Lateral Wedge with Medial Only Cardiac Shielding (LEMONADE) Technique in Left Breast Radiotherapy

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Abstract

This dosimetric study analyzed the lateral wedge with medial only cardiac shielding (LEMONADE) technique for left breast radiotherapy (LBRT) against three other commonly used techniques which is a follow-up from our earlier publication of LEMONADE technique in left chest wall (LCW) radiotherapy. Dosimetric parameters of 30 consecutive patients who underwent LBRT with LEMONADE technique (P1) after breast conserving surgery (BCS) were compared with 3 other virtually reconstructed plans: no cardiac shielding with paired wedges; P2 (paired wedges and medial only Y-direction shielding) and P3 (paired wedges and bilateral Y-direction shielding). P1 had target volume (TV) coverage [mean 90% isodose coverage of 89.00% ± 3.96 vs 86.28% ± 4.80 and 84.43% ± 5.70 for P2 and P3, respectively]. While there is 3.07% drop in TV coverage compared to no cardiac shielding, the V26Gy of heart dropped from 5.26% to a negligible 0.56% for P1. Low dose region (TV receiving < 30Gy) is also significantly lesser for P1 compared to P2 and P3 (1.50% vs 3.61% and 5.65%). The earlier positive LEMONADE dosimetric study of LCW radiotherapy has been replicated in this study with much better dose volume parameters likely due to the physical properties of intact breast. LEMONADE is an easily re-producible and simple radiotherapy technique that can be implemented in most radiotherapy centres. Further study is needed on the use of LEMONADE technique in extreme hypofractionation.

Keywords
Left breast radiotherapy, left breast carcinoma, cardiotoxicity, multileaf collimators, cardiac shielding
Introduction
In our earlier publication we have shown that lateral wedge with medial only cardiac shielding (LEMONADE) technique produces a good cardiac sparing with minimal compromise on the target volume coverage in post operative left chest wall (CW) irradiation [1]. This manuscript is a follow-up to the earlier publication with dosimetric analysis of patients who underwent breast conserving surgery (BCS) followed by post operative radiotherapy. BCS is near universally practiced nowadays and had shown to have better cosmetic outcome, quality of life and patients’ satisfaction. BCS followed by radiotherapy (RT) is also shown to have better OS as compared to mastectomy [2, 3].

Post-operative radiotherapy (RT) had 19% reduction in 5-year local recurrence rate and 5.4% 15-year overall survival (OS) benefit as reported in the Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) meta-analysis for patients undergoing breast conserving surgery [4]. The cardiac toxicity and excess cardiac deaths attributable to left breast irradiation had been recognized in a 1989 publication by Jones et.al. It is estimated that for every 1Gy of increase in the mean dose to heart the rate of major coronary events increase by 7.4% [5]. Radiation may damage heart structures such as the left anterior descending coronary artery (LADCA) with increased risk of ischaemic heart disease, myocardial musculature causing fibrosis, the valves, damage to pericardium causing pericardial effusion and cardiac arrhythmias due to damage to the conducting system [6, 7]. It is prudent to keep the dose to heart, especially to the LADCA as low as possible while ensuring optimal target volume (TV) coverage as there may not be an entirely safe threshold dose below which toxicity do not occur.

The LEMONADE technique has greatly eased the 3D-Conformal Radiotherapy (3D-CRT) planning for left breast carcinoma patients in our centre. Avoiding the use of medial wedge also reduced the time needed to deliver the required monitor units in the medial tangential field helping with the deep inspiratory breath holding (DIBH). While we have discussed in detail the benefits of LEMONADE technique in the earlier publication (dose to heart, LADCA, etc) it is not known if the magnitude of dosimetric benefits are similar in intact breast due to the tissue deficit with different anatomy. Hence, we retrospectively re-analyze the single lateral wedge and medial only multileaf collimators (MLC) based cardiac shielding with MLC in X-direction (LEMONADE) technique that is applicable to our Elekta TM 160 Agility leaf Linear Accelerator for patients who underwent BCS. Dosimetric comparison with 3 other commonly used RT techniques for BCS irradiation were virtually created and compared for each patient.

Materials and Methods
This study protocol has been reviewed and granted approval from Human Research Ethics Committee USM (HREC) under study protocol code USM/JEPeM/20050264.

Adjuvant RT plans of 30 consecutive patients using the LEMONADE technique at AMDI-USM from 10th August 2020 till 5th March 2021, which fulfilled the inclusion and exclusion criteria as below were identified.

Inclusion criteria:
- Left breast RT plan of female patients who had BCS with or without axillary clearance.
- CT-Scan based 3D-Conformal Radiotherapy (3D-CRT) plans using tangential photon beams.
- Patients treated with the LEMONADE technique (single lateral wedge and medial only X-direction MLC based cardiac shielding) with or without concomitant regional nodal irradiation
- Patients who are treated with standard fractionation of 40 – 50Gy in 15 – 28 fractions

Exclusion criteria:
- RT plans using non-tangential techniques such as IMRT/VMAT or direct electrons to the left breast.
- Previous intra-thoracic surgery that would have distorted the anatomy.
- RT plans not using the CT based 3D-Conformal technique.
- Patients who underwent extreme hypofractionation (e.g., 26Gy in 5 fractions)

**CT simulation and computerized treatment planning** *(treatment technique reproduced from our earlier LEMONADE publication for left chest wall irradiation)*

**CT simulation**
Patient is positioned supine on an angled breast board, with arms extended above the head (Med-Tec, Iowa, USA). The angled breast board makes the sternum more horizontal and reduces the need for angulation in treatment beam geometry of the tangential RT fields. Head, elbow and arm rests are used for patients' comfort and stability. Ball bearings are placed bilaterally at mid-axilla corresponding and aligned with lasers. The caudal border corresponds to 1.5cm below the right inframammary fold marked with lead wire. Patient is CT-Simulated with axial slice thickness of 3 mm. CT data (Toshiba, Japan) is acquired without contrast in deep inspiratory breath hold (DIBH) technique from mastoid to the umbilicus ensuring full lung is in the field. The data then imported into the Monaco treatment planning system (Elekta CMS, Maryland Heights, MO, USA) in DICOM format.

**Delineation of target volumes and organs at risk**
At the Monaco 5.1 TPS (Elekta CMS, Maryland Heights, MO, USA) workstation skin is delineated using the automated contour by the software. The target volume (TV) is contoured based on online Radiation Therapy Oncology Group (RTOG) Breast contouring atlas, which incorporates the consensus definition of anatomical borders, mastectomy scar where feasible and takes into consideration the referenced clinical chest wall at the time of CT-Simulation [8]. For organs at risk, the heart is contoured as all visible myocardium, the apex, the right auricle, atrium and infundibulum of the ventricle. The pulmonary trunk, root of the ascending aorta and superior vena cava is excluded. Other contoured organs at risk (OAR) include the contralateral breast, left lung and spinal cord.

**Treatment planning**
Standard 3D-CRT tangential photon fields covering the contoured TV based on RTOG atlas are used with the corresponding field borders generally at 1.5cm below inframammary fold caudally, medially at midline and anterior border of serratus anterior laterally. The cranial border of the tangential field differs slightly from the RTOG atlas as we use high tangents (defined as less than 2cm from the humeral head). In out centre we generally place cranial border of the tangents at 1.2cm below the humeral head.

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(a) Lateral field

(b) Medial field
Figure 1 illustrates LEMONADE technique (single lateral wedge and medial only cardiac shielding with MLCs’ in X-direction) for patients undergoing post operative left breast RT. Collimator is set at 0 degree and parallel opposed medial tangential field (MTF) and lateral tangential field (LTF) is created. No dynamic wedge can be applied in the MTF field due to machine limitation as MLC in X-direction for cardiac shielding is used [Figure 1 (b)]. For the LTF, collimator is rotated to 90 degrees and dynamic wedge is applied without cardiac shielding [Figure 1 (c)]. Patients are treated using 6 or 10 MV photons to a dose of 42.56Gy in 16 daily fractions over 3 1/2 weeks, treating 5 fractions a week. Dose is initially prescribed to mid-plane at 2/3 distance of a tangential line that connects the mid-point of half beam blocked tangents to the skin. Thereafter, the plan is optimized further and the prescription point adjusted as needed. Lung constraints are based on an earlier meta-analysis of early lung toxicity in breast irradiation (8). Use of concomitant regional nodal RT fields was not included in this analysis.

For each LEMONADE plan (P1) 3 other commonly used virtual plans are created for comparison, namely:

I. Paired wedges with no cardiac shielding on both tangents  
II. Paired wedges and medial only Y-direction MLC based cardiac shielding (P2)  
III. Paired wedges and bilateral with Y-direction MLCs’ based cardiac shielding (P3)

TV coverage (mean) by 90% and 80% of the prescription isodose (PI), mean percentage (%) of TV receiving <30Gy, the mean maximum dose (Dmax) of the heart, mean V20Gy (V_dose = volume in percentage receiving the mentioned dose or more) and mean V30Gy of the heart and lung dose parameters for each of the plan is analysed. Given the anatomical location, the supraclavicular (SCF), axillary and internal mammary nodal region RT fields are unlikely to influence the radiation dose received by heart and thus not analysed in this study.

Results
The summary of the TV coverage, heart dose, LADCA dose and left lung dose for the 30 consecutive patients is presented in the Table 1–4 respectively.
Table 1. Dosimetric comparison for target coverage in 30 left breast cancer patients.

<table>
<thead>
<tr>
<th>Mean ± sd</th>
<th>No Cardiac Shielding</th>
<th>LEMONADE (P1)</th>
<th>P2</th>
<th>P3</th>
<th>(P-value &lt; 0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90% isodose coverage of TV (%)</td>
<td>92.07 ± 3.50</td>
<td>89.00 ± 3.96</td>
<td>86.28 ± 4.80</td>
<td>84.43 ± 5.70</td>
<td>0.0000</td>
</tr>
<tr>
<td>80% isodose coverage of TV (%)</td>
<td>98.46 ± 1.04</td>
<td>96.83 ± 2.12</td>
<td>94.51 ± 4.03</td>
<td>92.61 ± 5.41</td>
<td>0.0000</td>
</tr>
<tr>
<td>TV receiving &lt;30Gy (%)</td>
<td>0.63 ± 0.66</td>
<td>1.50 ± 1.38</td>
<td>3.61 ± 3.58</td>
<td>5.65 ± 5.05</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

Table 2. Dosimetric comparison for heart in 30 left breast cancer patients.

<table>
<thead>
<tr>
<th>Mean ± sd</th>
<th>Heart volume (258.7 cc ± 7.7)</th>
<th>(P-value &lt; 0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dmax (Gy)</td>
<td>No Cardiac Shielding LEMONADE (P1)</td>
<td>P2</td>
</tr>
<tr>
<td>40.84 ± 2.82</td>
<td>33.47 ± 2.34</td>
<td>29.66 ± 1.96</td>
</tr>
<tr>
<td>V26Gy (%)</td>
<td>5.26 ± 3.97</td>
<td>0.56 ± 0.35</td>
</tr>
<tr>
<td>V30Gy (%)</td>
<td>4.43 ± 3.54</td>
<td>0.10 ± 0.11</td>
</tr>
</tbody>
</table>

Table 3. Dosimetric comparison for left lung in 30 left breast cancer patients.

<table>
<thead>
<tr>
<th>Mean ± sd</th>
<th>Left Lung volume (614.1 cc ± 5.9)</th>
<th>(P-value &lt; 0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dmax (Gy)</td>
<td>No Cardiac Shielding LEMONADE (P1)</td>
<td>P2</td>
</tr>
<tr>
<td>42.35 ± 2.67</td>
<td>41.85 ± 2.54</td>
<td>42.02 ± 2.58</td>
</tr>
<tr>
<td>Mean Dose (Gy)</td>
<td>1.24 ± 0.48</td>
<td>1.34 ± 0.47</td>
</tr>
<tr>
<td>V20Gy (%)</td>
<td>14.89 ± 5.63</td>
<td>14.56 ± 5.26</td>
</tr>
</tbody>
</table>

Table 4. Dosimetric comparison for LADCA in 30 left breast cancer patients.

<table>
<thead>
<tr>
<th>Mean ± sd</th>
<th>Coronary Artery volume (2.85 cc ± 0.0)</th>
<th>(P-value &lt; 0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Cardiac Shielding</td>
<td>LEMONADE (P1)</td>
<td>P2</td>
</tr>
</tbody>
</table>

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The mean 90% and 80% isodose TV coverage of LEMONADE technique is marginally smaller by 3.07% and 1.63% respectively compared to no cardiac shielding while it is significantly better compared to P2 and P3. The mean low dose (<30 Gy) region in TV is only marginally higher compared to no cardiac shielding by a mere 0.87% points for LEMONADE technique (Table 1).

While the mean Dmax is higher by 18.31 Gy in LEMONADE technique as compared to P3, the more significant dose parameters of $V_{26Gy}$ and $V_{30Gy}$ are different by only 0.56% and 0.10% respectively. In the no cardiac shielding plan, it is much higher at 5.26% and 4.43% respectively (Table 2). The mean LADCA D0.5cc and Dmax is higher by around 9 percentage points in the LEMONADE technique compared to P3 that applies complete cardiac shielding (Table 3).

The left lung dose parameters which is not the primary objective of this study was also analysed and showed no statistical significance (Table 4). The ipsilateral lung dose of all four plans are within the recommended tolerance in breast irradiation (ipsilateral $V_{20Gy}$ < 30% and MLD < 15 Gy).

**Discussion**

Due to machine limitation in most of the medical linear accelerator (Linac) brands, the dynamic wedge and the MLCs' cannot be in the same direction (they are fixed in opposite direction - X and Y). Hence when wedge is used, the MLCs' need to travel in the Y-direction in order to shield the heart which will inadvertently shield a small part of the TV without any extra benefit in sparing the heart. In the earlier LEMONADE publication, we have shown that unilateral cardiac shielding of the medial tangent and single wedge for the lateral tangent gives a reasonably good TV coverage and sparing of the heart [1].

There had been rapid progress in the treatment algorithm of breast cancer patients with significant improvement in the outcome whereby even in the metastatic setting long term survivors can be expected. Post-operative radiotherapy which is an integral part of breast cancer treatment that has consistently showed local control and survival benefit [4]. However, cardiac toxicity secondary to RT is a significant issue that may prove to be detrimental to survival and wash away any benefit derived from radiation in terms of disease control.

While advanced RT techniques such as intensity modulated radiation therapy (IMRT), volumetric arc therapy (VMAT), Tomotherapy and field in field planning in addition to respiratory gating are being employed to reduce the radiation induced damage to the heart, these techniques have their own set back. These advanced technologies are not available in all radiotherapy centres and there is a steep learning curve for the radiation oncologist, dosimetrist and physicist. Increased treatment time with IMRT/VMAT/Tomotherapy may impact on the patient compliance if DIBH technique is used. Small field dosimetric uncertainty, skin dose discrepancy and impact of air tissue interface especially with respiratory motion are important issues with the use of these techniques [9].

Without the use wedges in both tangents, the ability to manoeuvre TV dose coverage according to ICRU50 recommendations will be affected and we accept hotspots up to 25% of prescribed dose within the TV as the skin, chest wall and breast tissue may tolerate higher dose radiation with minimal morbidity. However, caution is needed for the use of LEMONADE technique in extreme hypofractionation since the therapeutic ratio is very narrow [10].

Based on this comparative dosimetric study performed at AMDI-USM, as with the previous analysis in chest wall irradiation LEMONADE technique also produced the best compromise between TV coverage and cardiac sparing compared to no cardiac shielding and 2 other commonly used techniques. The commonly accepted 80% isodose coverage in 3D-CRT of breast of 96.83% (mean) and a mean $V_{26Gy}$ heart of 0.56% can
be considered as very optimal in breast plans. While the LEMONADE technique reduced the dose (D0.5cc) to LADCA by nearly 11.5% points it is still around 10% points higher than bilateral shielding. It is not known if there is any clinical benefit in further reducing the LADCA dose at the expense of TV coverage. While the comparison of the lung dosimetric parameters were statistically not significant, LEMONADE plans conforms to the DVH constraints of the lung in RT for breast carcinomas [11].

An interesting finding is that the dosimetric parameters of TV coverage and cardiac sparing is better in current study compared to earlier LEMONADE publication of chest wall irradiation. We assume that the physical property of intact breast tissue would have contributed to this advantage. This further adds to the known benefits breast conserving surgery followed by surgery in contrast to mastectomy.

Conclusion
LEMONADE technique can achieve an optimal TV coverage and cardiac sparing in patients who underwent BCS. The earlier positive LEMONADE dosimetric study of chest wall irradiation has been replicated in this study with much better dose volume parameters likely due to the physical properties of intact breast. LEMONADE is an easily re-producible and simple radiotherapy technique that can be implemented in most radiotherapy centres. Further study is needed on the use of LEMONADE technique in extreme hypofractionation.

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The first author of this manuscript would like acknowledge Dr Karen Taylor, radiation oncologist at William Buckland Radiotherapy Centre, The Alfred, Melbourne who initially introduced this concept of single side cardiac shielding during his radiation oncology training years in 2011.

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