Moving from 2D to 3D-CRT Planning of Chest Wall for Postmastectomy Breast Cancer Patients: Mansoura University Experience

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Abstract

**Background:** This study evaluates the dose distribution of the wedged tangential beam three-dimensionally planned conformal radiotherapy (3D-CRT) compared to the previously used (5 years ago) two-dimensionally (2D-RT) planned radiotherapy of the chest wall for postmastectomy breast cancer patients in Clinical Oncology and Nuclear Medicine Department, Mansoura University.

**Patients and Methods:** Thirty six unselected breast cancer patients were planned by both the standard 3D-CRT and 2D-RT techniques for radiotherapy of the chest wall. Dose-volume histograms were carried out by the 3D treatment planning system. They were assessed for the PTV and organs at risk. The prescribed total dose was 50Gy in 25 fractions.

**Results:** The three-dimensionally planned conformal radiotherapy showed an improvement of the PTV coverage and statistically significant better in homogeneity index of the chest wall (p<0.001). The ipsilateral mean lung dose was significantly reduced with the tangential beam 3D-CRT plans with an average of 24.6% (1217cGy versus 1614cGy). For the left sided breast cancer patients, the mean heart dose was also reduced by an average of 48.6% (718cGy versus 1398cGy). The mean percentage dose of the contralateral breast to the prescribed dose was 8.2% for 3D-CRT, compared with 10.4% for 2D-RT tangential field techniques.

**Conclusions:** The tangential beam 3D-CRT planning demonstrated a significantly better homogeneity index for the PTV of the post-mastectomy breast cancer patients with a significant reduction in the mean doses of the ipsilateral lung and the heart for the left-sided breast cancer patients.

**Key Words:** Breast cancer — Post-mastectomy radiotherapy — Radiotherapy techniques — Three-dimensionally conformal radiotherapy.

Introduction

CARCINOMA of the breast is the most prevalent cancer among Egyptian women and constitutes 29% of National Cancer Institute (Egypt) cases.

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[i] In the United States and Europe, the most common treatment is breast conserving surgery followed by adjuvant radiotherapy [2]. In other parts of the world including the Middle East, the majority of the patients present in a more advanced stage of disease at diagnosis, and mastectomy is the most common treatment followed by adjuvant radiotherapy of the chest wall [3].

Post-mastectomy radiotherapy improves survival and local control in patients with high risk breast cancer [4,5]. The chest wall is the most frequent site of recurrence and delivering adequate radiation doses to the chest wall is crucial to reduce the risk of treatment failure. Keeping radiation-induced side effects as low as possible, while providing the intended dose to the chest wall remains a problem [6].

Treatment of the chest wall and regional nodes poses many challenges to the radiation oncologists. No significant technique is accepted as the "gold standard". The range of body position and close proximity of the internal mammary nodes (IMN) to the heart often necessitate individualized precise treatment planning. The risks of cardiac and pulmonary toxicity are highly technically dependent, so appropriate estimates of these risks could aid in clinical decision-making for the treatment of these patients [71.

There has been a general change in treatment planning from 2D using a simulator to 3D based on a CT scan and it has been shown that virtual simulation of breast cancer patients may be more time effective [8]. The technological development of accelerators with multi-leaf collimators has also offered some new possibilities for more time saving
Moving from 2D to 3D-CRT Planning of Chest Wall

treatment techniques compared to techniques with field matching between photon and electron fields [6].

Three-dimensional (3D) treatment planning refers to the use of software and hardware tools to design and implement more accurate and conformal radiation therapy. This is a major advance in oncology that should lead to the reduction of treatment-associated morbidity and facilitate safe dose escalation for many tumor sites. This technology affords the incorporation of physiologic and anatomic information into the treatment planning process, further enhancing our ability to improve the therapeutic ratio. However, as with any new technology, care must be taken when applying it in the clinic [9]. Dose-volume histograms (DVHs) are commonly used to compare radiation treatment beams designed using traditional techniques with those planned using 3D tools. The structures chosen for the DVHs comparison are typically those that are incidentally irradiated using traditional methods.

This study evaluates the dose distribution of the wedged tangential beam three-dimensionally planned conformal radiotherapy (3D-CRT) compared to the previously used conventional two-dimensionally (2D-RT) planned radiotherapy of the chest wall and through its effect on target coverage and normal tissue sparing for postmastectomy breast cancer patients.

Patients and Methods

Patients eligibility:
Eligibility criteria included patients attended the Clinical Oncology and Nuclear Medicine department, Mansoura University with non metastatic pathologically confirmed invasive breast cancer. The tumors sizes were more than 5cm and/or positive axillary lymph nodes. All of them underwent modified radical mastectomy without breast reconstruction during the period from January 2010 to March 2012.

A detailed prospective dosimetric comparison between 2D and 3D conformal radiotherapy planning for chest wall was performed on CT scans for thirty six selected breast cancer patients (twenty of them were left sided). While Axillary and internal mammary lymph nodes were irradiated when indicated.

Patient’s simulation:

Patients positioning and fixation:
Patients were positioned in the supine position, on an angled board such that the sternum was horizontal with ipsilateral arm abducted to 90°. The position of the patient must remain identical for localization on a CT scanner or simulator and during subsequent treatment. A headrest, elbow and armrests, knee supports and a footboard provide stability. Care must be taken at data acquisition to adapt all the supporting devices to the individual patient’s size and shape to maximize comfort, and so aid reproducibility for subsequent treatment.

Clinical landmarks:
The target was defined to consist of the chest wall and IMNs (defined to include those internal mammary nodal in interspaces (one to three) which were palpated clinically. The chest wall borders consisted of the medial border at the patient midline, the lateral border at the midaxillary line, the superior border at the sternal angle, and the inferior border at 1 cm below the contralateral inframammary fold. Clinical target volumes and scars were delineated on the treatment planning CT scans using radiopaque wires placed on the patient’s body.

Data transfer methods and algorithm:
Three-dimensional imaging (CT) scans multiple slices with slice thickness 5mm was obtained with the patient in the treatment position that was used throughout treatment. A reference point was defined and marked on the patient's chest wall. The patient returned home and the treatment planning proceeded on 3D imaging data sets.

CT cuts are transferred in Dicom format images. No special software for data transfer. Precise treatment planning system with Full-Integrated-Area-Algorithm was used to view the 3D relationship between structures of interest from any direction (including axial and nonaxial orientations). Elekta-Precise 3D treatment planning system was used to carry out the 2D and 3D plans for all patients under our study. Source to Axial Distance (SAD) technique was applied for all approved plans. High energy 6 MV Photon beams were used in planning and all data of approved plans were digitally transferred to Elekta Precise linear accelerator which contains Multileaf Collimator (MLC) of 80 leaves.

Target volume delineation:

2D Conventional radiotherapy planning:
For each patient, a standard 2D tangential wedged fields plan was adjusted and calculated on a single transverse contour taken on a CT cut midway between an upper border passing through the sternal angle and a lower one passing by a line.
1 cm below the contralateral inframmary fold, in the standard treatment position.

**3D Conformal radiotherapy planning:**

The planning target volume (PTV) definition for the chest wall was done according to the breast cancer atlas for radiation therapy planning consensus definitions of the Radiation Therapy Oncology Group (RTOG). The PTV included the chest wall with the pectoralis muscle, chest wall muscles and ribs with exclusion of the outermost 3mm from the superficial skin surface. The heart was defined as all visible myocardium, the apex, the right atricle, atrium, and infundibulum of the ventricle. The pulmonary trunk, root of the ascending aorta and superior vena cava were excluded. All soft tissue (down to deep fascia) of the contralateral breast was delineated.

**Dose prescription and constrains:**

The prescription dose and fractionation was 50Gy in 25 fractions, 5 fractions/week. The dose constraints for the treated volumes were minimum 90% and maximum 110% of the prescribed dose. The energy used was 6 MV photon using Elekta Precise linear accelerator.

Doses calculations and adjustments in beams weight, wedges, blocks, and beam orientations were made as desired in an interactive fashion. Beam orientations were selected and beams were 3D-shaped by using MLC based on the projection of the structures of interest as seen along the beam's-eye view.

Setup instructions to facilitate the implementation of treatment beams at the physical simulator and treatment machine were provided and included field size, gantry, collimator, and table position.

**Plan evaluation:**

To assess the target coverage and normal tissue sparing the following parameters were used.

- The treatment planning system calculated the volume of the target (or organs at risk) that received at least the given dose and plotted this volume (or percentage volume) versus dose (DVH). All cumulative DVH plots start at 100% of the volume for OcGy, since all of the volume receives at least no dose.

- For the PTV, mean, maximum and median (range) doses received, were calculated for both techniques.

- Radiation dose homogeneity index (HI), which was defined by Nutting et al. [HI as the difference in PTV dose between D1 and D99 divided by the prescription dose, was calculated. Smaller HI corresponds to more homogeneous dose distribution in PTV.

- The conformity index (CI) was calculated by using the following formula: [12].

$$CI = \frac{TV_{95}}{TV} - \frac{TV_{95}}{TV_{90}}$$

Where TV95 is the volume of target covered by the 95% isodose line, TV is the total target volume and TV95 is the volume of tissue covered by the 95% isodose line. The value of CI varies between 0 to 1 and a value close to 1 gives better conformity of dose to the PTV.

The sparing of organs at risk (lung, heart and contralateral breast) was evaluated by comparing their maximum, mean doses, lung $V_{20}$ (volume of lung receiving more than 20Gy), heart $V_{30}$ (volume of heart receiving more than 30Gy) in left sided patients and mean doses to contralateral breast.

The values of the above parameters for each patient planned by 2D-RT and 3D-CRT techniques were compared with the help of their dose volume histograms (DVH) using the 3D planning system.

The thickness of the chest wall was eventually adjusted with a bolus to obtain a match between the depth and the 85% isodose curve.

**Statistical analysis:**

Data was analyzed using SPSS (statistical package for social science) Version 15. The data were presented as mean±standard deviation (SD). Analysis was performed with the two-tailed paired t-test. Differences were considered statistically significant when $p$ was D105.

**Results**

The present work is a prospective study performed on 36 patients who met the inclusion criteria during the period of study. Postmastectomy radiotherapy for chest wall was decided for all included patients. Three-dimensionally conformal radiotherapy (3D-CRT) and two-dimensionally radiotherapy (2D-RT) plans were done for each patient. On comparing the plan parameters of the tangential beams of the chest wall, both 3D-CRT and 2D-RT planning techniques showed acceptable dose distributions to the plumed target volume (PTV) while 3D-CRT showed an improvement of the PTV coverage and sparing of organs at risk.
Dose distribution in the target volume:

The isodose distributions obtained on an axial slice at the isocenter plan were compared for each patient regarding the 3D-CRT and 2D-RT. The comparison of plan DVH curves for PTV and organs at risk (OARs) of a representative patient for 3D-CRT and 2D-RT are shown in (Fig. 1). The analyzed data of thirty six patients with the mean, maximum and median doses to the PTV and comparison of dose coverage with 3D-CRT and 2D-RT treatment plans is shown in (Table 1). The mean dose to the PTV for patients treated with 3D-CRT was 5070cGy (SD=72) with a median 5041 cGy (range 5008-5251). While the mean dose to the PTV for patients treated with 2D-RT was 5124cGy (SD=78) with a median 5125 cGy (range 5000-5290). The results indicate that there was a statistically significant and considerable difference in the dose coverage of PTV with 3D-CRT compared to 2D-RT plans (p=0.003).

The median value of HI for 3D-CRT was 0.219 with a range (0.19-0.30) while it was 0.324 with a range (0.19-0.44) for 2D-RT plan. Conformity index (CI) showed a median value of 0.915 with a range (0.71-0.96) for 3D-CRT while it was 0.840 with a range (0.63-0.96) for 2D-RT plan. The average lower values of HI and higher values of CI for 3D-CRT plans were compared to the 2D-RT with statistical significant difference (p<0.001) that confirm the advantage of 3D-CRT plans over 2D-RT plans.

Dose distribution in organs at risk (OARs):

The dose coverage of organs at risk (OARs) with 3D-CRT and 2D-RT plans is shown in (Table 2). Data represented were the mean values for each organ with their standard deviation.

For the left sided breast cancer patients (20 patients), the mean heart dose was reduced by an average of 48.6% in 3D-CRT plans compared to 2D-RT plans (718cGy versus 1398cGy). There was a significant (p<0.001) dose reduction in heart with 3D-CRT plans. The percentages of heart volumes receiving more than 30Gy (V30) were reduced with 3D-CRT plans (10.3%) compared to that of 2D-RT plans (23.0%) (p<0.001).

The ipsilateral mean lung dose was significantly reduced with the tangential beam delivered in 3D-CRT plans compared to that of 2D-RT plans with an average of 24.6% (1217cGy versus 1614cGy). There was a significant (p<0.001) dose reduction in lung with 3D-CRT plans compared to 2D-RT plans. The percentages of lung volumes exceeding a dose of 20Gy (V20) were 22.2% and 30% in 3D-CRT and 2D-RT plans, respectively (p<0.001).

The mean dose to the contralateral breast for patients treated with 3D-CRT was 409.4cGy (SD=97.4) with a median 407.5cGy (range 268-589), it represented 8.2% of the prescribed dose to the target. While the mean dose to the contralateral breast for patients treated with 2D-RT was 520.8cGy (SD=72.3) with a median 550.0cGy (range 398-610), it represented 10.4% of the prescribed dose to the target. The difference was statistically significant (p<0.0001).

Table (1): Comparison of the average dose parameters of 36 patients for the PTV between 3D and 2D radiotherapy planning techniques.

<table>
<thead>
<tr>
<th>PTV parameter</th>
<th>3D-CRT</th>
<th>2D-RT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum dose (cGy)</td>
<td>5463 ± 116</td>
<td>5429</td>
<td>5297-5723</td>
</tr>
<tr>
<td>Mean dose (cGy)</td>
<td>5070 ± 72</td>
<td>5041</td>
<td>5008-5251</td>
</tr>
<tr>
<td>HI</td>
<td>0.219 ± 0.024</td>
<td>0.219</td>
<td>0.19-0.30</td>
</tr>
<tr>
<td>CI</td>
<td>0.902 ± 0.061</td>
<td>0.915</td>
<td>0.71-0.96</td>
</tr>
<tr>
<td>DI</td>
<td>5748 ± 81</td>
<td>5755</td>
<td>5615-5934</td>
</tr>
<tr>
<td>D99</td>
<td>4655 ± 149</td>
<td>4677</td>
<td>4231-4930</td>
</tr>
</tbody>
</table>

//DIOS were statistically significant. HI : Homogeneity index. CI : Conformity index. DI : Dose to 1% of target volume.
Table (2): Comparison of the average dose distribution in the organs at risk (OARs) for 36 patients between 3D and 2D radiotherapy planning techniques.

<table>
<thead>
<tr>
<th>OARs parameter</th>
<th>3D-CRT Mean SD</th>
<th>2D-RT Mean SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart in left sided cases (20 patients):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum dose (cGy)</td>
<td>4623 291 4799 267</td>
<td>4430 174 4650 187</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean dose (cGy)</td>
<td>1217 279 1614 369</td>
<td>718 240 1398 374</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D40</td>
<td>122 78 226 142</td>
<td>251 39 544 138</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D20</td>
<td>816 76 1949 1272</td>
<td>489 81 1858 273</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V30</td>
<td>10.3% 5.3 23.0% 7.6</td>
<td>10.3% 5.3 23.0% 7.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Ipsilateral lung:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum dose (cGy)</td>
<td>4623 291 4799 267</td>
<td>4430 174 4650 187</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean dose (cGy)</td>
<td>1217 279 1614 369</td>
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<td>D40</td>
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<td>D20</td>
<td>816 76 1949 1272</td>
<td>489 81 1858 273</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V20</td>
<td>22.2% 5.3 30.0% 5.0</td>
<td>22.2% 5.3 30.0% 5.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Contralateral breast:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean dose (cGy)</td>
<td>409.4 97.4 520.8 72.3</td>
<td>4430 174 4650 187</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Discussion

Retrospective and prospective studies have demonstrated optimal locoregional control with radiotherapy after mastectomy in patients at high risk of locoregional recurrence [13,14]. Specifically, three randomized trials have demonstrated 9% benefit in survival at 10-15 years in patients randomized to comprehensive locoregional RT and chemotherapy or hormonal therapy. RT was delivered to the chest wall and regional nodes including the internal mammary nodes, in these studies [7].

In an ideal world, radiation treatment beams would fully encompass the target tissue and exclude all normal tissues. In practice, however, this is impossible due to the intimate relationship between tumors and surrounding normal structures. Radiation treatment planning, therefore, is based on a compromise between tumor and normal tissue considerations [9].

Conventional two-dimensional treatment planning is limited in its ability to represent the prescribed dose delivered to a specific target volume and to quantify the extent of irradiated normal tissue to estimate normal tissue toxicity. Analysis of the dose to normal tissues often performed using the DVHs that can be generated using three-dimensional treatment planning, providing estimates of the dose to target tissues and normal structures. A DVH is a plot of dose of radiation on the x-axis and percent volume of the structure of interest on the y-axis. The shape and area under the DVH curve are used to ensure that the target volume is adequately covered with a homogeneous dose and that dose to critical structures is within acceptable limits. A 3D planning system can calculate the dose in each pixel of the organ outlined and sum these to produce a DVH. 3D treatment planning is, therefore, a powerful tool that can be used to compare treatment techniques for adequacy of target coverage and complication risk mi.

A number of studies have demonstrated a dosimetric benefit of 3D-CRT compared to 2D-RT for the whole breast in early breast cancer patients [16], however such comparative studies for post-mastectomy patients are rare and there is a scarce data on such a subject. There are distinct geometric differences between the target volume of the chest wall and the whole breast, and these differences might have an impact on the resulting dose distribution.

In our study, we used standard tangential fields for chest wall irradiation and partial wide tangential fields (PWTFs) when IMNs were irradiated. This choice of field arrangements was based on data presented by Pierce et al., demonstrating that the use of standard tangents results in good coverage of the chest wall and PWTFs provides good coverage of both the chest wall and IMNs with little to no additional cardiac exposure to radiation compared with that observed with standard tangents [71].

One of the most important benefits of a DVH is that provides an accurate assessment of homogeneity in the PTV. The presence of defects in a dose distribution will negatively affect tumor control, and an accurate evaluation of homogeneity in the PTV is therefore essential to the efficacy of the treatment plan [17]. In the current study, we used both homogeneity index and conformity index to evaluate target coverage and dose homogeneity. Conformity index is used to evaluate the clinical evidence of better treatments. Improved conformity may help to deliver higher doses to the PTV without delivering more doses to the surrounding normal tissue [18]. Both indices where statistically better using 3D-CRT. This was clearly demonstrated by the isodose distributions and DVH curves.

Our data showed that tangential beam 3D-CRT of the chest wall compared to 2D-RT, significantly reduces the ipsilateral lung mean dose by 24.6% as well as lung V20 (22.2% versus 30%). V20 for the lung was chosen based on prior analysis identifying this value to be an independent predictor of pneumonitis [19]. On the other hand, it should
be noted, that actual clinical cases of pneumonitis are uncommon, and most often are either self-limited or treated with brief steroid course. Marks et al., reported a 2.6% risk of clinical pneumonitis primarily using tangential fields. Only 0.5% of patients, however, had persistent symptoms po.

Similarly radiation to the heart (for the left sided breast cancer patients) was markedly reduced using 3D-CRT. The calculated mean dose was decreased by 48.6% and heart V30 was (10.3% versus 23%). Gagliardi et al., demonstrated that volume of the heart receiving doses more than 30 Gy was the cutoff limit for the calculated risk of ischemic heart diseases [21]. Studies based on atomic bomb survivors also suggest a relationship between cardiac mortality and low radiation doses in the range of 0.4Gy [22-24]. The development of radiation-related heart disease is a complex process involving different heart structures with different radiosensitivities and pathomechanisms, and is still not well understood [25-27]. Furthermore, pre-existing cardiovascular risk factors as smoking, obesity, and hypertension as well as the use of cardiotoxic agents such as anthracyclines, paclitaxel and trastuzumab are likely to contribute to the development of radiation-related heart disease [28].

In the current study, The mean percentage dose of the contralateral breast to the prescribed dose was 8.2% for 3D-CRT, compared with 10.4% for 2D-RT tangential field techniques and this is in agreement with that reported by Bhatnagar et al., who compared the mean dose received to the contralateral breast by both IMRT (7.74%) and 3D-CRT (9.74%) [28].

Conclusion:

The tangential beam 3D-CRT planning demonstrated an improved coverage of PTV coverage and significantly better homogeneity and conformity indices for the of the post-mastectomy breast cancer patients with a significant reduction in the mean doses of the ipsilateral lung and the heart for the left-sided breast cancer patients with a lower mean percent of the prescribed dose to the contralateral breast.

References


