	0.87	0.24
Left chest wall	0.89	0.90	0.85

WT= Wide tangent; OPP= Oblique parasternal photon; OPE= Oblique parasternal electron; DHI= Dose homogeneity index.

As shown in Table 2, the lowest mean absorbed dose by the heart was obtained using the WT technique, while the highest absorbed dose was found in the OPP technique. All three techniques were found to be significantly different ($P<0.05$). In this regard, Emami reported that a mean dose <26 Gy delivered to the heart could cause pericarditis with a probability of 15% [17]. In our study, the mean absorbed dose by the heart was within the tolerance level of the heart in all three techniques (Table 1).

The DVHs of the countered organs in the three techniques are shown in Figure 4. In this figure, for better comparisons, the DVHs of the three techniques for each investigated organ were plotted separately. The maximum doses in the WT, OPP, and OPE techniques were 57.75, 58.20, and 58.85 Gy, respectively, using the TPS system.

Based on the TPS data, the DHI values of the left chest wall and the lymph nodes for the three techniques are summarized in Table 3. The DHI values were calculated according to the following equation [18]:

DHI= D≥ 95% (within PTV)/D≥5% (within PTV)

In this equation, the numerator of the fraction refers to the dose reaching 95% of the PTV (D≥95%), and the denominator denotes the dose reaching 5% (D≥5%) of the PTV.

Discussion

In most breast cancer patients, there are common problems in the irradiation of IMNs, as the anatomical position of these nodes leads to a higher dose received by the ipsilateral lung and the heart, especially in patients with left-sided breast cancer [19]. Many techniques can be used to reduce the dose delivered to healthy organs, while delivering the prescribed dose to the target volume. In many medical centers with advanced radiotherapy facilities, such as IMRT and DIBH, the problem of IMN irradiation has been considerably resolved. On the other hand, conventional methods are applied in radiotherapy centers that lack such facilities. Therefore, these methods should be compared to find the optimal one for reaching a more homogenous dose distribution in the target volume, while reducing the dose received by the OARs.

In the present dosimetric study, the dose received by the chest wall, lymph nodes, left lung, and heart during breast cancer radiotherapy of the RANDO phantom, as a mastectomy patient, was measured. Next, using the conventional radiotherapy equipment, the three breast cancer radiotherapy techniques were compared. According to the DVHs, the OPE technique could not cover the IMNs sufficiently, and the coverage of these nodes in the WT technique was better than the OPP technique. Also, the TLD measurements were consistent with the DVH results.

Based on the dose measurements using TLDs (Table 1), the dose received by the left IMNs was decreased in the OPE technique (39.87±16.24 Gy), compared to the WT and OPP techniques (47.93±4.06 Gy and 47.69±4.25 Gy, respectively). The insufficient dose coverage in the OPE technique is due to the rapid energy loss of electron beams and also the high thickness of the chest wall in the phantom. It should be noted that the average chest wall thickness of the RANDO phantom is approximately 4 cm in the parasternal region, whereas in a real mastectomy patient, the average chest wall thickness is about 1.6 cm [20].

In this regard, Dogan et al. [21] compared the coverage of IMNs, using three different breast cancer radiotherapy techniques, including wide field (WF), OPE, and perpendicular photon electron (PE) techniques. In the WF technique, the tangential fields contained mammary IMNs. Also, in the oblique and perpendicular PE techniques, a combination of electron and photon beams was planned obliquely or perpendicularly to cover the IMNs, respectively. They concluded that the coverage of IMNs in the WF technique was superior to the PE technique, which is in line with the results of the present study. In another study, Dogan et al. [16] compared the WF, OPE, perpendicular PE, and oblique-electron techniques and found similar results that confirmed their previous findings.

Based on the DVHs in Figure 4, the coverage of the supraclavicular and axillary lymph nodes and also the chest wall was similar in all three techniques. Also, the TLD measurements in Table 1 show that the mean dose reaching the regions of interest were approximately the same for all three techniques; also, the P-values shown in Table 2 did not indicate any significant differences between the three techniques. Moreover, the DHI values for the chest wall and contoured lymph nodes were compared between the three treatment plans. The results shown in Table 3 indicate that the dose homogeneity of the left supraclavicular and left axillary lymph nodes was almost the same in all three techniques (supraclavicular: 0.90, 0.89, and 0.89 and axillary: 0.89, 0.89, and 0.88 in the WT, OPP, and OPE techniques, respectively).

The WT technique produced a more homogenous dose distribution for the IMNs, compared to the other two techniques (0.90, 0.87, and 0.24 in the WT, OPP, and OPE techniques, respectively). The significant reduction in the DHI value for the OPE technique in this region is due to the low penetration of electron beams in the thick phantom chest wall, as previously described. The dose homogeneity distributions of the chest wall in the WT and OPP techniques were almost similar or even better than the OPE technique (0.89, 0.90, and 0.85 in the WT, OPP, and OPE techniques, respectively). According to a study by Petrova et al. [18], the DHI value in the tangent method was estimated to be 0.90±0.01 in early-stage breast cancer patients, which is consistent with the obtained value in this study. Also, in a dosimetric study by Deborah et al. [22], the partially wide tangent fields (PWTFs) and four-field photon/electron combination techniques were compared. It was concluded that the dose homogeneity in the PWTF technique was better than that of the four-field photon/electron technique, which is in line with the results of our study.

In the present study, the lung DVHs, as shown in Figure 4, indicated that the OPP technique delivered the highest dose to the left lung and that the OPE technique reduced the dose received by the left lung slightly more than the WT technique. In this regard, Emami reported that if the percentage of normal lung receiving at least 20 Gy (V20) was less than 22%, 31%, and 40%, the probability of pneumonia would be 5%, 10%, and 20%, respectively [17]. Based on the DVHs, the V20 for the left lung was about 25%, 28%, and 60% in the OPE, WT, and OPP techniques, respectively. Therefore, the OPE and WT techniques might cause pneumonia with a probability of 10%. Also, in the OPP technique, the dose reaching the lung was higher than its tolerance level. The study by Dogan et al. confirmed these results for the OPE and WT techniques. They concluded that there was no significant difference between the WF and PE techniques regarding the lung volume irradiation [21].

The TLD measurements, as shown in Table 1, indicated that the mean dose received by the left lung in the WT technique was lower than the OPP technique; however, the difference was not significant, which could be due to the large SD in the WT technique. The reason for the large SD is that in this organ, the TLDs were located outside and inside the field, respectively and received noticeably different doses. The mean dose of the left lung in the OPP technique was higher than the OPE technique, whereas this value was not significantly different between the WT and OPE techniques. According to a study by Emami [17], the mean lung doses of 7, 13, 20, 24, and 27 Gy led to pneumonia with probabilities of 5%, 10%, 20%, 30%, and 40%, respectively. According to the mentioned tolerance levels, the mean absorbed dose by the left lung in the OPP technique was not in the tolerance range. Moreover, the mean dose received by the left lung in the OPE and WT techniques caused pneumonia with probabilities of 20% and 40%, respectively. However, the discrepancy between the DVH and TLD results regarding the probability of pneumonia was attributed to the limited number of TLD chips for the measurements.

According to the findings summarized in Table 2, the mean dose received by the heart was significantly different between the three techniques. Table 1 indicates that the mean dose received by the heart was the highest using the OPP technique, while this value decreased in the WT technique, compared to the OPE technique. This finding is consistent with the results of a study by Dogan et al. [16, 21]. They reported that the irradiated cardiac volume was lower in the WF technique, compared to the PE technique. In the study by Emami [17], if the mean received dose of the heart was less than 26 Gy, it could cause pericarditis with a probability of <15%. Also, if the V25 of the heart was <10%, the probability of long-term cardiac mortality would be <1%. According to our measurements, the mean dose received by the heart was lower than its tolerance level in all of the examined techniques. The DVH and TLD measurements showed a similar trend for the absorbed dose by the heart. According to Figure 4, the V25 for the OPP and OPE techniques was about 1%, and no heart volume received a dose above 25 Gy in the WT technique.

Conclusion

Based on the present results, the WT technique was associated with a lower delivered dose to the heart and a better dose homogeneity distribution in the IMN area, relative to the other two techniques. The OPP technique produced an acceptable dose homogeneity distribution; however, in this technique, the lung dose was higher than its tolerance limit. Although the OPE technique might cause a slight decrease in the left lung dose, relative to the WT technique, it did not yield a satisfactory dose homogeneity distribution, owing to the thick chest wall of the RANDO phantom. However, if an electron beam with a higher energy level was available, there could be a homogeneous dose distribution in the IMN region. Also, it seems that for real mastectomy patients with less chest wall thickness than the phantom (less than half of the phantom chest thickness), the OPE technique may be preferred, although further research is needed to confirm this finding.

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