Significant reductions in heart and lung doses using IMRT for left sided breast cancer patients

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Abstract

Introduction
Various radiation techniques include Three Dimensional Conformal Radiotherapy (3DCRT), breath hold and Intensity Modulated Radiotherapy (IMRT) are used to irradiate the breast and to limit the dose to the heart and lungs. IMRT is used as a class solution for cardiac protection in left sided breast cancer patients.

Aim of the work
To evaluate heart and lung sparing effects of tangential beam IMRT whilst maintaining target coverage compared with tangential beam 3DCRT for left sided breast cancer patients

Methods
CT simulation was done for thirty left sided breast cancer patients who underwent conservative surgery. Planning target volume (PTV), heart and ipsilateral lung were contoured. 3DCRT and IMRT plans were generated for 50Gy using opposed tangential medial and lateral photon beams. Five segments were generated for each IMRT field. Heart V5, V20, V30, and V40 and ipsilateral lung V20, mean dose, PTV D95%, PTV Dmax and dose homogeneity index were compared using Wilcoxon Signed-Ranks test.

Results
IMRT plans achieved significant reduction of 12%, 15%, 21% & 53% in heart V5, V20, V30, and V40 and of 18% & 11% in ipsilateral lung mean dose and V20 compared with 3DCRT (p values <0.001). PTV coverage was adequate and comparable in both plans (P for PTV D95% & Dmax% =0.188 & 0.553). The dose homogeneity within PTV was significantly better with 3DCRT (P=0.004).

Conclusion
Tangential beam IMRT in left sided breast cancer leads to a significant dose reduction in heart and ipsilateral lung with comparable target coverage compared to tangential beam 3DCRT.

I declare that there is no conflict of interest with any financial organization regarding the material in this manuscript.

Key words: breast cancer, cardiac protection. dose reduction. IMRT

Introduction
Breast cancer is the most common malignancy in women (1). Early stage breast cancer is commonly treated using breast conserving surgery followed by adjuvant radiotherapy (2,3). Although Three Dimensional Conformal radiotherapy (3DCRT) is widely used for treatment of breast carcinoma because it increases dose conformity to target volume and reduce heart and lungs doses but there is still a risk of fatal cardiovascular events (4).

Various radiation cardiac sparing techniques are recently used to irradiate the breast and to limit the dose to the heart and lungs (5). These techniques include maneuvers that based on the increase in the distance between the heart and the chest wall such as breath hold, respiratory gating and prone patient positioning techniques (6).

Breath hold reduces the heart dose as the heart moves away from the chest wall so cardiac volumes exposed to radiation are reduced. Respiratory gating is another technique for cardiac sparing as radiation is delivered during respiratory expansion of the thorax where the distance between the heart and the radiation fields is enlarged (7).

In prone positioning technique the breast falls away from the chest wall so the edge of the radiation beam is positioned away from the heart. This is useful for cardiac protection especially in patients with pendulous breasts (8).

Using advanced techniques as IMRT or proton beam radiotherapy is another way of cardiac sparing (9,10).
Computerized leaves and dose planning algorithms of IMRT allow for shaping of radiation field and help to escalate the dose to the target. This is with significant reductions in the cardiac dose (11). IMRT is successfully used as a class solution for cardiac protection in left sided breast cases especially for patients with large breast (12,13,14). Proton beam radiotherapy is based on rapid dose fall off beyond the Bragg peak. This allows the dose reduction to structures beyond the target volume as heart and so reduces cardiac toxicities (15).

As there is evidence that patients treated with these techniques have a lower risk of cardiac toxicity (16,17,18) so this study aimed to evaluate the heart and lung sparing effects of tangential beam IMRT whilst maintaining target coverage compared with tangential beam 3DCRT for left sided breast cancer patients.

**Methods**

**CT simulation:**
CT simulation was done for thirty left sided breast cancer patients who underwent breast conservative surgery and referred to Alexandria Clinical Oncology Department (ACOD), Alexandria faculty of Medicine from June 2014 to May 2015. CT Simulation was performed in the supine position on breast board with the ipsilateral arm positioned above the head and patient head tilted to other side.

**Target and organs at risk delineation**
The CT data were transferred to treatment planning system (Precise Elekta) where all required structures were contoured. The Planning target volume (PTV) was outlined according to RTOG breast cancer atlas for radiation therapy planning (19). Organs at risk (OARs) including heart and ipsilateral lung were also contoured.

**Treatment Planning**

**3DCRT Planning**
3DCRT optimum plan was carried out using two opposed tangential medial and lateral 6MV photon beams. The gantry and wedge angles were chosen to optimize the coverage of the PTV and to protect the ipsilateral lung and heart which were also shielded using MLCs. To improve the target coverage in the buildup region one cm thickness of a tissue equivalent bolus was used.

**IMRT Planning**
Step and shoot IMRT optimized plans were generated using same beam orientations of the 3DCRT plan. Five segments were generated for each field; segment one covering PTV, segment two including PTV & excluding heart, segment three including PTV & excluding lung, segment four including PTV & excluding both heart and lung and segment five including PTV & excluding buildup region. The best dose volume constrains (DVCs) were selected after many trials (table 1).

**Dose Prescription and dose limitation**
The dose of 50Gy/25f was prescribed to the ICRU reference point which was located in the centre of the PTV volume. According to the International Commission on Radiation Units and Measurement (ICRU) Reports 50 (20) and 62 (21) recommendations the PTV dose coverage was assessed using dose to 95% of the volume (D$_{95\%}$) and the maximum dose point of the PTV (D$_{max}$). Dose homogeneity was assessed using homogeneity index HI (calculated as D$_{5\%}$/ D$_{95\%}$; where D$_{5\%}$ and D$_{95\%}$ are the minimum doses delivered to 5% and 95% of the PTV). For OARs; the volume of heart receiving 5Gy, 20Gy, 30Gy and 40Gy (V$_{5\%}$, V$_{20\%}$, V$_{30\%}$ and V$_{40\%}$) were selected for the comparison of cardiac sparing between 3DCRT and IMRT plans. The ipsilateral lung mean dose and the volume of ipsilateral lung receiving 20Gy (V$_{20\%}$) were also used for comparing lung protection.

This study had approval of Institutional Review Board as a retrospective one in which confidentiality of records was considered.

**Statistical analysis**
Dose volume histograms of the PTV, ipsilateral lung and heart of the 3DCRT and IMRT plans were generated for the thirty patients. Relevant dose volume histogram parameters of both plans were compared and tested for any statistically significant difference using Wilcoxon Signed-Ranks test of SPSS (version 16).

**Results**

Table 2 & Table 3 compares the relevant plan parameters of PTV, ipsilateral lung and heart of tangential beam IMRT and 3DCRT for the adjuvant radiotherapy of whole breast for thirty

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**Table 1: Optimization setup table**

<table>
<thead>
<tr>
<th>Structure</th>
<th>Type</th>
<th>Priority</th>
<th>Mean dose</th>
<th>Underdose (cGy)</th>
<th>Underdose Volume (%)</th>
<th>Overdose (cGy)</th>
<th>Overdose Volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>target</td>
<td>100</td>
<td>-</td>
<td>5000</td>
<td>95%</td>
<td>5500</td>
<td>5</td>
</tr>
<tr>
<td>ipsilateral lung</td>
<td>OAR</td>
<td>40</td>
<td>1200</td>
<td>-</td>
<td>-</td>
<td>4500</td>
<td>-</td>
</tr>
<tr>
<td>Heart</td>
<td>OAR</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4500</td>
<td>5</td>
</tr>
</tbody>
</table>
left sided breast cancer patients. Figure 1 demonstrates dose distributions of an IMRT and 3DCRT plan of the same patient.

Dose distribution within PTV

Table 2 & figure 2 (A) present the comparison and dosimetric analysis for the Planning Target volume (PTV) for

<table>
<thead>
<tr>
<th>PTV DVPs</th>
<th>Min</th>
<th>Max</th>
<th>Average</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D_{95%} (3DCRT)</td>
<td>94</td>
<td>102</td>
<td>97.16</td>
<td>1.80</td>
<td>0.188</td>
</tr>
<tr>
<td>D_{95%} (IMRT)</td>
<td>90</td>
<td>103</td>
<td>96.40</td>
<td>3.15</td>
<td></td>
</tr>
<tr>
<td>D_{\text{max}} (3DCRT)</td>
<td>103</td>
<td>119</td>
<td>114</td>
<td>4.06</td>
<td>0.553</td>
</tr>
<tr>
<td>D_{\text{max}} (IMRT)</td>
<td>110</td>
<td>120</td>
<td>114.9</td>
<td>2.74</td>
<td></td>
</tr>
<tr>
<td>HI (3DCRT)</td>
<td>1.07</td>
<td>1.19</td>
<td>1.11</td>
<td>0.02</td>
<td>0.004</td>
</tr>
<tr>
<td>HI (IMRT)</td>
<td>1.10</td>
<td>1.21</td>
<td>1.14</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Dose distribution displayed in axial, coronal & sagittal views (A & C) for 3DCRT & IMRT plans using opposed tangent fields for a left sided breast cancer patient and the room eye views of the same patient (B & D). Both show the colour wash of 95% of the dose (pink in A & C & white in B & D) match well the PTV shape.
tangential beam 3DCRT and IMRT plans. Regarding to target coverage; the average of PTV D95% & Dmax% 97.16% & 114% for 3DCRT plans compared to 96.40% & 114.9% for IMRT plans. So coverage is adequate in both plans but comparable as the differences in PTV D95% & Dmax% between the plans were not statistically significant (P=0.188 & 0.553). Regarding the dose homogeneity; 3DCRT plans shows significantly lower HI than IMRT plans (1.11 for 3DCRT Vs 1.14 for IMRT plans) so the dose homogeneity within PTV was significantly better with 3DCRT than with IMRT plans (P=0.004).

Dose distribution within organs at risk
Regarding to ipsilateral lung; tangential beam IMRT statistically significantly reduced the ipsilateral lung mean dose by an average of 18% (average 10.80Gy versus 13.23Gy) & the ipsilateral lung V20Gy by an average of 11% (average 21.10% versus 23.90%) for IMRT and 3DCRT respectively (P<0.001). So IMRT plans achieved a significant ipsilateral lung sparing compared to 3DCRT plans. (Table 3 & figure 2 (B)

Concerning the heart; tangential beam IMRT shows significant reduction of 12% (average 24.10% versus 28.53%), 15% (average 17.16% versus 21.10%), 21% (average 14.13% versus 18.36%) & 53% (average 6.80% versus 15.20%) in heart V5Gy, V20Gy, V30Gy and V40Gy for IMRT and 3DCRT respectively (P<0.001). So IMRT plans achieved significant heart sparing compared to 3DCRT plans. (Table 3 & figure 2 (B)

Discussion
In left sided breast cancer the target volume is located in close proximity to the heart, ipsilateral lung, and other critical organs. While conventional 3DCRT plans cannot adequately protect these organs, a number of studies reported the benefits of IMRT in protecting the heart and other critical organs compared to 3DCRT for the whole breast in early stage left sided breast cancer patients. So IMRT is successfully used as a class solution for cardiac protection (22, 23). This study aimed to evaluate the heart and lung sparing effects of tangential beam IMRT whilst maintaining target coverage compared with tangential beam 3DCRT for thirty left sided breast cancer patients who underwent breast conservative surgery.

In the current study 3DCRT and IMRT plans showed adequate and comparable PTV dose coverage as the differences in PTV D95% & Dmax% between the plans were not statistically significant. On the other hand, tangential IMRT plans showed significant worst dose homogeneity compared to 3DCRT plans. The worst dose homogeneity inside the breast compared to 3DCRT plans was supported by Mayo CS et-al 2005(26) & Beckham WA et-al 2007(25). On the other hand in contrast with the results of the current study, Rongsriyam K et-al 2008 (26) & Guang et-al study 2013(27) found that IMRT plans improved the target coverage, homogeneity and conformity compared with 3DCRT plans.

Figure 2. DVH for PTV (A), for Ipsilateral lung in blue and heart in pink (B) comparing 3DCRT (solid line) and IMRT plans for a left sided breast cancer patient

Regarding to heart sparing: current study showed that IMRT plans resulted in significant heart reductions in V5Gy, V20Gy, V30Gy and V40Gy compared to 3DCRT plans. The findings of the current study were supported by the results of Beckham WA et-al 2007(25) study; they found that heart V30Gy was lower for IMRT plans (1.7% for IMRT Vs 12.5% for 3DCRT plans). Li J S et-al 2004 (28) showed also that heart V30Gy was lower in IMRT plans compared with 3DCRT plans (0.5% in IMRT and 5% in 3DCRT plans); this is in accordance with the results of the current study. The results of the current study is also supported by Rongsriyam K et-al 2008(26) who found that heart V30Gy was significantly lower for IMRT plans compared to 3DCRT plans (3.12% vs 5.84%). Moorthy S et-al 2013(29) also found that the average V40Gy of heart was significantly lower for
IMRT compared with 3DCRT (7.5 % for 3DCRT and 2.13 % for IMRT).

**Regarding to Ipsilateral lung sparing:** In the current study IMRT resulted in significant lung sparing compared with 3DCRT plans. This is in accordance with Khullar P et-al 2014 (30); they reported that IMRT achieved a significant reduction in V_{20Gy} of the ipsilateral lung with IMRT (49.2% versus 59.8% of the conventional technique). Moorthy S et-al 2013 (29) also demonstrated that IMRT provided better dose distribution with significantly better mean dose and V_{30Gy} compared with 3DCRT (V_{20Gy} of ipsilateral lung was 37.9 % for 3DCRT and 22.4 % for IMRT). The results of the current study were also supported by Jagsi R et-al 2010 (18); they showed that the ipsilateral lung mean dose and V_{30Gy}, with the inverse tangential IMRT technique were lower than with 3DCRT plans. The results of the current study is also supported by Rongsriyam K et-al 2008 (26) who found that ipsilateral lung mean dose and V_{20Gy} were significantly lower for IMRT plans compared to 3DCRT plans (6.42Gy vs 8.82Gy & 0.88% vs 14.8%) respectively. Beckham WA et-al 2007 (25) also found that ipsilateral lung V_{20Gy} was significantly lower for IMRT plans compared to 3DCRT plans (17.1% Vs 26.6%).

**Conclusion**

Tangential beam IMRT in left sided breast cancer leads to a significant dose reduction in heart and ipsilateral lung with comparable target coverage compared to tangential beam 3DCRT.

**References**

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Table 3. Relevant plan parameters of OARs comparing tangential beam 3DCRT and tangential beam IMRT of the adjuvant radiotherapy of the whole breast in left sided breast cancer patients

<table>
<thead>
<tr>
<th>DVPs</th>
<th>Min</th>
<th>Max</th>
<th>Average</th>
<th>SD</th>
<th>P-value</th>
<th>Reduction%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V_{3Gy} (3DCRT)</td>
<td>3</td>
<td>62</td>
<td>28.53</td>
<td>13.9</td>
<td>&lt;0.001</td>
<td>12</td>
</tr>
<tr>
<td>V_{3Gy} (IMRT)</td>
<td>6</td>
<td>58</td>
<td>24.10</td>
<td>12.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V_{2Gy} (3DCRT)</td>
<td>2</td>
<td>51</td>
<td>21.10</td>
<td>12.1</td>
<td>&lt;0.001</td>
<td>15</td>
</tr>
<tr>
<td>V_{2Gy} (IMRT)</td>
<td>3</td>
<td>46</td>
<td>17.16</td>
<td>10.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V_{4Gy} (3DCRT)</td>
<td>2</td>
<td>47</td>
<td>18.36</td>
<td>11.01</td>
<td>&lt;0.001</td>
<td>21</td>
</tr>
<tr>
<td>V_{4Gy} (IMRT)</td>
<td>2</td>
<td>42</td>
<td>14.13</td>
<td>9.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V_{6Gy} (3DCRT)</td>
<td>1</td>
<td>44</td>
<td>15.20</td>
<td>10.12</td>
<td>&lt;0.001</td>
<td>53</td>
</tr>
<tr>
<td>V_{6Gy} (IMRT)</td>
<td>0</td>
<td>30</td>
<td>6.80</td>
<td>6.17</td>
<td></td>
<td></td>
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<tr>
<td><strong>Ipsilateral lung</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean dose (3DCRT)</td>
<td>7</td>
<td>21</td>
<td>13.23</td>
<td>2.80</td>
<td>&lt;0.001</td>
<td>18</td>
</tr>
<tr>
<td>Mean dose (IMRT)</td>
<td>5.5</td>
<td>19.5</td>
<td>10.80</td>
<td>2.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V_{3Gy} (3DCRT)</td>
<td>12</td>
<td>41</td>
<td>23.90</td>
<td>6.08</td>
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</tr>
<tr>
<td>V_{3Gy} (IMRT)</td>
<td>11</td>
<td>43</td>
<td>21.10</td>
<td>6.60</td>
<td>&lt;0.001</td>
<td>11</td>
</tr>
</tbody>
</table>


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