Post Mastectomy Chest Wall Irradiation Using Mixed Electron-photon Beams with or without Isocentric Technique

H. K. Hamdy, M. S. Zikry

Department of clinical Oncology, Faculty of Medicine – Al-Azhar University.

Abstract

Aim

To describe our technique in delivering post mastectomy radiotherapy to chest wall using electron-photon mixed beam with or without isocentric application of the tangential photon portals, and to evaluate the associated acute and delayed morbidities.

Patients and methods

Twenty-two females with invasive breast cancer were subjected to modified radical mastectomy with adequate axillary dissection. All the patients have either tumour $\geq$ 5 cm and/or positive axillary nodes >3. Chest wall was irradiated by a mixed beam of 6-Mev electrons (10Gy) and opposed tangential fields using 6 Mev-photons (36 Gy) followed by 6-Mev electrons boost to the scar of mastectomy for 4 Gy/2 fractions. We randomly allocated our patients to receive the photon beam with or without the isocentric technique.

Results

The mean dose to the planned target volume (PTV) by mixed beam was 44 Gy (96%) with a mean dose of 42 Gy (91%) to the overlying skin for the whole study group. In cases with right breast disease (17 cases), the mean right lung tissue volume within the PTV was 220 ml (15%). It was relatively higher with the non-iscocentric technique, 281 ml (19%), compared to the isocentric technique of 159 ml (10.5%). In cases with left breast disease (5 cases), the mean left lung volume within the PTV was 175 ml (14%). Larger volume of the lung tissue was included with the non-isocentric technique, 197 ml (16%) compared to the isocentric technique of 153 ml (12%).The mean scattered doses to the rest of the lung tissue, the rest of the heart in left breast cases, and the contra-lateral breast for the whole study group were 2.8 Gy, 1.8 Gy, and 1.4 Gy respectively and was comparable in both treatment arms. None of the cases developed any element of acute radiation related pneumonitis. Delayed radiation induced pneumonitis was seen in 2 cases (18%), with the chest wall treated with radiation with the non-isocentric technique.

Conclusion

This study clearly demonstrated the utility of mixed beam in irradiating the chest wall after mastectomy with the dose prescription we proposed. An adequate homogeneous dose level was delivered to the chest wall. The treatment was administered with accepted level of both acute and delayed treatment related morbidity especially when the photons were delivered by the isocentric technique.

Keywords

Chest wall irradiation, mixed electronphoton beam.

Introduction

Radiotherapy clearly reduces the risk of loco-regional failure (LRF) for patients with invasive breast cancer treated with mastectomy [1]. However for many years it has been controversial whether this reduction also results in decreased risks of distant failures and ultimately death due to cancer to patients who receive systemic therapy. Two large trials [2,3], were conducted to answer this question. Node-positive patients treated with radiation therapy after modified radical mastectomy, not only had reduced LRF

Correspondance address: Dr. Hassan Khalid, KCCC - Sabah, Department of Medical Oncology, Sabah Region, Shuwaikh, Kuwait Tel.: 7368730 Email: hassankhalid_57@yahoo.com

but also significantly had improved disease-free and overall or cause-specific survival rates.

Patients most likely to benefit from adjuvant radiation therapy are presumed to be those with an increased risk of LRF. Patients with tumours $\geq$ 4 cm or at least 4 involved axillary nodes experience LRF rates in excess of 20% and should be offered adjuvant radiation [4]. The chest wall is the site at greatest risk of recurrence after mastectomy. Hence the treatment of the chest wall is mandatory whenever radiation therapy is indicated [5].

However, it is difficult to irradiate the chest wall in a homogenous manner. It has a complex shape and is located at the body-air interface, often with rapid changes in contour and tissue separation, together with much inter patient variation, that can be more modified by surgery. Also, the dose-limiting organs at risk i.e. the lung and heart, especially in left sided tumours, are in close proximity to the under surface of the chest wall. Finally, there is the inhomogeneity produced by the lungs with its lower density leading to less attenuation of the primary beam with subsequent scattered radiation. There is no agreement to what an "adequate" or "optimal" radiotherapy technique for chest wall is. Different centers throughout the world use different techniques [6].

The most frequently used technique is the 2 opposed tangential photon beams across the chest wall. Its major disadvantage is the beam divergence into the underlying lung tissue and the heart. The use of isocentric technique with non-divergent posterior borders can reduce this problem. On the other hand, treating a large curved surface like the chest wall with single stationary electron field to avoid irradiation of the underlying vulnerable organs is less acceptable due to the expected dose inhomogeneity within the treatment volume. Combining both electrons and photons can improve the dose homogeneity or the chest wall and lowers the associated morbidity to the overlying skin and underlying organs at risk i.e lung and heart [7].

The aim of this study is to describe our technique in delivering post mastectomy radiotherapy to the chest wall using electron-photon mixed beams with or without isocentric application of the tangential photon portals. Also we evaluated the dosimetry of our technique, as well as, the expected acute and delayed morbidity.

Patients and Methods

This study included 22 females with invasive primary breast cancer at the non-metastatic stage. All were subjected to modified radical mastectomy with adequate axillary dissection, followed by adjuvant chemotherapy.

All the patients were at risk of chest wall recurrence, by having either tumour $\geq$ 5 cm or positive axillary nodes >3 in number and so all of them have been irradiated. We prescribed a total dose of 46 Gy/23 fractions with 5 fractions/ week for the chest wall. It was given via a mixed beam of 6-Mev electrons (10Gy) and opposed medial/lateral tangential fields using 6Mv-photons (36 Gy). This was followed by 6-Mev electrons boost to the scar of mastectomy for 4 Gy/2 fractions. Concerning the photon beams, we randomly allocated our patients to receive it with or without the isocentric technique.

Simulation

All patients were simulated for the photon tangential portals. The patients lied in the supine position, with the ipsilateral arm in the "Salute-position". An inclined plane was used and adjusted to compensate for the cranio-caudal variation in the chest wall outline. The treatment volume was defined in each patient as the chest wall at the anatomical site of the resected breast, and inevitably a segment of the underlying lung tissue, or the heart in left sided disease. The medial and lateral tangential portals configurations, angulations and collimations were displayed to include the treatment volume. Markings were applied at the skin to show the beam entry and lasers used to fix the patients set-up. Concerning the electron beam, it was delivered via suitable cones and usually kept 5 cm above the skin to avoid its contamination with secondary x-ray produced by the interaction of electrons with the cone. Also the gantry was rotated approximately 30° to compensate for the medio-lateral discrepancy of the chest wall.

All patients underwent CT scanning in the treatment position, with CT slices taken at the upper, middle and the lower borders of the treatment volume. Radio-opaque catheters were placed during scanning to determine the medial and lateral borders of the radiation fields.

Dosimetry

The CT slices were then transferred to a 2-D computerized planning system (Fig. 1), on which the target volume was accurately defined to include the chest wall at the anatomical site of the resected breast with exclusion of the superficial 5 mm of the skin surface. The tangential portals were applied at the marked borders on the scans. Whenever the isocenteric-technique was used, the isocenter was located from the CT cuts as well as the FSD at midline (P). The medial and lateral tangential angles were then calculated from the following equations:

Right-sided chest wall

- Medial tangential angle = 90 – a + B
- Lateral tangential angle = 270 –a + B

Left-sided chest wall

- Medial tangential angle = 270 – a + B
- Lateral tangential angle = 90 – a + B

Where a was measured, and

$$B = \tan^{-1}\frac{(0.5\ W)}{SAD}$$

- To apply on the patient, re-simulation was carried out, where the patient was fixed in the treatment position, with previously calculated FSD at midline (P). Shift the patient distance (X), to left or right for right, or, left sided chest wall irradiation respectively, to mark the isocentre on the patient. (Fig. 2)

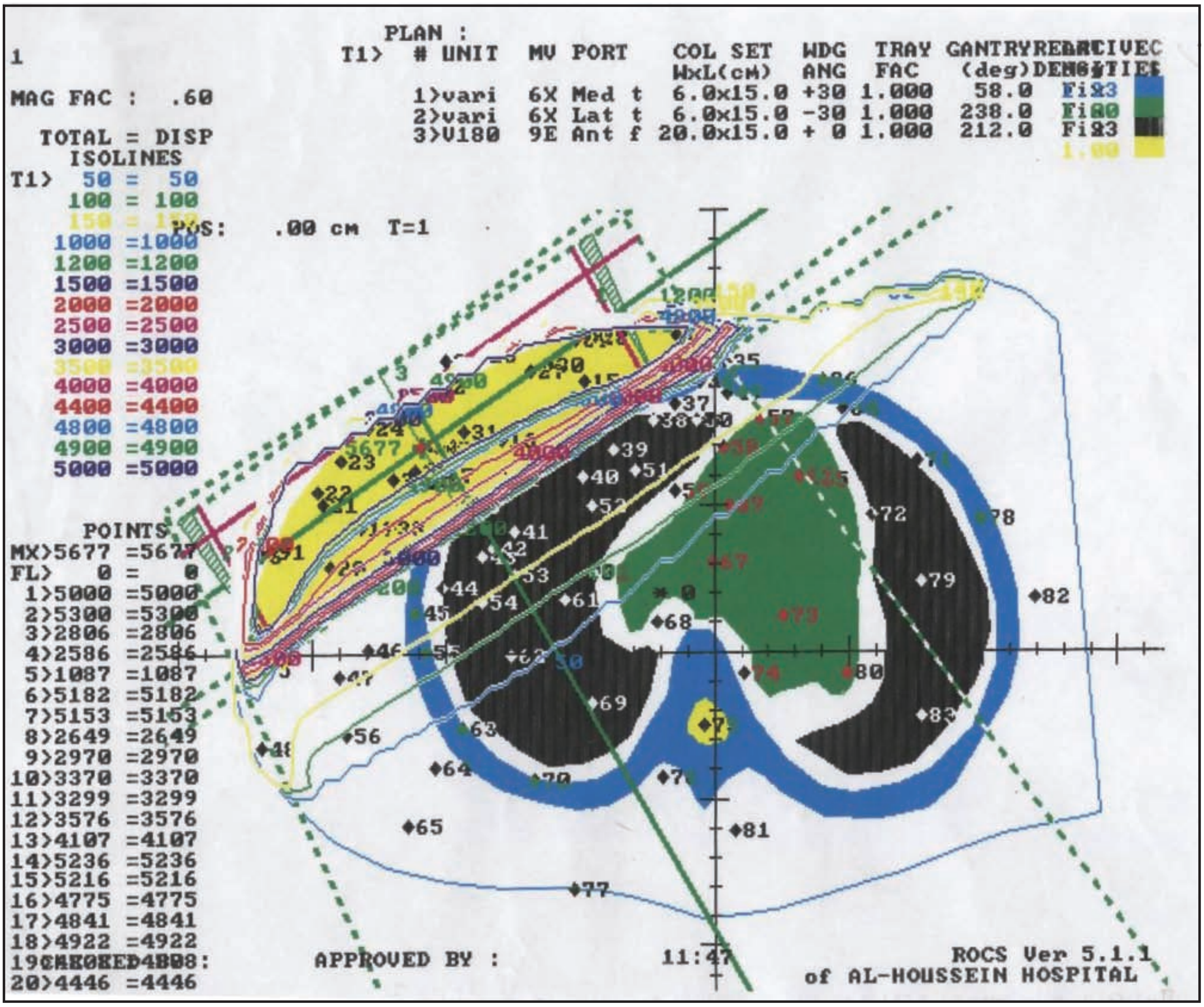

Fig. 1: Isodose distribution for mixed beams with isocentric technique

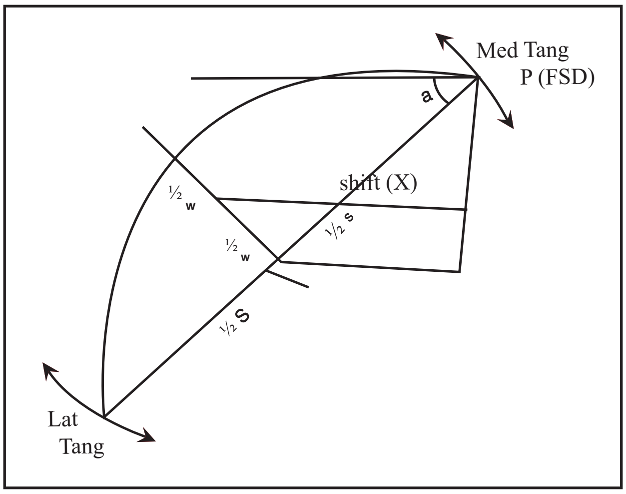

Fig. 2: Localisation of the isocentre

- Rotate the gantry to mark the medial and lateral tangential portals, as previously calculated.
- Adjust collimator angle to optimize coverage of chest wall.
- Check films were taken.
- Usually wedge filters were used with closure of air-groups and bolus was applied on the scar along the photon beam sessions.
- Finally the isodose curves contributed from the mixed electron-photon beams were displayed, always aiming to include the target volume within the 95% isodose curve.
- Whenever it was indicated to irradiate the supra-clavicular fossa $\pm$ axillary apex, we prescribed a total dose of 50 Gy/25 fractions, with 5 fractions/week using a mixed beam of 9 Mev electrons (14 Gy) and 6 Mv photons (36 Gy).

Aided by the check films, we calculated the central lung distance (CLD) for every patient, and accordingly we were able to calculate the volume of lung tissue included within the primary beam by the equations:-

- Irradiated left lung volume (Y) = 0.21 CLD^2 + 2.47 CLD + 2.95.
- Percentage of irradiated left lung volume $= \frac{Y \times 100}{1500}$
- Irradiated right lung volume (Z) = 0.01 CLD^2 + 0.17 CLD = 0.19.
- Percentage of irradiated right lung volume $= \frac{Z \times 100}{1245}$ [8]

We recorded also the mean dose of scattered radiation to the rest of the lung tissue, the mean dose to the pericardium and the contralateral breast tissue for each patient.

Follow up

After the radiation therapy was included, we kept our patients on regular follow-up every 3 months, aiming to monitor the disease local control and to evaluate the expected treatment related morbidity according to the RTOG/EORTC grading system [9] by thorough physical examination plain x-rays of chest, echocardiagram every six months, as well CT scan chest whenever required to confirm radiation induced pneumonitis and to estimate its extent.

Results

This study included 22 females with invasive breast carcinoma at the non-metastatic stage. All were subjected to modified radical mastectomy and adjuvant FAC-chemotherapy regimen for 6 cycles. They were under our care during the period from August 2002 to April 2003 for radiation therapy.

The median age of the whole study group was 52 years. The majority of the cases were pre-menopausal (68%), right breast 77%, T_3 (68%), Node positive (86%) [Table 1].

All the cases received post-operative radiotherapy to the chest wall using electron-photon mixed beam. Half of the cases, received the photon beams sessions with the isocentric technique. Thirteen cases (59%) received radiation to the supra clavicular fossa and axillary apex as they showed heavy axillary nodal infiltration (>3). None of the cases received whole axillary radiotherapy as all of them had adequate axillary dissection. [Table 2].

The mean dose to the planned target volume (PTV) by mixed beam was 44 Gy (96%) with a mean dose of 42 Gy (91%) to the overlying skin for the whole study group. This was followed by a boost confined to the scar of mastectomy using 6 Mev for a dose of 4 Gy/2 fractions. In all cases with right breast disease (17 cases), the mean right lung tissue volume within the PTV was 220 ml (15%). It was relatively higher with the non-iscocentric technique, 281 ml (19%), compared to the isocentric technique 159 ml (10.5%). Also, in cases with left breast disease (5 cases), the mean left lung volume within the PTV was 175 ml (14%). Similarly, larger volume of the lung tissue was included with the non-isocentric technique, 197 ml (16%) compared to the isocentric technique 153 ml (12%). [Table 3].

The mean scattered doses to the rest of the lung tissue, the rest of the heart in left breast cases, and the contra-lateral breast for the whole study group were 2.8 Gy, 1.8 Gy, and 1.4 Gy respectively. It was comparable in both treatment arms. [Table 4].

Along the course of radiotherapy, the patients were weekly evaluated for treatment related acute toxicity and recorded according to the EORTC/RTOG grading system for radiation toxicity. The prescribed treatment was regularly administered for the whole study group without serious acute toxicity (grade 3 & 4). None of the cases developed any element of acute radiation related pneumonitis. [Table 5].

Once the treatment was completed, all the cases were kept under regular follow-up. Non of them showed evidence of loco-regional relapse. No serious delayed treatment related morbidities were recorded (grade 3 & 4). Grade 2 delayed skin changes was recorded in

	Iso-centric Technique (11 patients)	Non Iso - centric Technique (11 patients)	Total (22-patients)
Age			
➢ Median age	52	53	52
➢ Range	32-61	35-59	32-61
Menstrual Status			
Pre-menopausal	8 (73%)	7 (64%)	15 (68%)
Post-menopausal	3 (27%)	4 (36%)	7 (32%)
Site			
Right Breast	8 (73%)	9 (82%)	17 (77%)
Left Breast	3 (27%)	2 (18%)	5 (23%)
pT-stage			
pT_2	4 (36%)	3 (27%)	7 (32%)
pT_3	7 (64%)	8 (73%)	15 (68%)
pN-stage			
pN_0	1 (9%)	2 (18%)	3 (14%)
pN_1	8 (73%)	7 (64%)	15 (68%)
pN_2	2 (18%)	2 (18%)	4 (18%)

Table 1: Patients Characteristics

	Isocentric	Non-Isocentric	Total
Chest wall	11 (100%)	11 (100%)	22 (100%)
Supraclavicular fossa & axillary apex	6 (55%)	7 (64%)	13 (59%)

Table 2: Irradiated Targets

	Iso-centric Technique	Non Iso - centric	Total
Mean dose to target volume	44 Gy (96%)	44 Gy (96%)	44 Gy (96%)
Mean Dose to over laying skin	42 Gy (91%)	42 Gy (91%)	42 Gy (91%)
Mean Right CLD	2.2 cm	3.1 cm	2.7 cm
Mean right lung volume within primary beam	159 ml (10.5%)	281 ml (19%)	220 ml (15%)
Mean left CLD	2.5 cm	2.9 cm	2.7 cm
Mean Left lung volume within primary beam	153 ml (12%)	197 ml (16%)	175 ml (14%)

Table 3: Dose/Volume distribution within primary beam

	Iso-centric technique	Non-Isocentric Technique	Total
Mean scattered dose to lung	2.6 Gy (5.7%)	3.0 Gy (6.5%)	2.8 Gy (6%)
Mean scattered dose to heart (left side)	1.5 Gy (3.2%)	2.0 Gy (4.2%)	1.8 Gy (4%)
Mean scattered dose to contra lateral breast	1.2 Gy (2.5%)	1.6 Gy (3.5%)	1.4 Gy (3%)

Table 4: Scattered radiation

	Isocentric technique	Non-Isocentric technique	Total
Skin			
0	1 (9%)	-----	1 (4.5%)
1	8 (73%)	8 (73%)	16 (73%)
2	2 (18%)	3 (27%)	5 (22.5%)
Oesophagitis (Dysphagia)			
0	1 (9%)	2 (18%)	3 (14%)
1	6 (55%)	7 (64%)	16 (59%)
2	4 (36%)	2 (18%)	6 (27%)

Table 5: Treatment related acute reaction according to EORTC/RTOG Grading system

	Isocentric technique	Non- Isocentric technique	Total
Skin			
0	1 (9%)	-----	1 (5%)
1	6 (55%)	7 (64%)	13 (59%)
2	4 (36%)	4 (36%)	8 (36%)
Delayed pneumonitis			
0	8 (73%)	6 (55%)	14 (64%)
1	3 (27%)	3 (27%)	6 (27%)
2	---------	2 (18%)	2 (9 %)

Table 6: Treatment related delayed morbidity according to EORTC/RTOG Grading system

8 cases (36.5%). Delayed radiation induced pneumonitis was seen in 2 cases (9%), both received the chest wall radiotherapy with the non-isocentric technique. No clinically detected radiation induced delayed cardiomyopathy was recorded in this series [Table 6].

Discussion

Loco-regional failure (LRF) after mastectomy is a substantial clinical problem, despite the use of chemotherapy with or without tamoxifen. LRF is difficult to control, and causes much morbidity [(1)]. Also it may reduce patient's chance of cure. The Danish [2] and British Columbia [3] trials established strong support for the general principle that attaining maximal loco-regional control is necessary to achieve the best possible outcome in patients with positive axillary nodes treated with mastectomy and chemotherapy. In the Danish trial, radiotherapy reduced the odds of any recurrence or death by 41% on multivariate analysis. In the British Colombia trial the reduction in the relative risk of any recurrence at 15 years was 33%. The relative reductions in the risk of death from any cause in these two trials were 29% and 26% respectively.

The Eastern Cooperative Oncology Group[1] reviewed 2016 females with breast cancer, all received combination chemotherapy with or without tamoxifen, but without radiotherapy. A total of 1099 patients (55%) experienced disease recurrence. Isolated LRF in 254 cases (13%), LRF with simultaneous distant failure in 166 cases (18%) and distant metastasis only in 679 cases (34%). The risk of LRF with, or, without simultaneous distant failure at 10 years was 12.9% in patients with 1-3 positive axillary nodes and 28.7% for patients with ≥ 4 positive nodes. Multivariate analysis showed that increasing tumour size, negative estrogen receptor, also significantly increased the rate of LRF. They stressed the value of post-mastectomy radiotherapy (PMRT) in presence of these poor risk factors.

In a total of 1031 patients treated with mastectomy and doxorubicin – based chemotherapy without irradiation at the M.D Anderson Cancer Center [4], patients with tumour > 4cm or at least with 4 involved axillary nodes experienced LRF rates in excess of 20%. They stressed that they should have offered PMRT.

Consequently, the American Society of Clinical Oncology (ASCO) – guidelines for PMRT, included cases with ≥ 4 positive axillary nodes, patients with T_3 lesions, and those with operable stage III tumours. [10].

The chest wall is however the site at greatest risk of recurrence after mastectomy. Hence the treatment of the chest wall is mandatory whenever PMRT is indicated [5].

The chest wall is however a difficult location to irradiate. Firstly, it has a complex 3D shape and is located at the body-air interface, leading to rapid changes in the contour and tissue separation, together with much inter-patient variation. This can present problems in terms of beam obliquity and increased radiation build-up in the subcutaneous tissue. Secondly, the dose limiting organs at risk (lung and heart) are in close proximity. Finally, there is also the issue of inhomogeneities produced by the lungs, which have a lower electron density than muscle and fat leading to less attenuation of the primary beam and less scattered radiation contribution [6].

There is no universal agreement concerning the optimal chest wall irradiation so that the ASCO found insufficient evidence to recommend or suggest specific technique, total dose or fraction size [10].

For radiotherapy to be successful in attaining long-term local control, it is assumed that any tumour clonogens remaining after surgery must be eliminated. A 10% reduction in the prescribed dose leads to a reduction in tumour control probability from 95% to 85%.[6] Many techniques for chest wall irradiation were developed to achieve this inquiry. The most frequently used is the opposed tangential photon beams across the chest wall. Its major disadvantage is the beam divergence into the underlying lung tissue and pericardium. To overcome this drawback, we can use a machine with a half-beam block facility, or even a half beam with a custom block, or using asymmetric collimator jaw, or using isocentric technique with non-divergent posterior borders. It seems that the latter technique is the cheapest and easiest in set-up and delivers the lowest contralateral breast dose [11].

Although the use of a single stationary electron field lowers the dose to the underlying structures, it is less acceptable due to the expected dose in-homogeneity within the target volume. Combining both electrons and photons especially when using the isocentric technique can improve the dose homogeneity within the chest wall, and expected to maximally lower the associated morbidities to the overlying skin and underlying organs at risk [7].

In this study we had 22 females with invasive breast cancinoma, subjected to modified radical mastectomy who received PMRT. All cases received chest wall radiotherapy using mixed electrons – photon beam for total dose of 46 Gy. Half of the cases received their photon session by an isocentric technique. The mean dose to the chest wall was 44 Gy (96%). This followed by boost to the scar . The mean dose to the overlying skin was 42 Gy (91%). The mean lung tissue volumes included within the primary beam was 220ml (15%) and 175 ml (14%) when irradiating the right and left chest walls respectively. Relatively larger lung tissue volume was included within the primary beam, whenever we delivered the photons with non-isocentric technique. The mean scattered doses to the lung, heart and contralateral breast was minimal, 2.8 Gy, 1.8 Gy and 1.4 Gy respectively. These were comparable in both treatment arms.

No serious treatment related toxicities was observed during the course of treatment. Delayed grade 2 skin changes were seen in 8 cases (36.5%). While grade 2 delayed radiation induced pneumonitis was diagnosed in 2 cases (9%). All received their photon sessions with non-isocentric procedure.

Conclusion

This study clearly demonstrated the utility of mixed beams (electrons-photons) in irradiating the chest wall after mastectomy with the dose prescription we proposed. An adequate homogeneous dose level was delivered to the chest wall, with accepted dose to the overlying skin. The treatment was administered with accepted level of both acute and delayed treatment related morbidities. Whenever the photons were delivered by the isocentric technique described in this study, less lung tissue was included within the primary beam, with subsequent diminished morbidity.

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