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Can dynamic wedges reduce thyroid dose in breast radiotherapy compared to physical wedges?

M. Joya[1], T. Kordane[2], A.H. Karimi[1], G. Geraily[1,3*]

[1]Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran
[3]Radiation Oncology Research Center, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran

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***Corresponding author:**
Ghazale Geraily, Ph.D.,
E-mail:
gh-geraily@sina.tums.ac.ir

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ABSTRACT

Background: In breast radiotherapy, enhanced dynamic wedge (EDW) and physical wedges are used to improve the homogeneity of the dose. Scattered photons are the major factor in the off-field organs' unwanted dose. In breast radiotherapy, the thyroid is a critical off-field organ at risk for scattered photons. This study was performed to compare the unwanted dose and the secondary fatal cancer risk to the thyroid in breast radiotherapy between EDW and physical wedge. ***Material and Methods:*** The 6-MV Varian 2100 C/D linac was used to irradiate the breast of a thorax phantom under two opposite tangential fields. The unwanted dose that reached the thyroid was estimated using Eclipse Treatment Planning System and Gafchromic film dosimetry. Corresponding fatal secondary cancer risks were also assessed according to the NCRP report 116 recommendations. ***Results:*** The measured dose for thyroid using a physical wedge and enhanced dynamic wedge were measured as 2.1 and 0.735 cGy, which are approximately 1% and 0.37% of the prescribed dose to the breast (2 Gy), respectively. In the case of radiotherapy with the physical wedge, the lifetime risk of secondary fatal cancer attributed to the thyroid is 0.0480 and 0.0504 % using TPS and measured data, respectively. In the case of the dynamic wedge, the above values were reduced to 0.0168 and 0.0176 %, respectively. ***Conclusions:*** Using an enhanced dynamic wedge in breast radiotherapy reduced the thyroid dose by about 65% compared to the physical wedge technique. As a result, it was concluded that the application of EDW is safer than the physical wedge in breast radiotherapy.

INTRODUCTION

Breast cancer is the most prevalent cancer and a significant mortality reason for women. World Health Organization (WHO) reported that over 2.3 million women were diagnosed, and 685 000 died from breast cancer around the world in 2020. Surgery and radiotherapy as the common treatments for female patients with breast cancer are used to control the disease in the breast and lymph nodes, while to reduce the risk of cancer metastasis, systemic therapy is required [1, 2]. Radiotherapy aims to deliver a destroying dose to the tumor and off-field organs at risk (OARs) and healthy tissues. The tangential opposed beams radiotherapy technique using physical wedge or enhanced dynamic wedge and field-in-field techniques are the common techniques for whole-breast irradiation to ensure the uniform dose distribution within the tumor [3-5]. Despite the usage of physical wedges and compensators in breast radiotherapy improving the uniformity and conformity of the tumor dose, on the other hand, they increase the periphery dose (PD) to the out-of-field critical organs such as the thyroid, lungs, and heart due to generating more scattered radiation which may lead to the long-term radiation-induced secondary cancers and other complications to the survivals in the future [2, 6]. An alternative technique using enhanced dynamic wedge (EDW) is also introduced to decrease the periphery dose and reduce future complications resulting from breast radiotherapy. The treatment planning systems (TPS) cannot accurately calculate the out-of-field dose, and therefore, the estimation of developing secondary cancer risk is not possible based on the data provided by TPS [7, 8]. Therefore, studies are needed to directly determine the level of dose absorbed by out-of-field OARs and estimate the possibility of future complications based on the International Radiation Protection Commission (ICRU)[9] and Biological Effects of Ionizing Radiation (BEIR) VII [10] guidelines. Some studies have been performed to measure the thyroid dose using different dosimetry systems and compared it with the dose constraint of the thyroid in breast radiotherapy. The Radiation Therapy Oncology Group (RTOG) recommended that the maximum dose received by the thyroid should not be more than 3% of the prescribed dose for breast radiotherapy [11, 12].

Studies demonstrated that the thyroid receives a

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considerable dose while external radiotherapy is used for breast cancer treatment. Vlachopoulou *et al.* [13], in an *in-vivo* study, measured the thyroid gland dose and calculated the possibility of secondary cancer as a result of two tangential fields of breast radiotherapy using metal-oxide-semiconductor field effect transistor (MOSFET) dosimeters and found that the thyroid received about 2.0 ± 0.8% of the prescribed dose with the corresponding risk factor of 0.3%. They concluded that the risk should be considered along with the pathology and patient's age. Momeni *et al.* [6] determined the mean thyroid dose and related risk resulting from breast tangential beam radiotherapy using thermoluminescent dosimeters (TLD) and measured the thyroid dose as 0.883±0.472% of the prescribed dose and the possible secondary fatal cancer risk of 9.974±4.318 after five years. Farhood *et al.* [14], using a TLD dosimeter, found that the average skin entrance dose (SED) for the thyroid was about 7% of the prescribed dose for the supraclavicular field, and Sulieman *et al.* [15], using TLD-100 chips, measured the thyroid dose on 69 patients and found that the mean thyroid dose was 3.7% of the prescribed dose to the breast. However, the authors did not specify whether they used a physical wedge or an enhanced dynamic wedge to improve dose uniformity in their treatment plans.

Follow-up studies showed that about 6-21% of patients developed hypothyroidism 2-7 years after breast radiotherapy. Those studies recommended that the thyroid should be shielded during irradiation, and after radiotherapy, routine thyroid function monitoring must be performed [16, 17]. In addition, complications such as brachial plexopathy, lymphedema, pneumonitis, rib fractures [18], congestive heart failure[19], secondary cancer, including soft tissue sarcoma, contralateral breast cancer, and leukemia were also have been reported after breast radiotherapy [20]. Therefore, the thyroid and other critical OARs doses in breast radiotherapy must be measured and controlled accurately for necessary protection concerns. The level of received dose by the thyroid depends on the radiotherapy technique, field size, and thyroid distance from the edge of irradiated field [6].

To the best of our knowledge, no or limited number of research was conducted on the measurement of the thyroid dose by gafchromic film in breast radiotherapy while using physical wedge and EDW. Therefore, this project aimed to address the unwanted dose and subsequently risk of fatal cancer attributed to the thyroid in patients undergoing breast radiotherapy.

MATERIALS AND METHODS

This research was implemented in the institute of cancer, Imam Khomeini Hospital, Tehran, Iran, during 2019-2020. Irradiation was carried out by 6-MV Varian 2100C/D linear accelerator (linac), and treatment planning was performed by the Eclipse software.

Calibration of EBT3 film

Analyzing and discussing EBT Gafchromic film characteristics such as uniformity, dose rate dependency, energy response, post-irradiation density growth, etc., have been discussed elsewhere [21, 22]. In this study, gafchromic EBT3 films with 8" × 10" of dimension were cut off into 33 pieces of 3×3 cm^2 shown as figure 1. Carefully handling was performed to keep the films clean in all steps of cutting, irradiation, and scanning by using latex gloves. A small sign was created on one side of each piece of the film to ensure the same alignment of films during irradiation and scanning. Three pieces of the film were kept aside without irradiation to determine and correct background radiation. Films were placed in turn within slab phantoms (RW3 Slab Phantom model T40006, PTW, Germany) to be irradiated for calibration purposes. Eight 10 mm thick slabs were placed under the films to achieve the full backscatter, and two slabs were put above the film. Films irradiation setting was SSD = 90 cm, field size = 10 × 10cm^2, gantry angle of zero, and dose rate 200 MU/min. Dose levels for films calibration were 0, 25, 50, 75, 100, 125, 150, 175, 200, 225, and 250 cGy. Exposed films were collected and kept inside a dark box per company recommendation for 24-48 h to reach color stabilization before scanning [23].

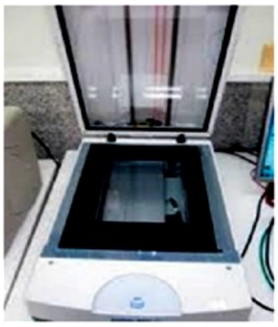

Figure 1. Microtek scanner (left) and calibration films images (right).

Phantom imaging and treatment planning phases

A spiral General Electric (GE) Computed Tomography (CT) scan with a slice thickness of 1 mm was used for imaging the homemade head & neck and heterogeneous thorax phantom. The phantom included heterogeneities of the lung from cork (0.23 g/cm3), heart from 61 transverse 5 mm thick slices colored Plexiglas, and the breast intact was constructed from plexiy (1.01g/cm^3). The phantom materials were selected based on the recommendations of report number 44 of ICRU [24-26]. Acquired Digital Imaging and Communications in Medicine (DICOM) images were transferred from the CT scan unit to the TPS. An oncologist contoured the target volume (right breast) and OARs, like the

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thyroid, according to the ICRU recommendations. Then, optimum treatment plans for two tangential opposed beams techniques using both physical and dynamic wedges were prepared by a medical physicist. The required parameters of the treatment plans, such as tumor dose, number of fractions, dose-volume histogram (DVH), and their monitor units, were calculated. Plans were sent to the treatment delivery system after the final acknowledgment by a medical oncologist.

Film placement and irradiation

When the treatment system received the treatment plan, the head & neck, and thorax phantom setup was performed on the treatment couch and tried to reproduce the same condition as it was determined in the imaging and treatment planning phases. Then, a piece of the calibrated gafchromic film (three times for each setup using physical wedge and EDW) was placed inside the thyroid (parallel to the beam axis). The film and phantom edges were precisely matched with each other. Then the breast phantom irradiation procedure was carried out for both techniques by 6-MV photon energy, Varian 2100C/D Linac. The exposed films were collected and placed in a dark box before scanning.

Scanning of EBT3 exposed films

Microtek ScanMaker 9800XL (Microtek, Taiwan) [27] scanner was used for scanning all the exposed films 24-48 h post-irradiation. This time is needed for self-development and stabilization of exposed films. Once the scanner was turned on, it was kept in transmission mode for half one hour for warm-up purposes. The scanner's screen was cleaned with sterilized gas and alcohol to remove any dust and contamination and decrease uncertainties during the film scanning process. Before starting scanning the films, 3-5 blank scanning were made for warm-up of the scanner's lamp and correcting defective pixels. First of all, un-exposed films, then the exposed calibration films, and finally the irradiated thyroid films were placed at the central part of the scanner and the scan of them three times, and their images were saved in pixelated tagged image file (TIF) format. Scan procedure was performed via Wizard Pro option, red, green blue (RGB) colors (48 bit) mode, and imaging resolution of 150 dots per inch (dpi) (figure 1) [28, 29].

In the next step for obtaining the optical density (OD) of the film pieces and establishing the relationship between dose and OD, ImageJ software (Eliceiri lab, University of Wisconsin-Madison, Wisconsin, United States) [30] was used for TIF image reading and pixel values measurement. As the EBT3 Gafchromic film is very sensitive to the wavelength of 636 nm [29] and also the applied dose in this project was lower than 10 Gy. Therefore, the red channel in ImageJ was used to measure the TIF image pixel values. Equal regions of interest (ROIs) at the central parts of all unexposed and calibration films were selected, and their pixel values were measured. Equation (1) was employed to convert the film pixel values to the optical densities.

$$\mathrm{OD} = \log\left(\frac{I_u}{I_i}\right) \quad (1)$$

Where OD is the film transmitted optical density, I_u and I_i are the mean pixel values of un-irradiated and irradiated films, respectively [31]. The calibration curve (dose vs. OD) was created by ImageJ software, and its fitting equation was also acquired. The fitting curve's equation was used to calculate doses received by films during breast irradiation with physical and enhanced dynamic wedges.

Lifetime risk of fatal cancer for thyroid

From the point of radiation protection view, it is interesting for physicists, radio-oncologists, and patients to estimate the risk of fatal cancer for the thyroid where the thyroid is more at risk of scattered photons, e.g., radiotherapy of breast cancer. Additionally, comparing the physical and dynamic wedge techniques based on the lifetime risk of fatal cancer that may be induced to the thyroid can be used to select the best technique from radiation protection aspects. Equation (2) presents the risk estimation based on NCRP Report 116.

$$\text{The lifetime risk of fatal cancer}_{\text{thyroid}}\ (\%) = \text{Dose}_{\text{Thyroid}} \times C_{\text{Thyroid}} \quad (2)$$

Where $\text{Dose}_{\text{Thyroid}}$ represents the dose received by the thyroid when 60-Gy photon dose is delivered to the breast (as the treatment target), and C_{Thyroid} is the thyroid coefficient (0.08) for fatal cancer risk based on NCRP Report 116 [32].

The excel software was used for calculation and comparison of dose and relative dose in this study. The simple averaging and relative difference were used to compare the results obtained for each technique in this study.

RESULTS

Dose-volume histogram (DVH)

TPS calculated the absorbed dose for all thyroid voxels for both techniques, which shows the pattern of dose distribution within the thyroid. The thyroid dose distributions are shown graphically as dose-volume histograms in figure 2. As the DVHs show the maximum dose that deposited in 100% of the thyroid volume in the presence of EDW and physical wedge were 0.25 cGy and 1.5 cGy, respectively. The prescribed dose for breast irradiation was 2.0 Gy for a single fraction.

EBT3 film calibration

The pixel values of films were extracted by ImageJ software 24-48 h later than irradiation.

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Optical densities for all calibration films were calculated from pixel values according to equation (1). Then the graph of optical density against dose was drawn, and the curve's linear fitting and its equation were also obtained figure 3. Then, the fitting equation was used for calculating the exposed films' doses.

Thyroid dose

The unwanted dose to the thyroid measured by Gafchromic film and calculated by TPS is given in table 1. The relative differences between the measured and calculated results were presented in the last column. Additionally, the relative differences in doses between the results of techniques using a physical wedge and dynamic wedge were reported in the last row.

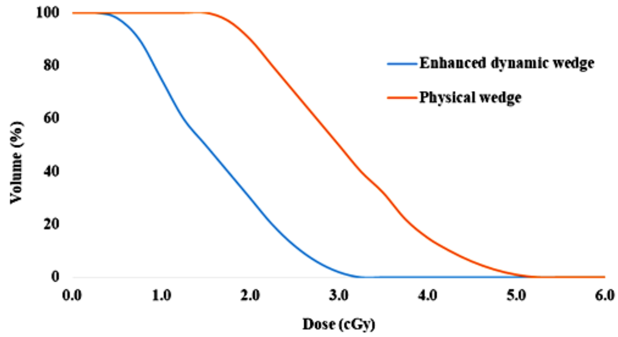

Figure 2. DVHs of thyroid dose in the presence of physical and enhanced dynamic wedges for breast radiotherapy.

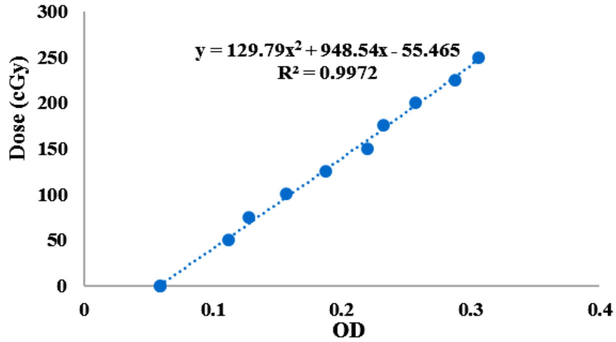

Figure 3. EBT3 calibration curve.

Table 2. Compression of fatal cancer risk for thyroid when 60-Gy photon dose is delivered to breast between two techniques: dynamic wedge vs. physical wedge.

Wedge	Thyroid mean dose (cGy)		Relative differences (%)
	TPS	Measurement	
Physical	2.00 (1.1-3.5)	2.1	-4.8
Dynamic	0.700 (0.2-3.6)	0.735	-4.8
Relative differences (%)	-65	-65	-

DISCUSSION

The results show that the measured doses do not differ significantly (< 5%) from those estimated by TPS. Nevertheless, underestimation of the dose by TPS is still observable. Generally, the TPS underestimates the off-field dose significantly in comparison with the measurement. In this study, underestimation is negligible (4.8 %), probably due to the proximity of the thyroid to the treatment field.

From table 1, the measured dose for thyroid as a result of 3D-conformal radiotherapy of the breast using a physical wedge and enhanced dynamic wedge are 2.1 and 0.735 cGy, which are approximately 1% and 0.37% of the prescribed dose for the breast (2 Gy), respectively which are lower than the limit of 3% of prescribed dose [11, 12]. Similar results have been reported in the literature. Thyroid dose with and without supraclavicular field irradiation was 8.0±2.0% and 2.0±0.8% of the prescribed dose, respectively [13]. Donovan *et al.* (2012) showed that the thyroid dose as a result of whole breast radiotherapy (WHRT) and accelerated partial breast irradiation (APBI) was 0.3% and 0.2% of the prescribed dose, respectively. Momeni *et al.* (2018) also found that the thyroid dose in breast radiotherapy is 3.02% of the prescribed dose [6]. On the other hand, Farhood *et al.* (2016) and Ansari *et al.* (2020) reported higher values of 7% and 13%, respectively. A study using TLDs resulted in 7% of the prescribed dose [14]. These discrepancies originate from the differences in radiotherapy technique, dosimetry systems, thyroid volume, and finally, the distance of the thyroid from the radiation field.

Table 2 highlights noticeable differences in thyroid dose (independent of dosimetry method) for when the breast is irradiated with a dynamic wedge compared to the physical wedge. As seen, the thyroid dose in radiotherapy of the breast with a dynamic wedge is relatively 65% lower than when the physical wedge is used. A typical physical wedge attenuates the radiation beam more and produces more scattered radiation. Therefore, higher monitor units (MUs) are needed to deliver a defined dose to the target compared to when EDW is used. As a result, more unwanted doses to the normal tissues outside the treatment field, e.g., the thyroid, are expected in breast radiotherapy.

Table 2. Compression of fatal cancer risk for thyroid when 60-Gy photon dose is delivered to breast between two techniques: dynamic wedge vs. physical wedge.

Wedge	The lifetime risk of fatal cancer for thyroid (%)		Absolute differences (%)
	TPS	Measurement	
Physical	0.0480	0.0504	0.0024
Dynamic	0.0168	0.0176	0.0008
Absolute differences (%)	0.0312	0.0328	-

However, based on the results of this study, for both dynamic wedge and physical wedge, the total thyroid dose when 60-Gy photon dose is prescribed to the breast is 0.22 and 0.63 Gy, respectively, which are still below the thyroid threshold dose of 3% of the prescribed dose. Accordingly, the authors believe there is some advantage for a dynamic wedge

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compared to a physical wedge in decreasing the unwanted dose to the thyroid for patients undergoing breast radiotherapy. However, the consequences were also re-analyzed via risk assessment.

The lifetime risk of fatal cancer-induced to the thyroid was estimated based on NCRP report 116 for circumstances that assumed that a 60-Gy photon dose was delivered to the breast. The estimation was performed for both measured and calculated data in each technique. Table 2 presents the risk assessment in detail.

It can be seen that there are no meaningful differences (below 0.0024 % absolutely) between risk assessment through TPS data and those estimated using measurement by the film. In the case of radiotherapy with the physical wedge, the lifetime risk of fatal cancer attributed to the thyroid is 0.00480 and 0.0504 % using TPS and measured data, respectively. In the case of the dynamic wedge, the above values are replaced with 0.0168 and 0.0176 %, respectively.

Given that the estimated values for fatal cancer risk are negligible (up to 0.0504 % or, in other words, five persons per 10,000 population), the authors believe that there is no significant relationship between the fatal cancer risk induced to thyroid after breast radiotherapy neither with dynamic wedge nor with a physical wedge. This finding is in agreement with Grantzau and Overgaard's study (2015), where for 322,461 breast cancer patients (37% of them had received radiotherapy between 1961 and 2007), there was no meaningful relation between secondary thyroid cancer and breast radiotherapy neither over passing the time nor in the total accumulated relative risk (RR) estimate, RR 1.05 (95% CI, 0.78-1.43) [33]. Similarly, Veiga *et al.* (2012) found that the association between second thyroid cancer and childhood radiotherapy is significant for childhood and increases as the age of exposure decreases [34]. Therefore, if an adult breast cancer patient grows thyroid cancer, it may be induced due to childhood exposure to the radiation [33] and not necessarily from adulthood breast cancer radiotherapy. However, in terms of lifetime risk estimation, Lee *et al.* (2014) found that lifetime attributable risk (LAR) to the thyroid per 10,000 population is 0.002 for 3D-conformal radiotherapy and much lower than 0.011 and 0.012 for Intensity Modulated Radiation Therapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT), respectively [2].

Contrary to the above findings, the LAR of the thyroid among 10,000 of the population for 100 years due to 3D-CRT, field-in-field (FiF) forward-planned, IMRT, VMAT, and Tomo-therapy (TOMO) were 50.6±17.6, 49.6±19.2, 86.8±28.0, 101.3±57.3 and 25.5±5.5 respectively [35]. The increase of LAR is associated with the scattered and leakage radiation and hence with the number of MUs. Therefore, the physical wedge is attributed to higher LAR due to the higher number of MUs. Selection of the best modality is vital for the younger patients with longer life expectancy to avoid facing higher LAR [35].

Generally, secondary cancer risk estimation is still a challenging issue in radiobiology since there is no organized data in this regard, and the available human knowledge was extracted only from the studies on the Hiroshima and Nagasaki survivors. To answer the common concerns among the public about secondary cancer risk due to medical radiation, more studies are recommended in this field, especially follow-up of the patients is a vital issue of interest.

CONCLUSION

Results showed that the usage of EDW in the Linac head for breast radiotherapy decreased the dose received by the thyroid compared to the application of physical wedge. Analyzing the results revealed that the probability of occurring fatal cancer risk is very low and secondary thyroid cancer after breast radiotherapy is not a significant concern for consideration. However, more efforts should be taken into account from radiation protection to decrease the risk of growing secondary cancer and hypothyroidism due to breast radiotherapy.

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Conflict of interest: The authors have no conflicts to disclose.

Ethical consideration: The research was phantom based, and there was no contribution of humans or animals.

Author statement: M.J.: Investigation, writing original draft-reviewing and editing. T.K.: Investigation, data curation, methodology, validation, visualization. A.H.K.: Writing original draft-reviewing and editing. G.G.: Software, conceptualization, project administration, supervision, writing- reviewing and editing.

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