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Research Article

Effect of three-dimensional conformal radiotherapy with full beam size technique on clinical outcomes for patients with left breast cancer

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Abstract

Background and objectives: Three-dimensional conformal radiotherapy (3DCRT) is used to treat breast cancer with multiple radiation beam fields with precision while sparing normal tissue. Noteworthy problem with treatment using different isocenters in 3DCRT technique is undesirably increased radiation doses due to superposition of fields of radiation beams. At this condition, the use of a single isocenter appears to be a suitable solution. The objective of this study was to evaluate the clinical outcomes of 3DCRT with full beam technique (single isocenter) and evaluate effect high-energy photon beam during whole breast irradiation on healthy tissues, planning target volume, dose homogeneity, and dose of organs at risk (such as heart, cord, right and left lungs, and spinal cord).

Methods: Radiotherapy treatment of 50 patients with left-sided breast cancer treated to a prescribed dose of 40.05 Gy in 20 fractions, 5 fractions per week during 4 weeks. The treatment plans executed by using Linear accelerator (Elekta Synergy) with single isocenter for evaluation of clinical outcomes based on three-dimensional conformal radiotherapy (3DCRT) technique with full beam plan.

Results: Mean dose Gy for planning target volume PVT was (40.53± 0.46 Gy). The dose for complete beam planning methods was 40.050Gy, and Conformity Index CI < 1. The mean heart doses were (476.7±314.6 cGy), and the heart was exposed to dose 4.4±4.5 cGy. The low dose volume in this technique was less than <20 Gy. Similarly, the left lung was exposed to the low dose volume (V20) was 0.020 cGy, but for the right lung (V20) was zero. The mean dose of the left lung was (10.18Gy), but with the right lung was (0.0882 Gy). The Spinal Cord Max dose <2 Gy

Conclusion: Complete planning treatment plan achieved improved dose homogeneity and superior outcome regarding dose to normal tissues.

Keywords: Breast cancer, Isocenter, Complete field, Radiotherapy, Supraclavicular

Background and objectives

The treatment management of breast cancer is by mastectomy and then chemotherapy and irradiation. External Beam Radiation Therapy (EBRT) is the most common type of radiation used to treat breast cancer. Three-dimensional conformal radiotherapy (3DCRT) is used to treat breast cancer with multiple radiation fields with precision while sparing normal tissue. 3DCRT/quadrant breast irradiation delivers radiation to a minimal portion of the breast. Multiple, targeted beams reduce the chances for irradiation of critical organs (healthy tissue) such as heart, spinal cord, and lungs. 3DCRT is a technique in which radiation beams used during cancer treatment are shaped to correspond with the tumor. Radiotherapy techniques in the treatment of breast cancer vary in different institutions[1-3].

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3D-CRT advantages are simple in delivering the whole breast dose and with great preventing of the contralateral breast tissues and lung volume. Sparing the contralateral lung is also one of the major clinical considerations of this type of treatment. Noteworthy problem with treatment using different isocenters in 3DCRT technigue is undesirably increased radiation doses due to superposition of fields of radiation beams. At this condition, the use of a single isocenter appears to be a suitable solution[4,5].

Generally, during radiotherapy for breast cancer, a percentage of the prescribed dose that is

delivered to the target volume (breast cancer) is absorbed by organs outside the radiation field such as heart, spinal cord, esophagus, and lungs. These organs may lie close to the radiation field, or remotely from it. This amount of dose is called peripheral dose peripheral dose (PD).
The peripheral dose is determined by three factors: a) the leakage radiation from the radiotherapy machine head due to the interaction of the photon beam with the primary collimators, b) the scatter of radiation in the irradiated volume inside the human body and c) the scatter of the radiation from the linear accelerators couch, the walls of the room, and the floor and the ceiling. The percentage of dose that is received by the regions outside the field is very small compared to the dose delivered to the target volume. Hence, this dose may cause secondary cellular abnormalities, which can induct secondary cancers.

Aim of this study to investigate effect of 3DCRT with complete beam technique on planning target volume, dose homogeneity, dose of organs at risk (heart, cord, Right lung (Rt lung), and Left lung (Lt lung),), the homogeneity Index, and conformity index in the target region.

Method

Study design

In this comparative study, 50 patients with early stage left-sided breast cancer were treated by using 3DCRT with complete beam plan. This study was performed on an Elekta Synergy LINAC, 2013, from the United Kingdom. The accelerator machine is equipped with Multi-Leaf Collimator (MLC) at the Zhianawa Cancer Center (ZCC) KR, from October 2016 to June 2019.

XiO planning system: Xio is a radiotherapy planning system software designed by CMS-Elekta for contouring, 3D-CRT planning and plan evaluation, it is version 5.00.02, that relates to the center's main network[6].

Linear accelerator (LINAC) of Elekta apparatus.

A Linear accelerator (LINAC) is the device most used for external beam radiation treatment for patient with cancer[7]. LINAC is used to treat all parts or organs of the body. It delivers high energy X-ray to the region of the patient’s tumor. As the name implies, the electrons are accelerated in a straight line and this is achieved using radio frequency (RF) waves of approximately 10 cm wavelength[8]. These radio waves are generated in a specially designed vacuum diode valve called a magnetron which operates in an intense magnetic field, or in an RF oscillator called klystrons.

An Elekta synergy Linear accelerator[9] (Fig.1) was used for all measurements. This accelerator has three photon energies (6 MV, 10 MV, and 18 MV) and eight electron energies (4 Mev, 6 Mev, 8 Mev, 10 Mev, 12 Mev, 15 Mev, 18 Mev and 22 Mev). Fig (1) (Elekta Synergy).

Figure 1. Linear accelerator (Elekta Synergy) [9]. Zhianawa cancer center- Sulimaniyah

The present study was conducted following the approval by the Ethical Committee of Hawler Medical University (KR, meeting code: 6, paper code: 8, date: 23/04/2016)

Computed tomography scan (CT scan) utilizes a combination of several X-ray measurements obtained from different angles which have been processed by computer to generate virtual "slices" of a specified object, thus, let the user to observe interior parts of the object, without the need for cutting.

All patients underwent imulation by computed tomography (CT) in the same treatment position. Using a computer to process a combination of X-rays, CT can produce pictures of human interior organs. It provides pictures with more detail compared to a regular X-ray. The obtained data from CT can be manipulated to show various structures inside body based on their capability in attracting the X-ray beams. Modern scanners have the ability to represent these data in various planes, or even produce volumetric 3D pictures of structures[10]

The planning target volume will provide the initial gross tumor volume (GTV) as well as a margin around the CTV to compensate for the variability of treatment setup . The GTV was specified as the gross volume of the tumor, while the CTV was defined to include both GTV and possible microscopic spreads along the routes. Also, planning target volume (PTV) was determined as CTV with a uniform margin, so that include both the organ motions and set-up errors. Parotids and spinal cord were landmarked on all CT images as organs-at-risk (OAR's).

The treatment plan for each patient was established by the use of a XIO planning system superposition algorithm, and 6, 10, 18 MV photon beams provided by an ELEKTA Synergy linear accelerator, equipped with a multi-leaf collimators (MLC), having 80-leaf with 1 cm width projected at the isocenter.

A dose of 40.05 Gy, 2.025 Gy per fraction, 5 fractions per week during four weeks (duration of treatment) to a reference point in PTV was prescribed, which satisfies most recommendations of International Commission of Radiation Units (ICRU). A region which was clinically relevant to PTV and had a low dose gradient was selected as the reference point. In order to control dose homogeneity, some additional dose points in PTV were considered[11].

Simulation

All patients underwent Computed Tomography (CT) simulation, which was obtained using a scanner with 16 detector arrays (LightSpeed Xtra; general electric GE Healthcare, Waukesha, WI, USA) while patients were in the supine position on a breast board with both arms above their heads, the elbow support. Marker and tattoos were taken for setting up the patients during

the treatment. Scanning was performed in 2.5-mm slices from the clavicle to the mid-abdomen during free-breathing (Khan, 2012).

The ipsilateral whole breast was contoured as the Clinical Target Volume (CTV). The Planning Target Volume (PTV) was constructed by adding 5-mm margins and editing 5-mm of the build-up region from the breast skin surface. Two opposed tangential fields were set up without wedges, and the gantry angles were optimized. Leaf margins of 2 cm were added to the skin side, and leaf margins of 3 mm to the other sides. Each patient's plan was normalized to a reference point at the interface of the breast and pectoralis major muscle at the nipple level. The target volumes were delineated according to the recommendation of ICRU, report No.50. GTV was contoured according to the information from CT-Scanner, MRI, pathology, and oncology reports. PTV was delineated after CTV. Healthy tissues and nearby organs were contoured (spinal cord, Left lung (Lt lung), Right lung (Rt lung), heart, and esophagus) as OARs. CTV included tumor volume, as well as Lt lung, Rt lung, heart, and spinal cord tissues as OARs (Figure 4). The lungs were automatically delineated on CT scans[14]. The dose was prescribed for all PTVs according to the type, size, and location of the tumor for each patient. Dose prescription and delineation processes were conducted by radiation oncologists at ZCC.

Dose limitation for the OARs was defined as:

D30% was for the Lt lung and Rt lung (equivalent V20%); it is defined as the dose received by 30% of Lt lung and must be <20Gy to avoid pneumonitis. Moreover, the equivalent dose for the V35% of the heart was D20%. This is defined as a received dose, which is equivalent to 20% of the heart and must be <20 Gy to avoid perica[12,13]. The prescribed dose by the oncologist was 40.050Gy/ (2.670Gy/fraction), and the number of fractions was 15. These fractions are based on guidelines from the International Commission of Radiation Units and Measurement (ICRU), report 50 and 62[14].

Comparison of Plans

In this study 3D-CRT have attempted to a apply two techniques that can prevent or reduce peripheral dose to radiosensitive organs by using two techniques:

- First, complete beam, full-field technique (consisted of 2 opposing wedged tangential fields) for irradiation of tangential breast fields and supraclavicular field with two opposing tangential fields. When indicated, supraclavicular lymph nodes have to be irradiated, and a third anterior field is applied.

The tangential breast fields are geometrically matched with the supraclavicular field by rotating the collimator and couch. The full-field length can be utilized for the tangential fields. With a single isocenter, the treatment delivery requires only one setup, thereby treatment time is significantly.

The full beam plan was calculated with superposition algorithm using heterogeneity correction Xio Planning System version 5.0 (Elekta AB). The prescribed dose to PTV was 40.05 Gy in 20 fractions and the optimization constraint adopted requires that at least 95% isodose line encompasses 95% of PTV (V95%, volume receiving ≥95% of the prescribed dose, ≥ 40.05 Gy). The level of statistical significance was set at a p value of <0.05 for all tests. The Elekta Synergy® S linear accelerator with (6, 10, 18 MV) photon energy was used.

Plan evaluation

Plan evaluation was based on the following dosimetry parameters from dose-volume histograms: homogeneity index (HI) and conformity index (CI) established according to definition proposed by the ICRU (vol. 10, Report 83-2010 and Report 62-1999, respectively, (http://www.icru.org) as follows:

Homogeneity Index (HI) is an objective tool that analyses the uniformity of dose distribution in the target volume. The values of D2% and D98% for PTVs were obtained from DVH. D2% represents the maximum

dose that is delivered to 2% of the PTV. Dp is the prescribed dose for PTV, and D98% is the minimum dose calculated for 98% of the PTV. The lower the HI, the better the dose homogeneity. HI=(D(2%)- D_(98%)) / (D_p)

The CI measures the degree of conformity, which is calculated as follows[15]

CI value indicates the conformity degree of the plan. If CI < 1, the PTV is under coverage. If CI > 1, the normal tissues receive a high dose. Lastly, if CI = 1, in this case, the prescribed dose conforms to the PTV shape.

CI= (volume covered by 95% of the prescribed dose)/(volume of PTV)[15]

Results

Demographic data

Fifty patients with early-stage left-sided breast cancer were included in this study. Patients were treated with radiation therapy using 3DCRT with a single isocenter with full field beam. The isocenter is placed in the junction of tangential and supraclavicular fields[16].

The range of the age of patients was between 35-65 years. The mean PTV of all patients with complete beam technique was 4053.4cGy (±46.0). Previous biopsy, histopathology report, CT-Scan report, oncologist report, as well as all information about the patient like cancer type and stage, were taken into account for dose prescription by radiation oncologists. The role of medical physicists is to implement ideal planning to distribute the dose prescribed for the target area and reduce the dose received by healthy tissue.

PTV

Table 1. Mean ± SD (Range) for the values of conformity index (CI) and homogeneity index (HI) in full or complete beam size for all 50 patients

		No	Mean ±SD (Range)
PTV Mean Dose (cGray) Complete Beam		50	4053.4±46.0 (3960-4163)
95% CI of the Difference			(-154.5 - -27.27)
P value			0.006*
HI Complete		50	0.2±0.1 (0.1-0.4)
95% CI of the Difference			(-0.048 - 0.014)
P value			0.273
CI Complete		50	0.9±0.2 (0.6-1.4)
PTV Tolerance mean dose (cGy) 4005	<4005	50	

A summary of Dose Volume Histogram DVH analysis can be found in Table 1, where mean values over the cohort of fifty patients are reported together with their standard deviation.

As shown in Table 1, complete beam plan showed the relative volume of planning target volume PTV was (4053.4±46.0 cGray). The use of complete beam plan on the fifty patients had the PTV95% coverage values of >95% of prescription dose. This result corresponds with Abo-Madyan[17].

As shown in Table 1, dose homogeneity was measured by HI. Indicate a more homogeneous dose distribution in PTV for patients that treated with complete beam (The lower the HI, the optimal the dose homogeneity).

Lower HI means a better and more uniform dose distribution that can be achieved in the target[18].

Table 2: Dose homogeneity (HI) value, and Conformity Index (CI) value, in 50 patients with complete beam plan.

		No	%
CI for PTV complete	No risk (<1)	45	90.0
	High risk (>1)	5	10.0
	Perfect (=1)	-	-

Dose conformity was measured by CI. CI value indicates the degree of conformity of the plan. Therefore, where CI < 1 this denotes that the planning target volume PTV was under coverage. Where CI > 1 this meant that the normal tissues were receiving a high dose. Finally, where CI = 1 this indicates that the prescribed dose conformed to the shape of the PTV[18].

Table 2 indicates the conformity index (CI) of 6 patients is >1. This indicated that the normal tissue received a high dose. However, for the other patients where CI < 1 this signified that the PTV was under coverage. Also, Table 2 indicates that the conformity index (CI) of 5 patients is >1. This indicates that the normal tissue received a high dose. However, for the other patients where CI < 1, the PTV was under coverage.

Heart

Table 3. Mean ±SD (Range) for the values of Mean dose delivered to the heart of 50 patients with full beam technique.

	No	Mean ±SD (Range)
Heart Mean Dose (cGy)	50	476.7±314.6 (201-1813)
V35<20 Gy	50	4.4±4.5 (0-19.8)
Heart Tolerance mean dose (cGy) <2600	50	

Table 3 shows that the mean dose to the heart with complete beam plan is (476.7 cGy), which is<2600 cGy.

The result indicated that the heart was exposed to doses in complete beam technique (4.4 Gy) <20 Gy. The low dose volume in this technique (V35) <20Gy. However, we found that there was no absolute safe dose. Our finding concurs with Taylor et al[19] who found that adjuvant RT to left sided breast cancers had a small but significant increase in the risk of both cerebrovascular and cardiac deaths.

Right lung (Rt-lung)

Table 4. Mean ±SD (Range) for the values of Mean dose delivered to the Right-Lung (Rt-lung) of 50 patients with full beam size technique

Dose of Radiation		No. of patients	Mean ±SD (Range)
Right-Lung(Rt-lung) Mean Dose (cGy)		50	88.2±119.6 (26-627)
The low dose volume V20<30 Gy		50	0±
Rt Lung Tolerance mean dose (cGy) <4000	<4000	50	

Table 4 shows the received mean dose volume of the Right lung (Rt-lung) by full beam size to be (88.2±119.6 cGy), and in this technique Rt Lung Tolerance mean dose (cGy) is <4000 cGy, and the low dose volume (V20) <30Gy. This was since the Rt lung was distant from the target.

Left lung (Lt-lung)

Table 5. Mean ±SD (Range) for the values of Mean dose delivered to the Left-Lung (Lt-lung) of 50 patients with full beam size technique

		No	Mean ±SD (Range)
Left lung (Lt Lung) Mean Dose (cGy)		50	1081.8±313.6 (442-1751)
V20<30 cGy		50	20.1±5.3 (8.1-29.6)
Left lung (Lt Lung) Tolerance mean dose (cGy) <4000	<4000	50	

In the present study (Table 4), the low dose volume (<30Gy) for the left lung with complete beam was (20.1 cGy) and the low dose volume (V20) <30Gy. The Left Lung (Lt-lung) Mean Dose (cGy) for complete beam was (1081.8). Lt Lung Tolerance mean dose (cGy) was <4000 cGy showing the Left lung is nearest from the target.

Spinal Cord

Table 6. Mean ±SD (Range) for the values of Max dose delivered to the spinal cord of 50 patients with complete beam technique

		No	Mean ±SD (Range)
Cord Max Dose (cGy)		50	795.9±475.6 (22-2101)
Cord Tolerance mean dose (cGy) <2000	<2000	50	

Table 6 indicates that Cord max dose was 795.9±475.6 cGy. Spinal cord max dose was <45Gy (4500 cGy), which coincides with Majumder et al[20].

Discussion

Breast radiotherapy is a form of radiotherapy technique and since breast cancer is still a servere problem due to both incidence and mortality rates, 3D planning is used as the most used methods. In general, for every patient, there is an optimum plan that treats the breast tissue while sparing the organs at risk. However, the technique one uses could vary depending on patient geometry or the technology available in the radiotherapy center, including the available treatment planning systems.

PTV max and PTV mean values obtained by single isocenter with complete beam technique. PTV in complete beam was (4053.4±46.0 cGy).

The aim of 3DCRT using single isocenter with complete beam is homogeneity dose distribution for breast cancer, as well as to achieve a marked decrease in volumes of heart, ipsilateral lung, and spinal cord exposed to high-dose. Cumulative DVHs were assessed according to their target volumes and healthy tissues. Quantitative data were considered from the DVHs and were based on three significant factors: PTV dose, conformity index (CI), and homogeneity index (HI). The $D_{2\%}$ represented the maximum dose delivered to 2% of the PTV for all fifty patients, and D98% was the minimum dose calculated for 98% of the PTV. The prescribed dose received by 95% of the PTV assisted in the evaluation of the dosimetry plans. The dosimetry plan in this study aimed to cover at least 95% of the PTV.

The small amount of HI indicated that a lesser dose exceeded the prescription dose. Dose conformity was measured by CI. CI value indicates the degree of conformity of the plan.

The CI measures the degree of conformity, which is calculated as follows[21]:

- CI value indicates the conformity degree of the plan. If CI < 1, the PTV is under coverage.
- If CI > 1, the normal tissues receive a high dose.
- Lastly, if CI = 1, in this case, the prescribed dose conforms to the PTV shape.

CI= (volume covered by 95% of the prescribed dose)/(volume of PTV)[22].

We compared the critical organs treated on the basis of the following parameters: heart max dose and volume receiving 30 Gy or greater

(V30), ipsilateral (left) lung mean dose and volume receiving 20 Gy or greater (V20), and contralateral (right) lung mean dose and volume receiving 5 Gy or greater (V5).

However, for the other patients where CI < 1 this signified that the PTV was under coverage. Lungs are one of the first organs to receive radiation beam and need to be protected during breast radiation[11]. However, in complete beam technique on Right lung (Rt-lung) via reduction of V5 in <5 Gy, there was a decrease in V20, V30, and D- mean values. In complete beam technique satisfied the objective for V5Gy, V20Gy and V30Gy for Lt- Lung. The lowest V20Gy were found in complete beam.

In general, our results showed that both V5 Gy, V20Gy, V30Gy, D- mean values, and Dmax were significantly higher in Lt-lung than the Rt-lung as a result of location of Lt lung which is close to the target area.

For heart, the objective V35<20GY or (2000 cGy) was achieved in complete beam techniques. Its lowest value was found in full beam size (2.2 Gy) <20 Gy our result agree with Smyth et al[23].

Our results showed that the mean dose to the heart with full beam size was (476.7cGy) <2600 cGy "Heart Tolerance mean dose (cGy)" this concurred with Latty et al[24]. Our study results have been confirmed by Gagliardi[25] who reported that coronary artery disease risk was significantly reduced at doses less than a few Gy. Clinical effects of radiation induced heart disease have been observed with therapeutic doses of >35 Gy to partial volumes of the heart.

The risks are increased especially during radiotherapy for the left breast. Patient related factors like gender, age, diabetes, smoking habits, hypertension, obesity, and hypercholesterolemia contribute significantly to these risks, still the most important factor is the dose received by the heart (Marks et al, 2005; Gagliardi et al, 2010). The spinal cord max dose was <45 Gy which corresponds with Majumder et al[26].

Conclusion

Any radiation dose may increase the risk of a second malignancy. Although no safe dose limits can be given, the risk may be minimized. In principle, the irradiated volume should be as minimal as possible. The 3DCRT with complete technique achieved a significant reduction in the volume of heart and ipsilateral lung when exposed to high-dose PTV (≥40.05 Gy). The 3DCRT-complete technique leads to reduction in the mean dose of heart and ipsilateral lung when exposed to high-dose of radiation (Heart Tolerance mean dose (cGy) <2600, and ipsilateral Lung Tolerance mean dose (cGy) <4000). This technique might also benefit patients with heart diseases, and wherever cardiac regions are exposed to doses <20 Gy (The low dose volume in this technique (V35) <20Gy), irrespective of the selected plan. Heart and lung are the primary organs of concern. In the current research, the relative volume of ipsilateral lung or heart receiving high-dose PTV (40.05Gy) was significantly reduced.

The RTP outcome that uses 3DCRT with complete beam plan for breast cancer may provide a guideline for selecting a possible treatment technique for breast cancer at Zhianawa Cancer Center (ZCC) – Sulaymaniyah-KR- Iraq

Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

Ethical Approval

The present study was conducted following the approval by the Ethical Committee of Hawler Medical University (KR, meeting code: 9, paper code: 1, date: 11/10/2020)

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