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Dosimetric Evaluation of Post-mastectomy Three-Dimensional Conformal Radiation Therapy (3DCRT) Breast Cancer Treatment Plans

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Abstract

Breast cancer is the most diagnosed cancer in women globally. External beam radiotherapy is one method to treat breast cancer, which can be given to the patients after mastectomy. The changes in anatomy of breast tissues after mastectomy makes the radiotherapy treatment very challenging to ensure the prescribed dose delivered to the tumour target while the radiation to the surrounding critical organs is kept to be low. This study aims to evaluate the dosimetric parameters of radiotherapy treatment plans for breast cancer patients after mastectomy delivered using 3DCRT technique. The evaluation includes the target coverage to the PTV, defined as the volume of PTV receiving 95% of the prescribed dose and the volume of PTV receiving 107% of the prescribed dose. The min, max and mean dose to the PTV were also recorded. The dosimetric parameters to the OARs were Dmean and V20 to the lung, Dmean and V25 to the heart, Dmean to esophagus and Dmax to the spinal cord. The result shows that target coverage is fulfilled in most of the plans, however the hot spot in the PTV also observed in the most of the plans. Dose to heart, left lung, esophagus and spinal cord are relatively low and below the constraint recommended by QUANTEC, however the V20 to the right lung exceeded the constraint in the most of the plans. The combination of photon and electron beam might be useful to reduce the excessive dose to the right lung.

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Introduction

Breast cancer is the most diagnosed cancer in female. Based on Globocan data 2020, breast cancer account for 11.7% of the total new cancer cases globally and account for 24.5% of the total cancer cases in female, which places the breast cancer as the most diagnosed cancer in

the world. The increase of breast cancer cases is influenced by hormonal risk and life style risk factors. The hormonal risk factors include menstruation at early age, menopause at late age, first pregnancy at late age, rare breastfeeding, oral contraception and hormone therapy. The life style risk factors include alcohol consumption, overweight, and less physical activities [1].

Breast cancer can be classified into non-invasive and invasive types. Non-invasive breast cancer does not infiltrate the surrounding fat and connective tissues. The examples of this category are ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). DCIS is more commonly found than LCIS, however, it can develop into invasive cancer if left untreated. Invasive breast cancer destroys ductal wall and lobule as well as infiltrating surrounding connective tissues. The examples of this category are invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC). IDC is more dominant which account for 70-80% of total breast cancer cases [2] Another type of breast cancer is inflammatory breast cancer (IBC) which quickly spread through lymphatic causing patient already found in the metastasis stadium at time of diagnosis procedure [3], [4].

The common management of breast cancer includes surgery, chemotherapy, and radiotherapy. The surgical treatment involves the removal of nodule known as lumpectomy and the removal of breast tissue known as mastectomy. In chemotherapy, the anti-cancer drugs are given to the patients which can be administered before surgery, aiming to shrink the tumor size, or given after surgery. Radiotherapy uses a high energetic radiation to eradicate tumor. In breast cancer management, radiotherapy is often given post after surgery [2], [4]. The aim is to eradicate the remained diseases and to minimize the cancer recurrence [3]. Post-mastectomy radiation therapy has been shown to increase the local control of breast cancer patients [5]. New approaches for breast cancer management are gene therapy, hormone therapy and immunotherapy [6], [7].

The goal of radiotherapy is to deliver lethal dose to the tumor and minimize the dose to the normal tissues surrounding the tumor. The introduction of Three-Dimensional Conformal Radiation Therapy (3DCRT) enables sparing normal tissues by producing conformal dose distribution. Typically, three to five beams are used to treat the chest wall region and lymphatic region. The use of opposed tangential beams can reduce the radiation to the contralateral breast and minimize the dose to the normal lung and heart. The general dose prescription for chest wall treatment is 50 - 50.4 Gy in 25 - 28 fractions. There are several acute and chronic risks of post-mastectomy radiotherapy. The acute risks are fatigue, sore throat, and dermatitis. The chronic risks are hyperpigmentation, fibrosis of chest wall, radiation pneumonitis and rib fracture [5].

To ensure that the radiotherapy beneficial for the patients, the treatment plan was designed and optimized to full fill the objective of the treatment. The objective is to deliver the prescribed dose to the target and to minimize the dose to the OARS. The ICRU Report No 50 give the guidelines of the dose homogeneity within the target, which should be within +7% and - 5% of the prescribed dose [8]. The dose constraint to the normal structures follows the recommendation from QUANTEC [9]. For breast cancer treatment, the critical organs should be considered are lung and heart. The radiation exposure to the lung is related to radiation pneumonitis with $V20Gy \leq 30\%$ with the endpoint of 20% radiation pneumonitis risk [10]. While the dose constraint for heart is $V25Gy \leq 10\%$ associated with cardiac damage less than 1% [11].

Radiotherapy is often given as an adjuvant treatment in the breast cancer management after patient underwent mastectomy which includes removal of all breast tissues. This treatment is recommended for the breast cancer patients with early stage and carcinoma in situ. The mastectomy procedure changes the breast tissues, in which radiotherapy might cause a high dose irradiation to the organs beneath the breast such as lung and heart which might manifesting in high complication probabilities for those normal tissues. A study of left-breast cancer cases by Wang et al. (2013) and Liu et al. (2016) shows that the dose received by the left lung during post-mastectomy radiotherapy is slightly higher from the defined dose constraint [12], [13]. This study aims to evaluate the dosimetric parameters of the 3DCRT plan delivered for the right-side breast cancer treatment in our local hospital. This is because the breast cancer is dominant cancer cases treated in local hospital using external photon beam therapy.

Materials and Methods

Treatment plan

Forty-one clinical treatment plans of breast cancer cases previously designed in Monaco Treatment Planning System (TPS) software version 5.11.03 were studied retrospectively. All the studied plans were from female patients. All the plans had the tumor located at the right side of the breast. The Planning Treatment Volume (PTV) size ranged from 582.56 cm³ to 1613.23 cm³ with the median value of 1051.40 cm³. The radiation was given after mastectomy with the prescribed dose of 50 Gy given in 25 fractions, five fractions per week. Each plan consisted of four beams which are two opposed tangential beams and a pair of beams for supraclavicular regions. The beam from mediolateral had the gantry angle of 303-318 degree and the beam from lateral-medio had the gantry angle of 123-138 degree for chest wall area. For the supraclavicular region, the beam angles were 345 and 165 degrees. All the patients were treated using a 6 MV photon beam produced from the Elekta Synergy Platform (Elekta AB, Stockholm, Sweden) with the 3DCRT technique.

Treatment plan Evaluation

Dose volume histogram (DVH) was generated for each plan after the designed beam was computed using the dose calculation algorithm in the TPS. The cone convolution algorithm was chosen for the dose computation. The cumulative DVH for each treatment plans were used to derive the dosimetric parameters of the PTV and Organ at Risks (OARs). The dosimetric parameters to the PTV were the percentage of the PTV volume receiving the dose $\geq 95\%$ of the prescribed dose (V95) and the percentage of the PTV volume receiving the dose $\geq 107\%$ of the prescribed dose (V107). The maximum, mean and minimum dose to the PTV were also recorded. The objective of the treatment was $V95 \geq 95\%$ of the PTV volume and $V107 \leq 1\%$ of the PTV volume.

The OARs evaluated in this study were normal ipsilateral and contralateral lung, heart, spinal cord, and esophagus. The dosimetric for the normal lung was mean dose (Dmean) and volume of the lung receiving the dose ≥ 20 Gy (V20). For the heart, besides Dmean, the volume of the heart receiving the dose ≥ 25 Gy (V25) was recorded. The maximum dose (Dmax) to the spinal cord and the mean dose to the esophagus were also recorded.

Data Analysis

The dosimetric parameters of the PTV were evaluated using ICRU Report 50 and 62 recommendations, which has been adopted by the local hospital with a slightly adjustment.

The objective of the treatment was $V95 \geq 95\%$ of the PTV volume and $V107 \leq 1\%$ of the PTV volume. The dose received by the PTV was evaluated to ensure whether this objective was fulfilled or not. The evaluation of the dose to OARs was performed by comparing the dose received by the OARs to the dose constraints recommended by the QUANTEC, as shown in Table 1.

Table 1. Dose constraints for OARs in breast cancer therapy based on QUANTEC recommendations

No	OARs	Parameters	Endpoints
1	Lung	$V20 \leq 30\%$ $D_{mean} \leq 20$ Gy	Symptomatic pneumonitis
2	Heart	$D_{mean} < 26$ Gy $V25 < 10\%$	Pericarditis Long term cardiac mortality
3	Spinal Cord	$D_{max} = 50$ Gy	Myelopathy
4	Esophagus	$D_{mean} < 34$ Gy	Grade ≥ 3 acute esophagitis

Result and Discussion

Dosimetric parameters of the PTV

Target coverage to the PTV for the forty-one plans is shown in Figure 1. It shows that most of the plans have the PTV target coverage $V95 \geq 95\%$, except in one plan (plan 7). Although slightly lower than the objective, the target coverage in plan 7 is still cover 92% of the PTV volume. Regarding the volume of the PTV receiving the dose larger than 107% of the prescribed dose ($V107$), the result shows that there are only four plans having $V107 < 1\%$ of the PTV, while the rest of the plans have $V107 > 1\%$. The value of $V107$ ranges from 0.48% to 47.31% with the median value of 4.45%. There are seven plans which have $V107\%$ larger than 10% of the PTV volume. This indicates that there is hotspot in the PTV volume and the objective $V107 \leq 1\%$ was not meet in the majority of the plans.

The value of D_{min} , D_{max} and D_{mean} to the PTV is given in Table 2. The D_{min} to the PTV ranges from 4.85 Gy - 24.95 Gy with the average value of 15.76 ± 6.36 Gy. For the D_{max} to the PTV, the value ranges from 51.77 Gy - 57.97 Gy with the average value of 55.18 ± 1.12 Gy. The D_{mean} to the PTV has an average value of 51.07 ± 0.42 Gy. This shows that the mean dose received by the PTV is slightly higher than the prescribed dose.

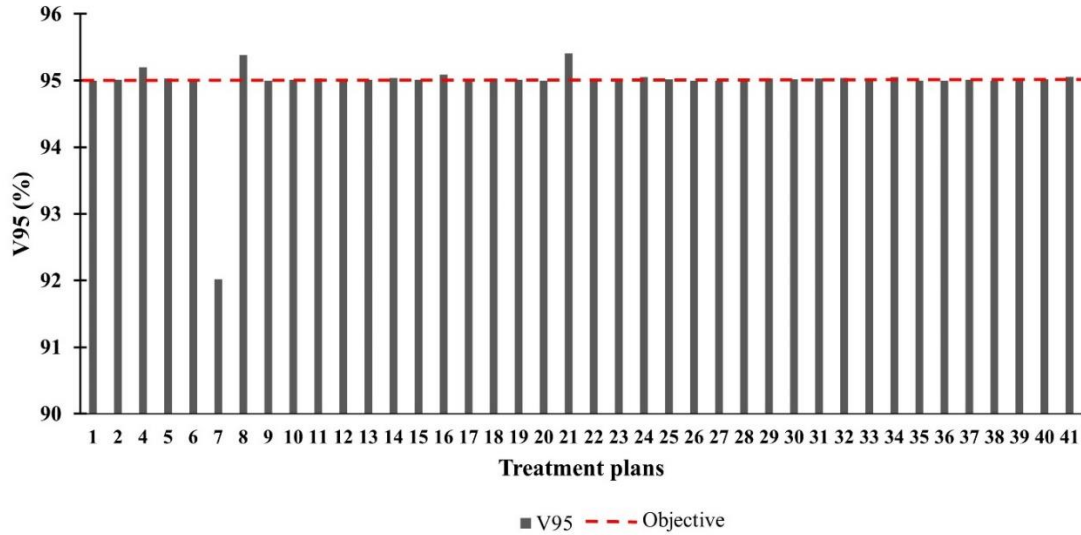


Figure 1. Distribution of the V95 of the PTV for all studied treatment plans. The objective is V95 ≥95% shown as the dashed line on the graph.

Table 2. Dosimetric parameters to the PTV and OARs

No	Structure	Parameter	Objective	Range	Median	Average
1	PTV	V95	≥95%	92.02 – 95.41 %	95.02%	94.97±0.47%
		V107	<1%	0.48 – 47.31 %	4.45%	7.59±9.63%
		Dmin		4.85 – 24.95 Gy	17.95%	15.76±6.36 Gy
		Dmax		51.77 – 57.97 Gy	55.02 Gy	55.18±1.12 Gy
		Dmean		50.46 – 52.42 Gy	51.02 Gy	51.07±0.42 Gy
2	Ipsilateral Lung	V20	≤30%	27.73-47.27%	39.50 Gy	39.72±4.26
		Dmean	20 Gy	14.27 – 23.22 Gy	19.45 Gy	19.66±1.95
3	Contralateral Lung	V20	≤30%	0.00%	0.00%	0.00 %
		Dmean	20Gy	0.65-0.93 Gy	0.76 Gy	0.76±0.06 Gy
4	Heart	V25	<10%	0.00 – 1.60%	0.00%	0.08±0.28%
		Dmean	<26 Gy	0.98 – 2.64 Gy	1.32 Gy	1.43±0.33 Gy
5	Spinal Cord	Dmax	50 Gy	5.40-54.80 Gy	24.37 Gy	25.06±11.01 Gy
6	Esophagus	Dmean	<34 Gy	1.98 – 12.04 Gy	3.50 Gy	4.54±2.83 Gy

Dosimetric Parameters to OARs

Table 2 also summarizes the dosimetric parameters to the OARs. The dose received by normal lung is shown in Figure 2. For the ipsilateral lung (i.e., right lung), most of plans having V20 > 30%, except in one plan. The V20 value of the ipsilateral lung ranges from 27.73% to 47.27% with the median value of 39.5%. While for the contralateral lung (i.e., left lung), the V20 is zero for all plans. The distribution of mean dose in the ipsilateral lung is

shown in Figure 3. It is shown that there are 17 plans having the Dmean higher than the dose constraint recommended by the QUANTEC, i.e., 20 Gy. While for the contralateral lung, the Dmean are relatively low and below the constraint from the QUANTEC. This is because the tumor is located at the right side of the breast, therefore the right lung received a relatively higher dose compared to the left lung. As shown in Figure 4, the right lung received more radiation doses compared to the left lung.

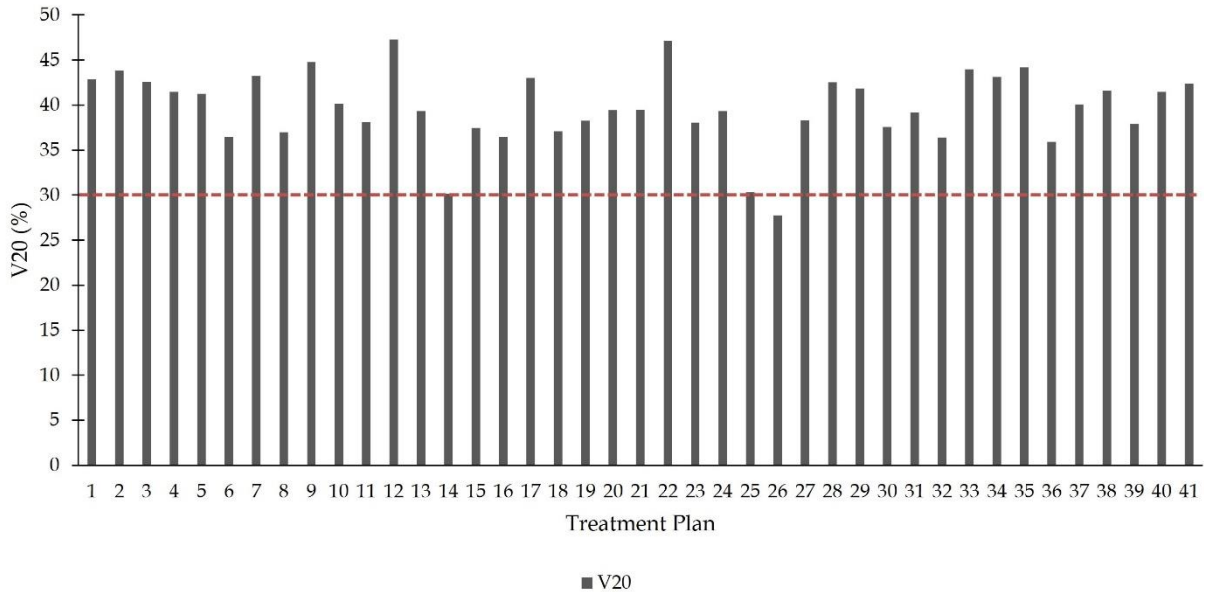


Figure 2. The distribution of the V20 parameter to the right lung. The dose constraint is $V20 \leq 30\%$ shown as the dashed line.

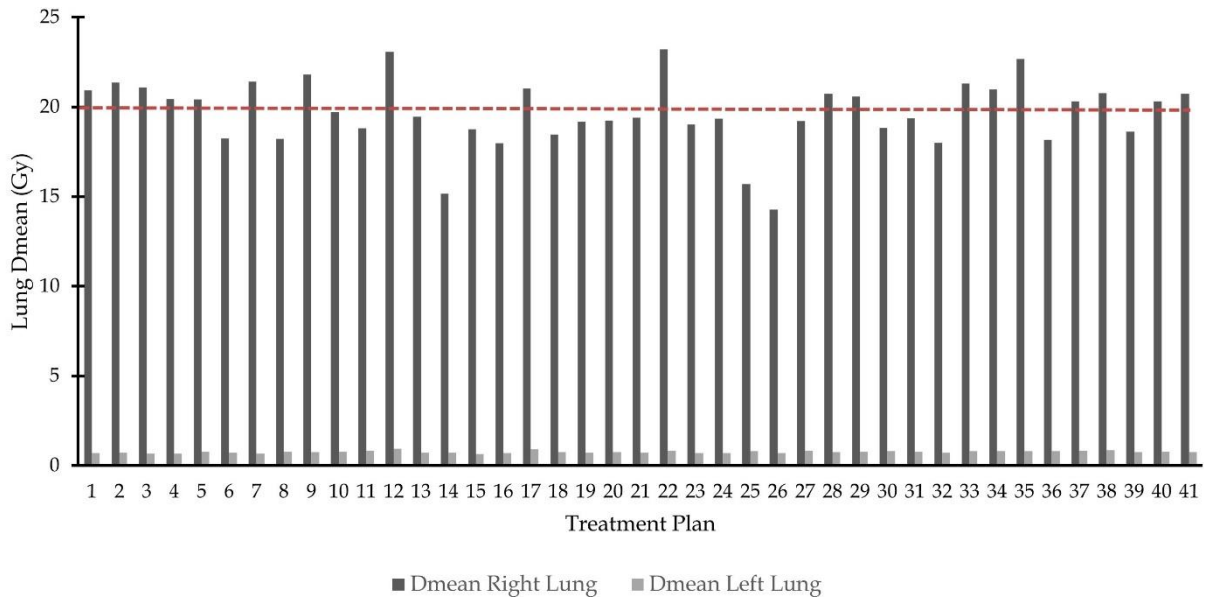


Figure 3. The Dmean received by the right and left lung. The dashed line indicates the dose constraint, $Dmean \leq 20$ Gy.

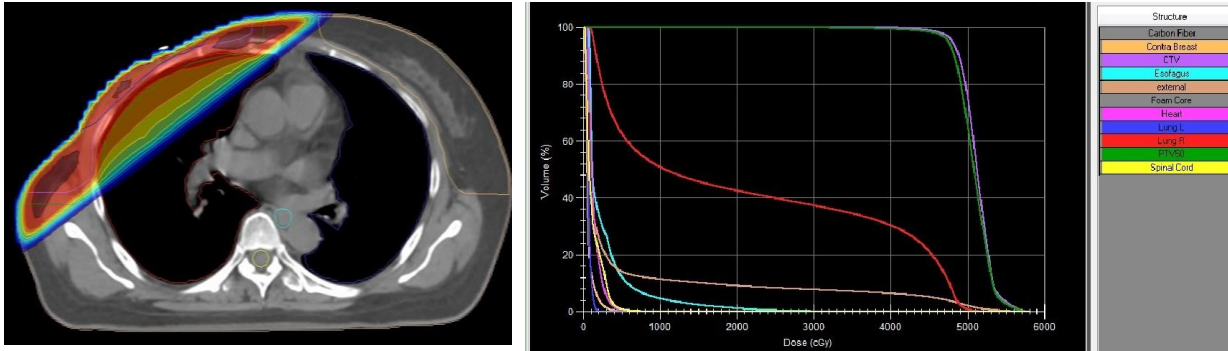


Figure 4. The dose distribution of one breast cancer plan: a) the isodose line distribution, b) cumulative dose volume histogram of the plan

The dose received by the heart is given in Table 2. The result shows that all the plans have the Dmean to the heart lower than the QUANTEC recommendations with the average value of 1.43 ± 0.33 Gy, ranging from 0.98 - 2.64 Gy. The value of V25 of the heart is very low and below the constraint from the QUANTEC, ranging from 0 - 1.6%. The reason of low dose value received by the heart structure is because the location of the tumor volume is at the right side of the thorax. Therefore, the heart structure does not suffer from a high radiation exposure.

Figure 5 shows the distribution of the Dmax received by the spinal cord. The average value is 25.06 ± 11.01 Gy. The lowest Dmax is received by the plan 41 and the highest Dmax is received by the plan 19. The majority of the plan have the Dmax value below the constraint from the QUANTEC (i.e., 50 Gy). However, there are two plans which have the Dmax value higher than the constraint, i.e., plan 19 and plan 36.

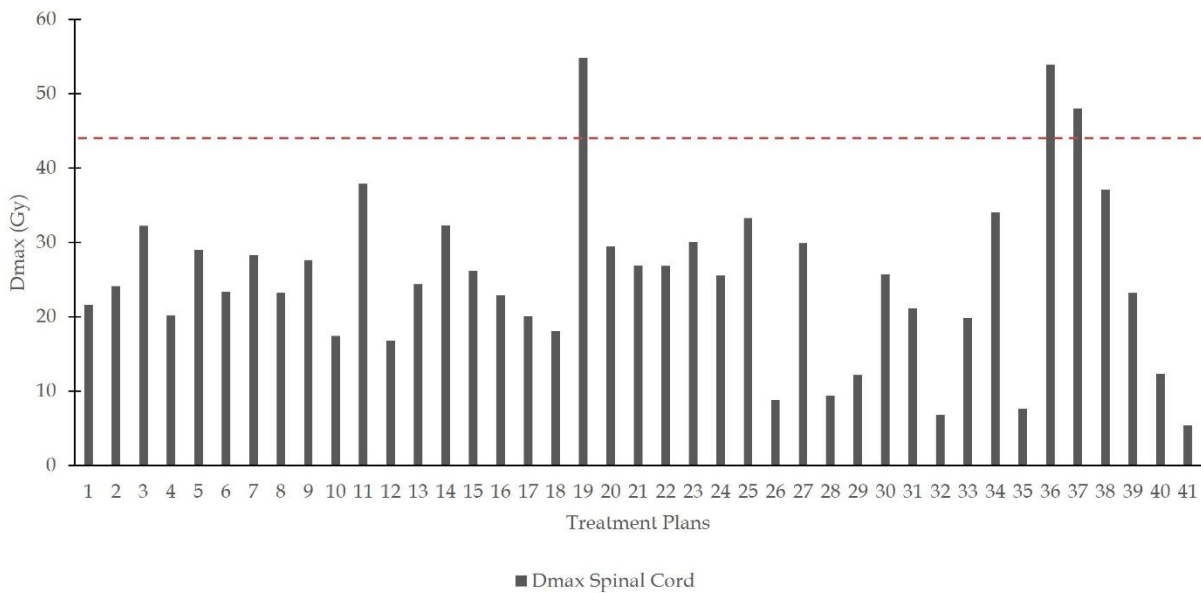


Figure 5. The distribution of the Dmax received by the spinal cord in forty plans.

The dose received by the esophagus is relatively low and far below the constraint from the QUANTEC (i.e., 34 Gy). The Dmean to the esophagus ranges from 1.98 – 12.04 Gy, with an average value of 4.54 ± 2.83 Gy.

Discussions

This study evaluates forty-one breast cancer treatment plans treated using a 6 MV photon beam radiotherapy with the 3DCRT technique in the local hospital. The results shows that the target coverage (V95 of the prescribed dose) is fulfilled in the most of the treatment plans. However, the target volume receiving the dose larger than 107% of the prescribed dose exceeds 1% in the majority of the treatment plans. Regarding the dose received by the OARs, only the dose received by the right lung which needs a greater concern, since the majority of the plans receive the dose higher than the constraint recommended by the QUANTEC. This applies for both the V20 to the lung and the Dmean to the lung parameters. On the other hand, the dose received by the left lung, the heart, the spinal cord and the esophagus are still below the constraint from the QUANTEC. Exception is two plans which has the Dmax value to the spinal cord slightly higher than the constraint.

The factor that causes the high hot spot and the high dose received by the right lung organ is because there is a change in the breast anatomy of the breast cancer patients after mastectomy procedure as shown in Figure 4a. The removal of the breast tissue causes the target volume of the treatment becomes closer to the skin surface. This also increases the doses received by the skin tissues as reported by [14]. Since the treatment uses the photon beam, the doses will reach a maximum value at a certain depth, depending on the photon energy used in the treatment. At the skin surface, the photon dose is lower due to a build-up factor, as the characteristics of the photon beam. To obtain the higher dose on the skin surface, in order to achieve the target coverage objective, i.e., $V95 \geq 95\%$, the dose needs to be increased. As a consequence, the hotspot volume becomes higher as well as the dose received by the right lung organ which lies under the treated breast tissue also becomes higher. Several studies reported that the Intensity Modulated Radiation Therapy (IMRT) offers a dose reduction to the OARs such as skin and lung [12]-[14].

The use of electron beam could be considered as an alternative for treating the tumor located close to the surface, aiming for reducing the dose received by the lung organs. The study by Kesava Ramgopal (2014) shows that the use of single energy electron beam reduced the dose received by the lung and heart organs [15]. This is because the electron beam has a shorter range, in order of cm, thus the penetration is shallower compared to the photon beam [16] Another alternative is the addition of bolus from the tissue equivalent material to increase the dose received by the skin surface [17] However, the use of bolus should be taken carefully as its use is reported could increase the risk of grade 3 radiation dermatitis.

Although in this study the dose received by the right lung exceeds the dose constraint recommended by the QUANTEC, it should be considered that lung organ is tissue with a parallel functional unit. The smallest functional unit in the lung organ is alveolus, in which each alveolus works independently from other alveoli. This parallel architecture allows the lung organ to perform its function although part of its tissues received the a relatively

radiation dose. However, the concern should be paid on the amount of the lung volume received the high dose, to ensure it is not exceeded 1/3 of the total lung volume.

Conclusion

External photon beam radiation therapy using 3DCRT technique for the right-sided breast cancer treatment after mastectomy has fulfilled the objective of 95% target coverage of the PTV in most of the plans. The objective of V107 to the PTV less than 1% is only met in four out of forty-one plans. A greater concern should be paid on the dose received by the right lung, which is located beneath the tumor target, since the value is higher than the recommended dose by the QUANTEC. The change of breast anatomy after mastectomy might contribute to a higher dose received by the right lung. The dose received by the other organs are still below the constraint from the QUANTEC. To reduce the doses to the ipsilateral lung, a combination of the photon and electron beams as well as the use of IMRT technique and hybrid IMRT might be considered in the future.

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