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RESEARCH PAPER

Lateral wedge with medial only cardiac shielding (LEMONADE) technique in left chest wall adjuvant radiotherapy

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ABSTRACT

Background: This dosimetric study compared lateral wedge with medial only cardiac shielding (LEMONADE) technique, for left chest wall (LCW) irradiation against three other commonly used techniques.

Materials and methods: Dosimetric parameters of 22 consecutive LBC patients treated using the P1 (LEMONADE technique) 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).

Results: P1 showed better target volume (TV) coverage with the mean 90% isodose coverage of 85.59% ± 5.44 compared to 78.90% ± 8.59 and 74.22% ± 9.50 for P2 and P3, respectively. Compared to no cardiac shielding, for a 4.65% drop in TV coverage the V26Gy of heart dropped from 6.68% to a negligible 0.85% for P1. TV receiving < 30Gy is also significantly lesser for P1 compared to P2 and P3 (5.42% vs 10.64% and 15.8%), whilst there is a small difference of 2.75% between no cardiac shielding and P1.

Conclusion: With the improvement in BC survival rate, cardiac toxicity associated with adjuvant irradiation for LBC is a major concern. P1 (LEMONADE) technique has a good compromise between cardiac sparing and target coverage and should suffice for most LCW irradiations. Furthermore, the LEMONADE technique is a simple, reproducible and involves fast planning for cardiac sparing, which is ideal for under-resourced departments with heavy workload.

Key words: left chest wall radiotherapy; left breast carcinoma; cardiotoxicity; multileaf collimators; cardiac shielding

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Introduction

Post-operative or adjuvant radiotherapy (RT) is an important component of breast cancer (BC) treatment algorithm, both in the breast conservative surgery and mastectomy. The most important manuscript to date, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis 2014 showed a 10-year recurrence free and 20-year BC mortality benefit for adjuvant RT after mastectomy [1]. Despite the known advantages, radiation induced cardiac toxicity leading to an increase in cardiac related deaths is a major issue with adjuvant RT for left BC. One of the earliest manuscript

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with regards to this issue is by Jones et al. in 1989. He reported on 35-year follow up of 1461 patients who were subjected to immediate post-operative RT or delayed RT at the time of recurrence. There was a significant increase in mortality attributable to deaths from cardiovascular disease which was seen after 15 years of follow up. However, the RT techniques used then would be considered archaic today and, hence, the applicability of the study [2]. In another EBCTCG 2005 publication looking at 42,000 women in 78 randomized treatment comparisons, there was an excess mortality mainly from heart disease (rate ratio: 1.27, SE: 0.07, 2p = 0.0001) which was more pronounced in older radiotherapy regimens [3].

The left anterior descending coronary artery (LADCA) is directly below the left chest wall which can be damaged by the adjuvant RT to the left chest wall (LCW) or left breast leading to ischemic heart disease. Other damages to the heart include fibrosis of the myocardial musculature leading to reduced contractility, damage to the valves, damage to the conductive system causing cardiac arrhythmias and also pericardial damage causing effusion [4, 5].

With the improvement in BC treatment algorithm and outcome, many women will live to experience the delayed effects of radiation, of which cardiotoxicity is a major concern. Techniques that reduce radiation injury to the heart while maintaining the efficacy will translate into reduced morbidity and mortality and also a better all cause survival rates. While it is known that the risk of cardiac events increases with increasing radiation dose, there appears to be no safe threshold dose below which it is entirely safe, and it is estimated that the rate of major coronary events is increased by 7.4% for each 1Gy of increase in the mean radiation dose to the heart [6].

While there are many RT techniques being employed for left BC to reduce the dose to the heart, these techniques, such as IMRT, VMAT, Tomotherapy and Electron beam therapy, are not without their own setbacks. Furthermore, immobilization and patient reproducibility plays a very important role when these advanced modalities with steep radiation dose gradients are used. At centre A, we further fine-tuned a simple technique of single lateral wedge and medial only MLC based cardiac shielding coming in the X-direction which we call a LEMONADE technique that is applicable to our Elekta TM 160 Agility leaf Linear Accelerator, to shield the heart. We actively use this technique in 3D-Conformal RT (3D-CRT) planning for adjuvant RT to LCW or left breast. In this manuscript, we describe the LEMONADE planning technique and made dosimetric comparison with 3 other commonly used LCW RT techniques that were virtually created for each patient.

Materials and methods

Adjuvant RT plans of 22 consecutive patients who underwent LCW RT using the LEMONADE technique at centre A from 7th April 2016 till 1st August 2016 and who fulfilled the inclusion and exclusion criteria as identified below.

Inclusion criteria:

- LCW RT plans of female left BC patients who had mastectomy 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 MLC based cardiac shielding coming in the X-direction) with or without concomitant locoregional nodal irradiation.

Exclusion criteria:

- RT plans using non-tangential techniques such as IMRT/VMAT or direct electrons to the LCW;
- previous intra-thoracic surgery that would have distorted the anatomy;
- RT plans not using the CT based 3D-Conformal technique.

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 the mid-axilla corresponding and aligned with lasers. The caudal border corresponds to 1.5 cm below the right inframammary fold and cranial border at 2nd rib-sternal junction are also wired. Patient is CT-Simulated with axial slice thickness of 3 mm. CT data (Toshiba, Japan) is acquired without contrast in the deep inspiratory breath hold (DIBH) technique from the mastoid to the umbilicus ensuring full lung is in the field. The data is 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 the 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 [7]. 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 are excluded. Other contoured organs at risk (OAR) include the contralateral breast, left lung, left anterior descending coronary artery (LADCA) 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 the inframammary fold caudally, medially at the midline and anterior border of the 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). At centre A, we generally place the cranial border of the tangents at 1.2cm below the humeral head. Figure 1A–C illustrates the LEMONADE technique (single lateral wedge and medial only cardiac shielding us-

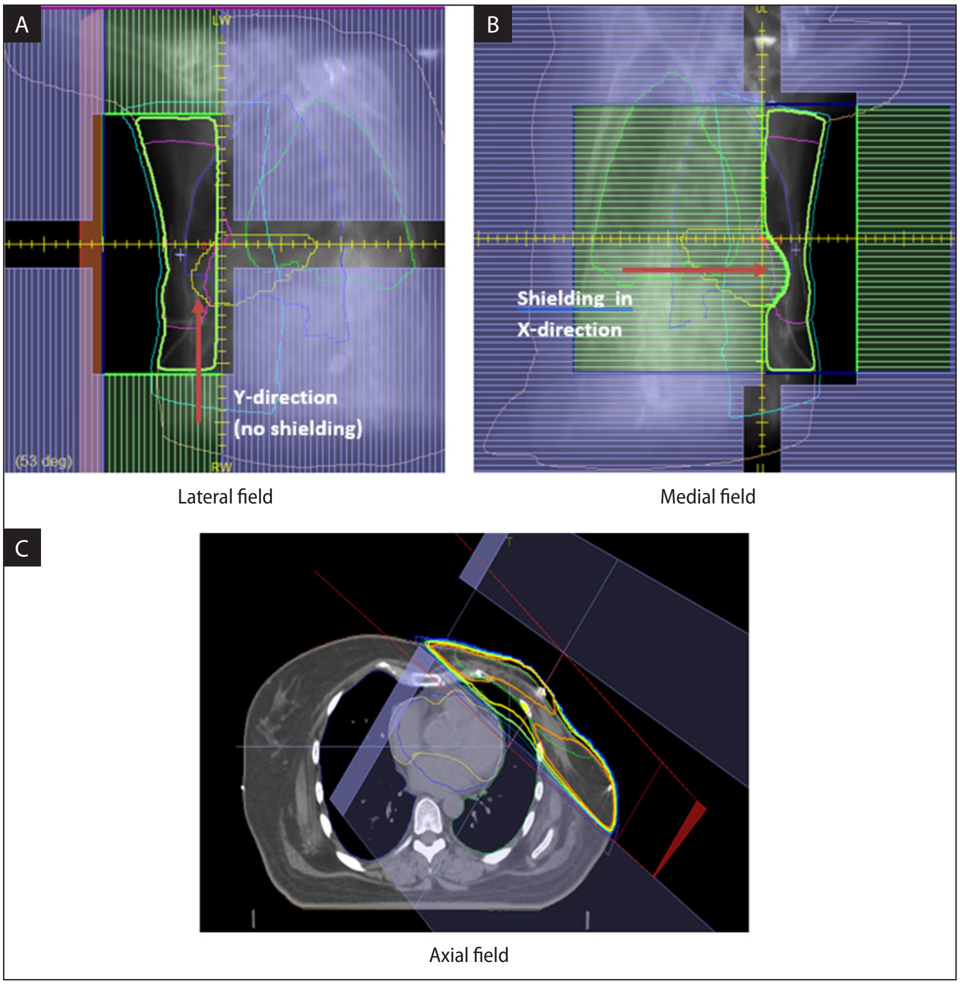

Figure 1. LEMONADE plan (single lateral wedge and medial only cardiac shielding using MLCs' in X-direction)

ing MLCs' in X-direction) for patients undergoing adjuvant LCW RT. Collimator is set at 0 degree and parallel opposed medial tangential field (MTF) and lateral tangential field (LTF) are created. No dynamic wedge can be applied in the MTF field due to machine limitation with the use of MLC in X-direction for cardiac shielding (Fig. 1B). For the LTF, collimator is rotated to 90 degrees and dynamic wedge is applied without cardiac shielding (Fig. 1A). Patients are treated using 6 or 10 MV photons to a dose of 42.56 Gy 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 by adjusting the physical properties of the radiation beam delivery not limited to the prescription point. Lung constraints are based on an earlier meta-analysis of early lung toxicity in breast irradiation [8]. At centre A, we rarely use the field in field technique or other modalities, such as IMRT, as this aforementioned LEMONADE technique gives a good dose distribution once the planning dosimetrist have mastered optimization methods. Use of concomitant regional or locoregional radiotherapy fields was not considered in this analysis.

For this comparative study, 3 other commonly used virtual plans are created for each LEMONADE plan, namely:

- paired wedges with no cardiac shielding on both tangents;
- paired wedges and medial only MLC based cardiac shielding with MLCs' coming in Y-direction (Plan 2; P2);
- paired wedges and bilateral cardiac shielding with MLCs' coming in Y-direction (Plan 3; P3).

TV coverage by 90% and 80% prescription isodose (PI), mean percentage (%) of TV receiving < 30 Gy, the mean maximum (mean Dmax) heart dose, mean % of V26 (volume of heart receiving more than 26 Gy) and mean % of V30 (volume of heart receiving more than 30 Gy), lung dose and also Dmax D0.5cc to the LADCA region for each of the plan are analyzed.

Results

The summary of the TV coverage, heart dose, left lung and LADCA dose for the 22 consecutive patients who are analyzed is presented in the Tables 1–4, respectively. While the 90% isodose TV coverage of P1 (LEMONADE) is compromised by 6.51% points compared to no shielding, it is much better than P2 and P3 at 13.20% and 17.88% points, respectively. The margin is even smaller at 4.65% points compared to no cardiac shielding for 80% isodose TV coverage. For TV receiving lower dose of radiation (< 30 Gy), there is only a mere 1.87% points difference between the P1 and no cardiac shielding, whereas it is 8.09% points in P2 and 13.25% points in P3.

P3 has very good cardiac shielding with mean Dmax of only 24.74Gy compared to no cardiac

Table 1. Dosimetric comparison for target volume coverage in the 22 patients

Mean ± SD	No cardiac shielding	LEMONADE (P1)	P2	P3	p-value < 0.001
90% isodose coverage of TV (%)	92.10 ± 4.11	85.59 ± 5.44	78.90 ± 8.59	74.22 ± 9.50	0.0000
80% isodose coverage of TV (%)	96.54 ± 4.11	91.89 ± 3.85	85.97 ± 7.13	81.33 ± 8.30	0.0000
TV receiving < 30 Gy (%)	2.55 ± 2.41	5.42 ± 3.14	10.64 ± 6.25	15.80 ± 7.70	0.0000

SD — standard deviation; LEMONADE — lateral wedge with medial only cardiac shielding; TV — target volume

Table 2. Dosimetric comparison for heart dose in the 22 patients

Mean ± SD	Heart volume (258.7 cc ± 7.7)				p-value < 0.001
	No cardiac shielding	LEMONADE (P1)	P2	P3	
Dmax [Gy]	42.36 ± 1.66	34.49 ± 1.94	32.04 ± 2.13	24.74 ± 2.21	0.0000
V26 (%)	6.68 ± 4.04	0.85 ± 0.47	0.25 ± 0.20	0.00 ± 0.00	0.0000
V30 (%)	5.88 ± 3.76	0.18 ± 0.16	0.03 ± 0.05	0.00 ± 0.00	0.0000

SD — standard deviation; LEMONADE — lateral wedge with medial only cardiac shielding

Table 3. Dosimetric comparison for left lung dose in the 22 patients

Mean ± SD	Left lung volume (614.1 cc ± 5.9)				p-value < 0.001
	No cardiac shielding	LEMONADE (P1)	P2	P3	
Dmax [Gy]	43.67 ± 1.40	42.71 ± 1.52	42.71 ± 1.50	40.30 ± 8.40	0.0887
Mean dose [Gy]	6.63 ± 7.71	6.42 ± 7.51	1.24 ± 0.42	4.54 ± 5.70	0.0184
V20 (%)	16.66 ± 5.53	15.24 ± 5.94	16.00 ± 5.36	12.57 ± 5.29	0.0933

SD — standard deviation; LEMONADE — lateral wedge with medial only cardiac shielding

Table 4. Dosimetric comparison for left anterior descending coronary artery (LADCA) region in 22 left breast cancer patients

Mean ± SD	LADCA region volume (3.61 cc ± 1.27)				p-value < 0.001
	No cardiac shielding	LEMONADE(P1)	P2	P3	
D0.5cc [Gy]	37.89 ± 6.71	22.54 ± 4.80	20.97 ± 3.91	12.10 ± 3.67	0.0000
Dmax [Gy]	41.26 ± 3.83	29.89 ± 4.13	28.87 ± 3.70	23.08 ± 4.34	0.0000

SD — standard deviation; LEMONADE — lateral wedge with medial only cardiac shielding

shielding (42.36 Gy), P1 (34.49 Gy) and P2(32.04 Gy). However, further analysis done at V_{26Gy} and V_{30Gy} (volume of heart receiving the dose; V_{dose}) showed very good cardiac sparing for P1 with only 0.85% and 0.18% points difference, respectively, compared to P3 which did not receive any dose above 25 Gy. While the mean Dmax and D0.5cc to LADCA were the lowest in P3 due to bilateral cardiac shielding, the LEMONADE technique demonstrates 1.02 Gy difference in mean Dmax compared to P2.

The left lung dose, though not the primary objective of this study, was also analyzed. The ipsilateral lung dose of all four plans are below the recommended tolerance in breast irradiation (ipsilateral V20 Gy < 30% and MLD < 15 Gy) [8].The supraclavicular (SCF), axillary and internal mammary nodal region RT fields are not included in this study as the addition of these RT fields are likely to have minimal impact on the radiation dose received by the heart due to the geographical location. Whereas in the case of lung dose analysis, the radiated volume will increase at the same ratio for all 4 plans.

Discussion

With the advent of highly effective systemic therapy and modern treatment algorithm, the cure rates of BC patients have improved significantly over the last 2 decades. More than half of the newly diagnosed breast cancer patients will eventually become cancer survivors or at times long term survivors even in metastatic setting. Hence, long term toxicity of the given treatment is becoming an important issue in this group of patients. Adjuvant RT to the chest wall or breast is an important part of treatment algorithm which has consistently showed survival benefit [1]. However, for the treatment of left BC with RT, cardiac toxicity is a major issue to be dealt with. Though radiation induced pericarditis and cardiovascular mortality are well-described in the literature, the tolerance dose for the left anterior descending coronary artery (LADCA) has not yet been established and the available evidence indicate that this should be kept as low as possible in patients with left-sided breast cancer [9].

With modern RT, many techniques are being employed to reduce the radiation induced damage to the heart. Breath holding or gating is usually employed to reduce the target position and OAR uncertainties associated with breathing motion. Despite the breath holding technique to reduce the field margins, invariably, some part of the heart will be inside the tangential fields employed to treat the left breast or LCW. Although other techniques are available in dealing with this issue, such as IMRT, Tomotherapy or field in field planning, these methods are time consuming and will have a significant impact on the available resources. Furthermore, the use of these techniques is not without its own setbacks such as longer treatment time which may reduce patient's compliance with DIBH and small beam dosimetry in IMRT that may not be accurate even with minimal breathing motion.

Due to the machine limitations in most medical linear accelerator (Linac) brands that are commercially available, the dynamic wedges are fixed either in the X or Y directions only and MLCs in the opposite direction. As such, when wedges are used in adjuvant breast or chest wall irradiation in the 3D-CRT technique, MLCs need to travel from inferior (Y-direction) to the shield the heart. This may inadvertently shield a small part of the TV without any extra benefit in sparing the heart. Anatomically, the closest part of the heart to the ribcage is more anterior-medial; hence, cardiac shielding of the MTF is more important than the LTF in LCW RT.

Bearing this in mind, Radiation Oncology department of centre A fine-tuned and improvised this simple and practical LEMONADE technique. With this technique inadvertent shielding of the breast tissue at the inferior aspect of the breast or chest wall (as happens in MLCs coming in the Y-direction) is avoided. Expectedly, without the use of bilateral wedges, the ability to modify or conform the TV dose coverage to ICRU50 recommendations will be affected. However, larger variations are acceptable provided that it is more of overdose rather than under dose as the skin, chest wall and breast tissue may tolerate higher dose radiation with minimal morbidity. Hence, in our institution, we strictly adhere to cardiac shielding and cardiac dose constraints at the expense of target volume dose in-homogeneity of up to 25% hotspot inside the TV.

Based on this comparative dosimetric study performed at centre A, though the P3 gives the best cardiac sparing parameters (Dmax 25.84, V26 Gy and V_{30Gy} of 0%), the TV coverage is very low. Mean TV coverage of 74.22% ± 9.50 for 90% isodose and 81.33% ± 8.30 for 80% isodose cannot be considered as acceptable in today's radiotherapy standards and, as such, this plan should not be used for LCW RT. Due to the physical nature of static tangential photon beams, it is unlikely to achieve the ICRU50 criteria of 95% isodose coverage of the PTV (planning target volume). Unless a half beam block is used in all directions, the 95% isodose will stretch to > 5 mm from the edge of the field. It is difficult to extend the field borders, especially the lateral and medial borders without inducing unnecessary toxicity to the OARs, especially the heart in LCW RT. This effect is seen even when no cardiac shielding is applied with the mean 90% isodose coverage of the TV of 92.10% ± 4.11.

Due to the technical issues mentioned, many radiation oncologists accept 80% isodose coverage of the TV as a reasonable figure for LCW RT. For 80% isodose coverage, P1 differs from no cardiac shielding by 4.65% points only compared to P2 that differs by 10.57% points. Furthermore, the advantage of P2 over P1 in terms of cardiac sparing is only 0.85% points and 0.03% points for V_{26Gy} and V_{30Gy}, respectively. With this strong dosimetric data, the authors suggest that the P1 plan should be strongly considered for simple and straightforward tangential photon treatments of the left BC patients undergoing adjuvant RT. The analysis of the lung dosimetric parameters shows that the P1 plan conforms to the DVH constraints of the lung in RT for BC [8].

Although single wedge techniques for left BC adjuvant RT has been described in textbooks, to our knowledge based on extensive literature search, there is no dosimetric study on the advantages of different shielding techniques and the use of uni/bi-directional wedges especially in the era of MLCs till date. We would like to name this technique which is used in conjunction with DIBH for 3D-CRT of left BC as LEMONADE technique in appreciation of the 2nd author of this manuscript who has popularized this treatment technique at centre A for past 8 years. This technique is used for both left CW and left breast irradiation.

Conclusion

With the improvement in breast cancer treatment and survival rates, long term toxicities are becoming a major issue, especially the cardiac toxicity associated with left BC adjuvant RT. The dosimetric comparison between the 4 different plans in this study confirmed that the LEMONADE technique has the best compromise between cardiac sparing and target coverage. The LEMONADE technique should suffice for most patients needing LCW RT. However, the treating radiation oncologist's clinical judgement should take precedence on the type of treatment modality to be used.

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Ethics approval

This study protocol has been reviewed and granted approval from Human Research Ethics Committee

USM (HREC) under study protocol code USM/JEPeM/20050264.

Conflict of interest

Authors report no conflict of interest

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