Iranian Journal of Medical Physics

ijmp.mums.ac.ir

Evaluation of 3D-CRT Radiotherapy Treatment Planning with Radiobiological Effects in Patient-Specific 3D Printed Anthropomorphic Phantom Postmastectomy Breast Cancer Axillary Metastases

Endarko Endarko[1*], Aditya Prayugo Hariyanto[1], Siti Aisyah[1], Nandia Kavilani[2], Ahmad Syafi'i[2]

1. Department of Physics, Institut Teknologi Sepuluh Nopember, Kampus ITS - Sukolilo Surabaya 60111, East Java, Indonesia.
2. Medical Physicist of Radiotherapy Installation, Naval Hospital Dr. Ramelan, Surabaya 60244, East Java, Indonesia

ARTICLE INFO

Article type:
Original Paper

Article history:
Received: July 23, 2023
Accepted: Feb 12, 2024

Keywords:
Radiation Therapy
Three-Dimensional
Conformal Radiation
Therapy (3D-CRT)
Phantom
Breast Cancer
Dosimetry Radiation
Protection

ABSTRACT

Introduction: The aim of this study was to evaluate and measure the effectiveness of a particular radiotherapy treatment planning system, namely 3D conformal radiation therapy (3D-CRT), and radiobiological effects in postmastectomy breast cancer axillary lymph metastases using a patient-specific 3D printed anthropomorphic phantom of the right breast after surgery.

Material and Methods: The chest wall and axilla were the two treatment targets for 3D-CRT planning techniques. Each target was subjected to variations of two and three irradiation fields, with a dose of 50.00 Gy and fractionation of 2.00 Gy. From the variations, the radiation dose received by planning target volume (PTV) chest wall, PTV-Axillary, and organs at risk (OARs) was evaluated to determine the best planning technique through dosimetry verification. The thermoluminescent dosimeter (TLD) 100 Chip and EBT3 film were employed to measure the radiation dose at the PTV and OARs.

Results: The planning system evaluation based on dose volume histogram showed no significant difference (p = 0.993) between two and three irradiation fields in both the chest wall and axillary planning 3D-CRT technique. Normal tissue complication probability for OARs has values below 5%, while the smallest value was obtained for the left lung. Finally, the point dose verification between planning and measurement using TLD100 and EBT3 film indicated an average difference of 9.14% and 4.34%, respectively, with no significant difference.

Conclusion: This study successfully demonstrated the dosimetry evaluation and radiobiological effects of postmastectomy right breast cancer treatment using a patient-specific 3D printed anthropomorphic phantom, which met the established standards.

► *Please cite this article as:*
Endarko E, Hariyanto AP, Aisyah S, Kavilani N, Syafi'i A. Evaluation of 3D-CRT Radiotherapy Treatment Planning with Radiobiological Effects in Patient-Specific 3D Printed Anthropomorphic Phantom Postmastectomy Breast Cancer Axillary Metastases. Iran J Med Phys 2024; 21: 314-322. 10.22038/ijmp.2024.73930.2309.

Introduction

Based on data from the Global Cancer Observatory, 2.29 million women were diagnosed with breast cancer and 666,103 deaths worldwide in 2022 [1]. This makes it the cancer with the highest risk of death in women. Breast cancer treatment requires a multidisciplinary team approach that combines surgery, chemotherapy, radiation therapy, and hormone therapy [2]. Although no precise treatment is designed to kill cancer cells, radiation therapy is the primary cancer treatment, and more than 60% of cases require radiation therapy. An important aspect of breast cancer treatment can be minimizing the risk of regional recurrence and increasing the overall survival of early and advanced breast cancer after mastectomy. Radiotherapy aims to deliver the maximum dose to target cells, and healthy organs receive the minimum dose simultaneously [3]. The primary limitation of radiotherapy is damage to normal cells surrounding the tumor cells [4]. Therefore, planning, technique, and evaluation of dose delivery should be a significant concern in radiotherapy.

Irradiation of the chest wall and regional lymph nodes such as supraclavicular, axillary, and internal mammary glands is one of the most challenging radiation strategies as it requires special care to dose the lungs and heart. Post-mastectomy breast cancer treatment includes external beam radiation therapy with three-dimensional conformal radiation therapy (3D-CRT) and intensity-modulated radiation therapy (IMRT) techniques. The two planning techniques are most used for post-mastectomy breast cancer treatment [5, 6]. However, 3D-CRT is superior to IMRT because of its uncomplicated application and ability to

*Corresponding Author: Tel: +62-31-5943351; Fax: +62-31-5943351; Email: endarko@physics.its.ac.id

minimize the contralateral exposure of healthy tissues in the heart, lungs, and breast to irradiation [5, 7]. Assessment of pulmonary, cardiac, and cutaneous accurate dose levels is challenging due to variations in chest wall thickness, and the considerable heterogeneity in tissue density must be considered in the treatment plan [8]. This shows that assessing radiation dose is very important to verify whether the therapy planning system can provide the expected dose distribution before being administered to the patient. The measurement and assessment of the dose cannot be done directly on the patient as doing so may harm the patient, and it is impossible to insert a dosimeter into the patient. This can be done by using anthropomorphic phantoms that can replace humans.

The phantom is a tissue-mimicking model with radiation characteristics similar to the mimicked organ [9]. Thoracic anthropomorphic phantoms comprise soft tissue, lung, heart, and bones [6,10]. Dose evaluation in targets and healthy organs makes inserting dosimeters into targets and organs possible to provide end-to-end validation. Thermoluminescent Dosimeter (TLD) and EBT3 radiochromic film can be applied in radiation dose assessment. These two dosimeters are reliable for verifying external radiation therapy doses [11, 12]. They include gold-standard dosimeter programs recommended for quality assurance of machine calibration, dosimetry planning, and dose calculation [12]. Butson et al. and Abdemanafi et al. performed in vitro dosimetry verification with TLDs using a standard thoracic anthropomorphic phantom. Their results consistently showed that the treatment planning system (TPS) overestimated the dose levels compared to TLD measurements [12, 13].

Therefore, this study aims to evaluate and quantify the radiation dose to the planning target volume (PTV) and organs at risk (OAR) using the radiation therapy oncology group (RTOG) 0413 guideline, as well as determine the radiobiological effects on postmastectomy right-sided axillary lymph metastasis of breast cancer using a specific thoracic anthropomorphic phantom. In addition, the simulation results and actual measurements will be compared with TLD100 and EBT3 film.

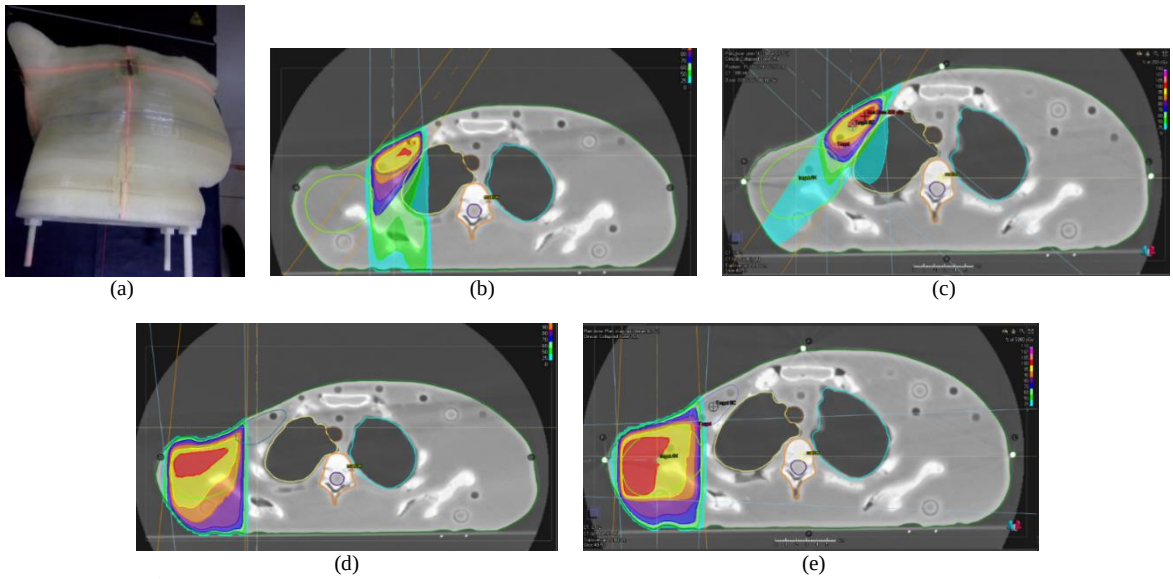
Materials and Methods

Thoracic anthropomorphic phantom for postmastectomy right breast

The thoracic anthropomorphic phantom for postmastectomy breast cancer referred to the registered patent No. P00202102195 [14] with dimensions of 437 × 372.7 × 265.7 mm^3. Furthermore, the phantom contains artificial tissues like the spine, ribs, lungs, and heart. It was cut axially to a thickness of 1.5 cm, and there were holes for placing the Harshaw chip TLD100 detector, as shown in Figure 1(a) [14].

3D-CRT radiotherapy treatment planning system

The 3D-CRT planning started with creating a virtual model of an anthropomorphic thoracic phantom using the Philips Big Bore Brilliance Computed Tomography (CT) Scanner (Philips Medical Eindhoven, The Netherlands) containing a tube voltage of 120 kV, a thickness of 5 mm, and 512 × 512 image matrix. According to Figure 1(b), while carrying out the CT-Simulator procedure, the phantom was given a metal and paper tape marker for adjustment to maintain the exact positioning during radiotherapy treatment. Furthermore, the virtual phantom model passed through a delineation process to determine the boundaries of the PTV and OARs. This is important for evaluating dosimetry and radiobiological effects in the treatment planning system (TPS).



(a) (b) (c) (d) (e)

Figure 1. (a) Setting of anthropomorphic phantom placement during CT simulation procedures and radiotherapy treatment. The results of dose distribution from TPS chest wall planning using (b) two irradiation fields and (c) three irradiation fields with the 3D-CRT technique. The results of the distribution of dose from TPS axillary planning using (d) two irradiation fields and (e) three irradiation fields with the 3D-CRT technique.

The TPS was constructed using RayPlan9A software with multicenter targets known as the chest wall (CW) and axillary (Ax) plans, which are presented in Figure 1 (b-e). The plan utilized variations of two and three irradiation fields with a photon energy level of 6 MV from an Elekta Precise Treatment linear accelerator (Elekta Solution AB, Stockholm, Sweden) with a dose fractionation of 2 Gy x 50 referring to RTOG protocol 0413. The settings for each TPS variation in post-mastectomy breast cancer cases with axillary lymph metastasis using the 3D-CRT technique are shown in Tables 1 and 2.

Evaluation of dosimetry and radiobiological effects of 3D-CRT plans

The PTV's homogeneity index (HI) and conformity index (CI) parameters were evaluated in this study. The HI value was determined based on the recommendations of ICRU Reports 83 [15], while the CI was obtained using the method proposed by Feuvret et al. [16].

The maximum dose Quantec recommends for organs at risk (OARs), such as the lung, is an average of 20–23 Gy, with a V20 < 30 – 35%. The heart's dose should be V25< 10%, while the spinal cord should not receive more than 50 Gy [17]. RADBIOMOD software was employed to determine the effects of radiation therapy treatment on OARs through the probability normal tissue complication parameter (NTCP) using the Lyman-Kutcher-Burman (LKB) model [18].

Dosimeters calibration

Two dosimeters used in this study were TLD100 (Harshaw Bicron, USA) and 3 × 2.5 cm^2 EBT3 film. Their calibration was carried out by inserting the dosimeters into a solid water phantom (PTW, Freiburg, Germany) at a depth of 1.5 cm. The irradiation area was 10 × 10 cm^2, and the source axis distance (SAD) was 100 cm. The TLD calibration method was based on the one described by Liuzzi et al. [19]. The TLD irradiation process used 0.25 – 2.75 Gy variations in multiples of 0.25 Gy. At the same time, the EBT3 film was irradiated between 0 and 7 Gy in multiples of 1 Gy. The pixel values of the EBT3 film were converted to net optical density (*netOD*) values using the equation published by Sipilä et al. [20]. Furthermore, the TLD and EBT3 film readings were presented as calibration curves of thermoluminescence (TL) signal (μC) and *netOD* against the dose absorbed by the solid water phantom (in Gy). There was an unirradiated dosimeter as a control for background measurements.

Dosimetry verification between 3D-CRT planning and actual measurement

Dosimetry verification was carried out using one fraction of 2 Gy due to the treatment process performed with fractionation. Additionally, the verification with point dose was evaluated based on AAPM TG 119 by comparing the results of 3D-CRT planning and direct measurement. Both dose measurements were compared using the equation below [21]:

$$Discrepancy\ (\%) = \frac{Dose_{calculated} - Dose_{measured}}{Dose_{measured}} \times 100$$

The scheme for dosimetry verification through measurement and planning is shown in Figure 2.

Table 1. The set-up of a chest wall (CW) treatment planning system using two- and three-field variations of 6 MV photon 3D-CRT technique irradiation on a specific anthropomorphic phantom for post-mastectomy breast cancer

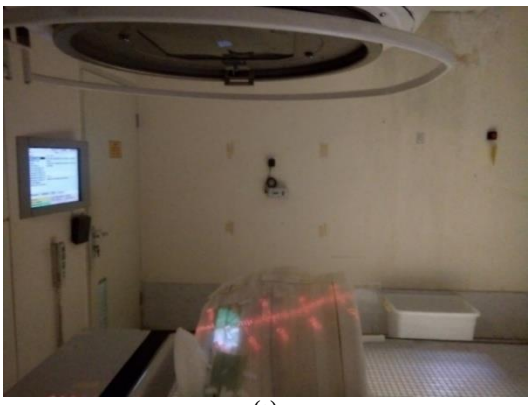
Plan CW	Beam	Weight	SSD (cm)	Gantry (deg)	Coll (deg)	Couch (deg)	MU/fx	Jaw maximum aperture (cm)			
								X1	X2	Y1	Y2
2 beams	1	16.2%	96.56	33.8º	0º	0º	33.61	-2.03	2.57	-2.30	1.83
	2	83.8%	98.19	358.7º	0º	0º	173.91	-2.75	3.65	-2.29	1.81
3 beams	1	56.7%	96.56	33.8º	0º	0º	119.85	-2.03	2.57	-2.30	1.83
	2	24.5%	98.19	358.7º	0º	0º	51.79	-2.75	3.60	-2.29	1.81
	3	18.9%	98.36	312.5º	0º	0º	39.87	-3.27	3.89	-2.27	1.78

Coll: collimator
CW: chest wall
MU/fx : monitor unit per fraction

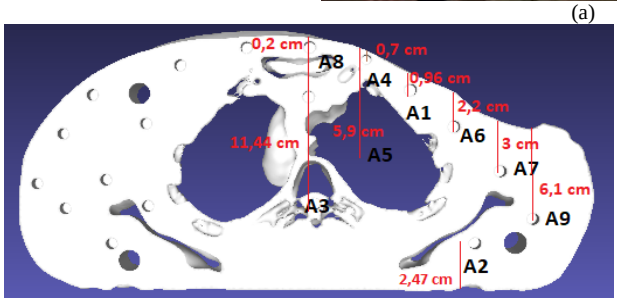
Table 2. The set-up of an Axillary (Ax) treatment planning system using two- and three-field variations of 6 MV photon 3D-CRT technique irradiation on a specific anthropomorphic phantom for post-mastectomy breast cancer

Plan Ax	Beam	Weight	SSD (cm)	Gantry (deg)	Coll (deg)	Couch (deg)	MU/fx	Jaw maximum aperture (cm)			
								X1	X2	Y1	Y2
2 beams	1	84.1%	96.35	0º	0º	0º	177.71	-4.43	4.65	-2.40	2.25
	2	15.9%	93.10	180º	0º	0º	33.61	-4.43	4.34	-2.40	2.25
3 beams	1	47.2%	96.35	0º	0º	0º	102.79	-4.45	4.43	-2.40	2.25
	2	36.9%	93.19	180º	0º	0º	80.26	-4.43	4.67	-2.47	2.25
	3	15.9%	95.05	270º	0º	0º	34.64	-4.21	4.54	-2.43	2.25

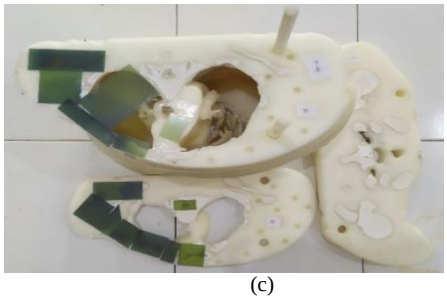
Coll: collimator
Ax : axillary
MU/fx : monitor unit per fraction



(a)



(b)



(c)

Figure 2. (a) Irradiation setup of a postmastectomy thoracic anthropomorphic phantom for dosimetry verification in a case of breast cancer with axillary lymph node metastasis after surgery; schematic showing the position of the dosimeters labeled at each point (b) positioning of the TLD at each label hole, and (c) EBT3 film over the label holes.

Statistical analysis

Statistical analysis was performed using an unpaired t-test to determine the differences between the models using R-software (version 2.5.1). With a p-value <0.05, the results were considered statistically significant. A p-value > 0.05 indicated no significant difference between the two models.

Results

The evaluation of dosimeters calibration

Figure 3(a) shows the response curve of the TLD to dose variations from 0 – 2.75 Gy for a 6 MV photon beam. A quadratic fitting approach was used to determine the behavior of the TLD response to several photon doses. The regression analysis results showed a very high R^2 value of 0.998. Based on Figure 3(b), at netOD values of 0 – 7 Gy, the red and green channels had higher netOD sensitivity than the blue channel. These align with the study conducted by Ataei et al., 2019; Casanova Borca et al., 2013 that the red channel had a higher sensitivity than blue [22, 23].

Evaluation of dose-volume histogram

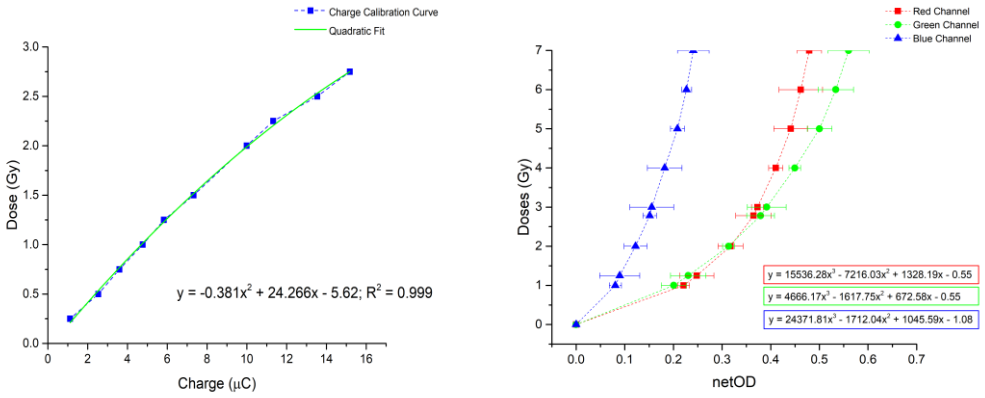
Figures 4(a) and (b) show that the 100% volume PTV CW and Ax received the same dose of 35.00Gy from the prescribed dose. The maximum treatment PTV CW and Ax received using two or three irradiation fields did not exceed 107% of the prescribed dose. The statistical results showed no significant difference between using both fields, with a p-value of 0.993.

Figures 4(c) and (d) show the DVH curves of OARs from the right breast cancer treatment after mastectomy. The maximum dose for OARs from the CW and Ax plans using either two or three-field irradiation was below 14.05 Gy. Except for the right lung from the Ax plan, both irradiation fields received a maximum dose of 30.90 and 21.79 Gy, respectively. The statistical test showed a significant difference (p = 0.005) in the Ax planning. However, the CW plan had no significant difference (p = 0.440).

Evaluation of homogeneity index and dose limitation

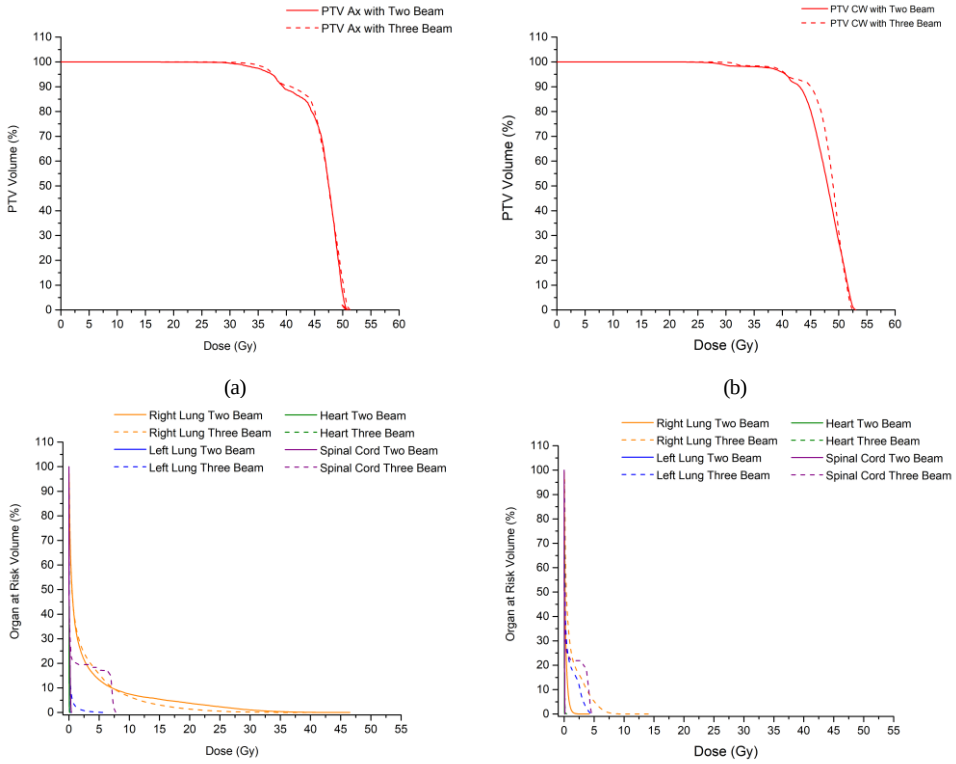
The ideal homogeneity index value is close to zero. Table 3 shows that the TPS HI value significantly differed from the ideal HI, with p-values of 0.035 and 0.021 for the Ax and CW plans, respectively. However, the HI value between the number of irradiated fields was not significantly different (p = 0.364). Based on the CI for CW planning, the three irradiated fields showed a difference, namely, 0.17 greater than the two irradiation fields. The statistical testing indicated no significant difference between both field values.

Table 4 shows the results of the analysis of the dose received by OARs based on Quantec recommendations. Furthermore, all OARs met the dose limits set by Quantec. Based on the evaluation of the values of HI, CI, and dose limitation, the planning with two or three fields attained the established standards and the same. Therefore, only the target point dose and OARs were verified using two fields on 3D-CRT TPS.



(a) (b)

Figure 3. (a) TLD calibration curve irradiated with 6 MV photons in a dose range of 0.20 – 2.75 Gy. The green line represents the quadratic fitting. (b) The results of fitting the calibration curve of EBT3 film using the third-order polynomial equation to determine the absorbed dose value of 6 MV photons when interacting with the material for the allowed dose range were 0 – 7 Gy.



(a) (b)

(c) (d)

Figure 4. (a) Comparison of dose-volume histograms of the planning target volume (PTV) of the axillary and (b) comparison of dose-volume histograms of the pla nning target volume (PTV) of the chest wall with variations in the number of beam fields. (c) Comparison of dose-volume histograms of organs at risk in planning axillary, and (d) planning chest wall with variation in the number of beam fields.

Table 3. The results of the homogeneity index (HI) and conformity index (CI) calculations of the planning target volume (PTV) using axillary and chest wall planning with varying numbers of beam fields.

Patients Data	Homogeneity Index	p-value	Conformity Index	p-value
Plan Ax (2 fields)	0.351	0.035	0.5	0.001
Plan Ax (3 fields)	0.314		0.5	
Plan CW (2 fields)	0.309	0.021	0.565	0.152
Plan CW (3 fields)	0.289		0.735	

Ax : axillary
CW: chest wall

Table 4. Radiation dose received by organs at risk at V_{20} (%), V_{30} (%), and maximum dose of 6 MV photon 3DCRT treatment planning system

Planning	Organs	V_{20}(%)	V_{30}(%)	D_{max} (Gy)
Plan Ax (2 fields)	Right Lung	3.782	1.051	30.90
	Left Lung	0	0	0.13
	Heart	0	0	0.08
	Spinal Cord	0	0	0.38
Plan Ax (3 fields)	Right Lung	0.137	0.179	21.79
	Left Lung	0	0	2.12
	Heart	0	0	0.09
	Spinal Cord	0	0	7.52
Plan CW (2 fields)	Right Lung	0	0	1.49
	Left Lung	0	0	0.07
	Heart	0	0	0.07
	Spinal Cord	0	0	0.11
Plan CW (3 fields)	Right Lung	0	0	6.91
	Left Lung	0	0	4.13
	Heart	0	0	0.18
	Spinal Cord	0	0	4.51

Ax: axillary
CW: chest wall

Table 5. Evaluation of radiobiologic effects using normal tissue complication probability (NTCP) of axillary and chest wall planning 3D-CRT technique

Planning	Structure	NTCP (%) 2 fields	NTCP (%) 3 fields	p-value
Ax	Right Lung	4.202	4.921	0.050
	Left Lung	0.567	0.654	0.007
	Heart	1.587	1.587	0.001
	Spinal Cord	4.979	4.977	0.001
CW	Right Lung	4.967	4.908	0.004
	Left Lung	0.612	0.689	0.027
	Heart	1.587	1.587	0.001
	Spinal Cord	4.977	4.977	0.001

The p-value is the result of the t-test obtained by making a comparison with the ideal NTCP value = 0
Ax: axillary
CW: chest wall

Table 6. Comparison of point dose at target and organs at risk between planning and actual measurements using two dosimeters (TLD and EBT3 film)

Code	Target	Planning (Gy)		Total	TLD-100 (Gy)			EBT3 film (Gy)		
		Ax	CW		Quadratic	%disc	*p*-value	Rc	%disc	*p*-value
A1	PTV-CW	0.05	1.94	1.99	2.3575	18.47		1.9901	0.01	
A4	Out PTV-CW	0.02	0.20	0.22	2.365	5.40	0.858	0.2627	5.08	0.967
A6	PTV-CW	0.40	1.94	2.34	2.5636	9.56		2.4529	4.82	
A2	PTV-Ax	1.66	1.20	2.86	3.0110	5.28		2.8276	1.13	
A7	PTV-Ax	2.06	0.35	2.41	2.7515	14.17	0.533	2.4593	2.05	0.930
A9	PTV-Ax	1.99	0.30	2.29	2.3455	2.42		2.3386	2.12	
A3	Spine	0.02	0.01	0.03	0.0263	12.33		0.0238	15.33	
A5	Right Lung	0.02	1.01	1.03	1.1664	6.04	0.968	1.0456	4.95	0.970
A8	Heart	0.01	0.04	0.05	0.0543	8.60		0.0518	3.60	

Disc: discrepancy; Rc: Red channel
Ax: axillary
CW: chest wall
PTV-CW: planning target volume chest wall
PTV-Ax: planning target volume axillary

Table 5. shows the results of the NTCP analysis conducted using the LKB model for OARs, where the average complication rate was less than 5%. However, the NTCP for planning with three fields was lower than that for two fields, namely 0.16% (CW plan). For the two-field Ax plan, the value obtained was 0.20% lower. Based on the

statistical analysis results, there was no significant difference (p-value > 0.05).

Comparative evaluation between planned and measured dose

Table 6 shows the results of the summation of dose for the Ax and CW plans, and the distribution was above 2 Gy in the planning target area. The percentage discrepancy of TLD100 between the measurement and planning ranged from 2.42–18.47%, and the global average discrepancy was 9.14%. Meanwhile, the percentage difference between EBT3 film measurement and planning was 0.01–15.33%, and the global average discrepancy was 4.34%. Comparing the two dosimeters, the EBT3 film with red channel showed a better confidence level than the TLD100 Chip for verification of point dose per fraction with a p-value = 0.9.

Discussion

The most exciting result from Figure 3(a) regarding the calibration curve was that the curve fit had a linear behavior below a dose of 1.50 Gy. Additionally, the TLD response curve showed results in line with Bahreyni Toossi et al., where the TLD response curves were linear for doses up to 1.20 Gy. For higher doses, they were supralinear [24]. From Figure 3(b), the blue channel had low sensitivity for verification of 2 Gy doses due to the visible light absorption spectrum of the EBT3 film being less than that of the red and green channels. EBT3 film has two different absorption peaks, one at 633 nm in the red wavelength (600 – 700 nm) and one around 595 nm in the green wavelength (500 – 600 nm) [25, 26]. Based on AAPM TG 235, dose analysis with the red channel using the EBT, EBT2, and EBT3 film models with a dose range below 10 Gy is in good agreement. However, the dose analysis of the red channel with a dose above 10 Gy is less suitable because the sensitivity at a higher dose is saturated at some points above 10 Gy. The analysis of higher doses is well achieved using the blue and green channels [26, 27]. TLD and EBT film response values significantly affect dosimetry, specifically in modern high-complexity radiotherapy treatments, where in vitro dosimetry can be recommended to improve quality assurance and control. The calibration curve does not involve variations in the beam field, incident angle, or air gap, and it can be used as a reference for future studies.

This study evaluated the dose and radiobiological effects of 3DCRT radiotherapy for treating postmastectomy breast cancer with axillary metastases. The technique was validated with two dosimeters, namely TLD and EBT3 film. Dosimetry and radiobiologic parameters assessed the dose to target and normal tissues. The results of TPS with plans CW and Ax for variations of two and three fields met the recommendations of the ICRU Report 50, with a PTV dose range of 95-107% [15]. The HI and CI parameters showed the uniformity of the dose received on the PTV structure's volume and shape. The type of planning technique, cancer shape and location, tissue density, and experience of the medical physicist affect the HI and CI values. The HI obtained ranged from 0.289 to 0.351, lower than the 1.16 obtained by Aras et al. using the 3D-CRT technique [28]. The CI values for Ax and CW planning were 0.5 and 0.735, respectively. In addition, the HI values obtained were close to those of more advanced radiotherapy planning techniques. From the study conducted by Xie et al., the HI values of volumetric modulated arc therapy (VMAT), intensity modulated radiation therapy (IMRT), and tomotherapy planning techniques were 0.1. Mixed beam therapy planning had a HI value of 0.2 for postmastectomy breast cancer treatment planning [29]. The HI difference between VMAT, IMRT, and tomotherapy techniques with the results obtained is 0.189, and mixed beam therapy is 0.089. The best HI value is the HI value that is close to zero or has many zero decimal digits. This shows that the HI value of the 3DCRT technique is considered because it has HI that is close to the advanced radiotherapy technique. The NTCP results for the heart and left lung are 1.587 and 0.654, with the lowest complication rates compared to other OARs. This is because the heart and left lung are far from the treatment target. The dose received may be due to secondary scattering that occurs internally. The NTCP results for the right lung showed the highest NTCP value of 4.9. The study results by Xie et al. [29] obtained an NTCP value of 3.8 which is smaller than the study results for the same case. This difference can occur due to the multileaf collimator (MLC) factor in Xie et al.'s research using a dynamic type of MLC, meaning that the MLC can adjust the target shape accurately and computerized. This study uses a static type of MLC so that the target shape adjustment is done manually. Overall, the NTCP value for heart and left lung complications should have been lower than 5% to avoid the effects of organ dysfunction [30].

Furthermore, tumor control and patient condition must be considered. The results showed no significant difference in the NTCP value of the right lung between the two or three field plans, namely, below 5%, with a p-value > 0.05. These are consistent with Zhang et al., who obtained 4.1% for the ipsilateral lung using the IMRT technique [31]. The dose limitation evaluation results met the OARs dose-limiting standard recommended by Quantec [17]. The 3D-CRT technique can be used as a radiotherapy treatment for postmastectomy breast cancer with axillary lymph metastases in the Ax and CW areas.

During the TPS dose evaluation, the right lung received a dose between 0.06 and 1.24 Gy per 2 Gy fraction. This is important because such a dose can increase the risk of secondary cancer development. Point dose measurements in the lung area using TLD obtained a mean discrepancy of 9.14%. Meanwhile, Abdemanafi et al. 2020 obtained a discrepancy of 4.46% from the measurement of lung dose with TLD100 [13]. Point dose measurements in the lung area using EBT3 film have an average discrepancy of 4.34% from the TPS. This discrepancy can be possible from the

calibration uncertainty factor between the dosimeter and Linac, the reader's calibration factor, and the uncertainty of the TLD and EBT3 film position. Furthermore, the discrepancy between the planned and measured dose was due to increased secondary radiation to the tissues within the treatment area. This condition was caused by artifacts or air gaps in the phantom and variations in the phantom material density, which can increase the Compton interaction. The dose difference from the plan was at -11.8% and similar to the previous study by Higgins et al. Spatially, high-energy photons of the MV range can cause measurement differences of more than 10% for the calculated values [32]. The presence of a scattering dose received by the detector, where only a portion of the diode is illuminated, can cause considerable uncertainty of 5 - 10% in the response between the planned and measured dose. This is in line with Alaei et al. [33], who found that the influence of the radiation angle affected the detector's sensitivity, which initiated measurement inaccuracies. However, this study obtained promising results, with an average percentage difference of < 10%.

Measurements obtained with the EBT3 film had more minor differences than TLD values compared to the TPS results. Although EBT3 cannot be reused like TLD after irradiation, it is easy to use and has an accessible reader. Comparison of the results of the two detectors, showing dose measurements on a case-specific anthropomorphic phantom of postmastectomy breast cancer with axillary metastases, there is a significant difference between TLD and EBT3 film readings. Good measurement results were obtained in dose readings with EBT3 film. EBT3 film can be cut into different shapes and sizes to customize the measurement site on the phantom or the patient. In addition, EBT3 film includes 2D dosimetry, has a high spatial resolution, can be read repeatedly, and is not sensitive to light, which may make it a better dosimeter than TLD [34]. The limitation of this study is that the dose measurement was performed using a phantom and has not been used on patients. This study's in vitro dosimetry evaluation using a specific anthropomorphic phantom produced results that were close to real-life clinical treatment. However, organ movement and breathing variability were not considered.

Conclusion

This study conducted the dosimetry evaluation and measurement of 3D-CRT Radiotherapy Treatment Planning and analysis of radiobiological effects. A specific thoracic anthropomorphic phantom for postmastectomy right breast cancer with axillary lymph metastases was used for the experiment, both TPS and direct measurement. Furthermore, verification of point dosimetry between TPS and actual measurements using TLD100 and EBT3 film obtained a good match with a global difference of 9.14% and 4.34% from the planning. Facts showed that quality assurance and control with specific phantoms had been successfully carried out and proven. Anthropomorphic phantoms are vital in quality assurance and control procedures or in developing other techniques.

Acknowledgment

The authors are grateful to the management of Dr. Ramelan Naval Hospital in Surabaya, Indonesia, for the permission to conduct this study as well as collect and analyze data at the Radiotherapy Facility.

References

1. The Global Cancer Observatory. World Factsheet of Cancer Today: Breast Cancer Incident and Mortality in the World. International Agency for Research on Cancer 2022.https://gco.iarc.who.int/media/globocan/factsheets/populations/900-world-fact-sheet.pdf .
2. Chakrabarty S, Sharma S, Maji A, Biswas L, Mandal S. Prospective study to compare the dose distribution and acute toxicity of three-dimentional conformal radiation therapy with intensity-modulated radiation therapy for post-mastectomy radiotherapy in carcinoma breast. J Med Sci Res. 2022;10(3):133–40.
3. Emami B, Lyman J, Brown A, Cola L, Goitein M, Munzenrider JE, et al. Tolerance of normal tissue to therapeutic irradiation. International Journal of Radiation Oncology* Biology* Physics. 1991 May 15;21(1):109-22.
4. Sprung CN, Chao M, Leong T, McKay MJ. Chromosomal radiosensitivity in two cell lineages derived from clinically radiosensitive cancer patients. Clinical cancer research. 2005 Sep 1;11(17):6352-8.
5. Xie X, Ouyang S, Wang H, Yang W, Jin H, Hu B, et al. Dosimetric comparison of left-sided whole breast irradiation with 3D-CRT, IP-IMRT and hybrid IMRT. Oncology reports. 2014 May 1;31(5):2195-205.
6. Lobo D, Challapalli S, Banerjee S, Putha SK, Saxena PP, Holla R, et al. Fabrication and development of a thorax phantom to evaluate 3D CRT treatment planning techniques for post-mastectomy chest wall radiotherapy. Physical and Engineering Sciences in Medicine. 2021 Jun;44:425-32.
7. Prior PW, Sparks I, Wilson JF, Li XA, White JR. Use of three dimensional conformal radiation therapy (3DCRT) for node positive breast cancer does not result in excess lung and heart irradiation. International Journal of Radiation Oncology, Biology, Physics. 2011 Oct 1;81(2):S805.
8. Pierce LJ, Butler JB, Martel MK, Normolle DP, Koelling T, Marsh RB, et al. Postmastectomy radiotherapy of the chest wall: dosimetric comparison of common techniques. International Journal of Radiation Oncology* Biology* Physics. 2002 Apr 1;52(5):1220-30.
9. White DR. The design and manufacture of anthropomorphic phantoms. Radiation Protection Dosimetry. 1993 Sep 1;49(1-3):359-69.
10. Winslow JF, Hyer DE, Fisher RF, Tien CJ, Hintenlang DE. Construction of anthropomorphic phantoms for use in dosimetry studies. Journal of Applied Clinical Medical Physics. 2009 Jun;10(3):195-204.

11. Choi Y, Lee IJ, Park K, Park KR, Cho Y, Kim JW, et al. Patient-specific quality assurance using a 3D-printed chest phantom for intraoperative radiotherapy in breast cancer. Frontiers in Oncology. 2021 Mar 15;11:629927.
12. Butson MJ, Elferink R, Cheung T, Peter KN, Stokes M, Quach KY, et al. Verification of lung dose in an anthropomorphic phantom calculated by the collapsed cone convolution method. Physics in Medicine & Biology. 2000 Nov 1;45(11):N143.
13. Abdemanafi M, Tavakoli MB, Akhavan A, Abedi I. Evaluation of the lung dose in three-dimensional conformal radiation therapy of left-sided breast cancer: A phantom study. Journal of Medical Signals & Sensors. 2020 Jan 1;10(1):48-52.
14. E. Endarko and A. P. Hariyanto. 3D Fantom Antropomorfik Untuk Jaminan Kualitas Radioterapi Pada Kasus Kanker Payudara Pasca-Mastektomi. Patent Indonesia 2021;P00202102195.
15. Hodapp N. The ICRU Report 83: prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT). Strahlentherapie und Onkologie: Organ der Deutschen Rontgengesellschaft...[et al]. 2012 Jan;188(1):97-9.
16. Feuvret L, Noël G, Mazeron JJ, Bey P. Conformity index: a review. International Journal of Radiation Oncology* Biology* Physics. 2006 Feb 1;64(2):333-42.
17. Bentzen SM, Constine LS, Deasy JO, Eisbruch A, Jackson A, Marks LB, Ten Haken RK, Yorke ED. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC): an introduction to the scientific issues. International Journal of Radiation Oncology* Biology* Physics. 2010 Mar 1;76(3):S3-9.
18. Chang JH, Gehrke C, Prabhakar R, Gill S, Wada M, Joon DL, Khoo V. RADBIOMOD: a simple program for utilising biological modelling in radiotherapy plan evaluation. Physica Medica. 2016 Jan 1;32(1):248-54.
19. Liuzzi R, Piccolo C, D'Avino V, Clemente S, Oliviero C, Cella L, et al. Dose–response of TLD-100 in the dose range useful for hypofractionated radiotherapy. Dose-Response. 2020 Feb 11;18(1):1559325819894081.
20. Sipilä P, Ojala J, Kaijaluoto S, Jokelainen I, Kosunen A. Gafchromic EBT3 film dosimetry in electron beams—energy dependence and improved film read-out. Journal of applied clinical medical physics. 2016 Jan;17(1):360-73.
21. Ezzell GA, Burmeister JW, Dogan N, LoSasso TJ, Mechalakos JG, Mihailidis D, et al. IMRT commissioning: multiple institution planning and dosimetry comparisons, a report from AAPM Task Group 119. Medical physics. 2009 Nov;36(11):5359-73.
22. Ataei G, Rezaei M, Gorji KE, Banaei A, Goushbolagh NA, Farhood B, et al. Evaluation of dose rate and photon energy dependence of gafchromic EBT3 film irradiating with 6 MV and Co-60 photon beams. Journal of Medical Signals & Sensors. 2019 Jul 1;9(3):204-10.
23. Borca VC, Pasquino M, Russo G, Grosso P, Cante D, Sciacero P, et al. Dosimetric characterization and use of GAFCHROMIC EBT3 film for IMRT dose verification. Journal of applied clinical medical physics. 2013 Mar;14(2):158-71.
24. Bahreyni Toossi MT, Gholamhosseinian H, Vejdani Noghreiyan A. Assessment of the Effects of Radiation Type and Energy on the Calibration of TLD-100. Iranian Journal of Medical Physics. 2018 Jul 1;15(3):140-5.
25. Callens M, Crijns W, Simons V, De Wolf I, Depuydt T, Maes F, Haustermans K, D'hooge J, D'Agostino E, Wevers M, Pfeiffer H. A spectroscopic study of the chromatic properties of GafChromic™ EBT3 films. Medical physics. 2016 Mar;43(3):1156-66.
26. Niroomand-Rad A, Chiu-Tsao ST, Grams MP, Lewis DF, Soares CG, Van Battum LJ, et al. Report of AAPM task group 235 radiochromic film dosimetry: an update to TG-55. Medical physics. 2020 Dec;47(12):5986-6025.
27. Khachonkham S, Dreindl R, Heilemann G, Lechner W, Fuchs H, Palmans H, et al. Characteristic of EBT-XD and EBT3 radiochromic film dosimetry for photon and proton beams. Physics in Medicine & Biology. 2018 Mar 15;63(6):065007.
28. Aras S, İkizceli T, Aktan M. Dosimetric comparison of three-dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiotherapy techniques (IMRT) with radiotherapy dose simulations for left-sided mastectomy patients. European journal of breast health. 2019 Apr;15(2):85.
29. Xie Y, Bourgeois D, Guo B, Zhang R. Postmastectomy radiotherapy for left-sided breast cancer patients: Comparison of advanced techniques. Medical dosimetry. 2020 Mar 1;45(1):34-40.
30. Sardaro A, Petruzzelli MF, D'Errico MP, Grimaldi L, Pili G, Portaluri M. Radiation-induced cardiac damage in early left breast cancer patients: risk factors, biological mechanisms, radiobiology, and dosimetric constraints. Radiotherapy and Oncology. 2012 May 1;103(2):133-42.
31. Zhang Y, Huang Y, Ding S, Yuan X, Shu Y, Liang J, Mao Q, Jiang C, Li J. A dosimetric and radiobiological evaluation of VMAT following mastectomy for patients with left-sided breast cancer. Radiation Oncology. 2021 Dec;16:1-1.
32. Higgins PD, Alaei P, Gerbi BJ, Dusenbery KE. In vivo diode dosimetry for routine quality assurance in IMRT. Medical physics. 2003 Dec;30(12):3118-23.
33. Alaei P, Higgins PD, Gerbi BJ. In vivo diode dosimetry for IMRT treatments generated by Pinnacle treatment planning system. Medical Dosimetry. 2009 Mar 1;34(1):26-9.
34. Fokou M, Hasford F, Ndontchueng MM, Tagoe SA, Njantang RN, Dery TB, Simo A, Larbi KO, Mantheaw P, Eduful E, Motapon O. In-vivo dosimetry with EBT-3 gafchromic films and thermoluminescent dosimeters in breast cancer radiotherapy treatments. Health and Technology. 2023 Jul;13(4):585-600.