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Original Research Article

Postmastectomy chest wall radiation of left-sided carcinoma breast - a dosimetric comparison between electrons and photons

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ABSTRACT

Background: For carcinoma breast patients requiring post mastectomy radiation therapy (PMRT), tangential photon beam (PB) is commonly used technique. The physical nature of electrons results in sharp dose fall off and reduces organs at risk (OAR) doses. Aim of the present study is to compare the coverage of chest wall and doses received by OARs – heart and lung between electron and photon beam plans in left sided breast cancer patients requiring PMRT.
Methods: This study was done in 22 left sided carcinoma breast patients treated at GSL Medical College between May to December 2017. Both tangential PB plans and electron beam (EB) plans were generated on simulation computed tomography (CT) for each patient and both plans were compared. A dose of 50 Gy was prescribed to planning target volume (PTV) in 25 fractions.
Results: The PB plans provided superior homogeneity index (HI) and conformity index CI compared to the EB plans ($p<0.05$). There was significant difference in favour of electron-beam plans for mean heart dose ($p=0.0312$), V25 Gy ($p=0.029$), V45 Gy ($p=0.001$) and V20 Gy of left lung ($p=0.042$). There was no significant difference in mean lung dose.
Conclusions: Dosimetric data from this study suggests that PMRT with the electron beam can reduce doses to the heart and left lung with acceptable target coverage. It needs further research in the clinical setting.

Keywords: Electron beam, Photon beam, Post mastectomy radiation therapy, Locally advanced breast carcinoma

INTRODUCTION

According to GLOBOCON 2020, breast cancer is the most commonly diagnosed cancer in women, with an expected 2.3 million new cases each year, accounting for 11.7 percent of all cancer cases and the primary cause of cancer death.[1]

Treatment of breast cancer involves multidisciplinary discussions which include surgery, chemotherapy, Radiation. In patients with locally advanced breast cancer (LABC) who have undergone modified radical mastectomy (MRM) and pathologically node positive, margin positive and T3-4 tumors,"postmastectomy radiation therapy" (PMRT) has become the standard. Based on the results from several large randomized trials and meta-analyses, PMRT reduced locoregional recurrence by 19%, resulting in a 9% reduction in mortality due to breast cancer.[2]

There are many techniques of PMRT. Depending on beam arrangements and beam characteristics, different techniques face different dosimetric problems. It is the decision of radiation oncologist to choose a particular radiation therapy technique such that the highest possible radiation dose is delivered to the target volume and negligible radiation to normal organs at risk (OAR). In many developing countries like India, cost of the treatment is also deciding factor in choosing a particular technique of radiotherapy.

The PMRT of the chest wall is commonly treated with two parallel opposed tangential beams. Part of the anterior thoracic cavity, as well as OARs, including the lung and heart and contralateral breast (in some patients) are included in the tangential beams. In left-sided breast cancers, heart is an additional organ at risk compared to right side breast cancers. It is important to decrease complications due to radiotherapy, as most breast cancer patients have long survival.

Radiation induced heart disease (RIHD) is a late effect of radiotherapy. The spectrum of RIHD includes cardiomyopathy, pericarditis, coronary artery disease, valvular heart disease and conduction system abnormalities and the severity ranges from mild to severe, and sometimes even leading to death.[3] There is wide range of incidence of each kind of RIHD among breast cancer patients, from 0.5% to 37%.[4]

Darby et al study concluded that exposure of heart to ionising radiotherapy increases the subsequent rate of ischemic heart disease. There was a linear increase in the rates of major coronary events with the mean cardiac dose by 7.4% per Gray (Gy) highlighting heart as an important OAR.[5] The relative incidence of RIHD was more in women who received radiation to the left side chest wall than compared to the right side. Women who have preexisting cardiac risk factors have greater absolute risk from radiotherapy than other women.[6]

Lungs are also a major OAR, because of the risk of radiation pneumonitis (RP) and radiation fibrosis.[7] RP is as early side effect of radiation which manifests 4 to 12 weeks post radiotherapy and is characterized by a chronic cough, fever, and infiltrates on chest X-ray. Whereas fibrosis is a late complication occurring 6 months after radiotherapy. The incidence of RP varies based on technique, fractionation, treatment portals, total dose, and use of photons/electrons from 14-40%.[8]

In a dosimetric study by Pierce et al comparing the common techniques in left sided PMRT, he stated that no single technique was found to be superior to another in terms of target coverage and optimal sparing of lung and heart.[9]

Two parallel opposed tangential photon beams (PB) and electrons beams (EB) are common and cost effective techniques for PMRT. Photons are non-particulate ionising radiation with no charge. Electrons are particulate ionising radiation with a negative charge. The particulate nature of electrons results in an abrupt dose fall off and shallow depth of penetration when compared to photons. Hence electrons are suitable to treat superficial targets. Modern linear accelerators are also equipped with electron applicators.

Hence we chose to do a dosimetric comparison of the above techniques of PMRT i.e. single enfaced EB and two parallel opposed tangential photons beams.

Aims and objectives

Aims and objectives include: to compare the coverage of chest wall and doses received by OARs – heart and lung between electron and PB plans in left sided breast cancer patients requiring PMRT.

METHODS

Present study is an observational study based on dosimetry comparing electrons with tangential PBs. This study was done on 22 left sided LABC who underwent MRM and PMRT at GSL Medical College between May to December 2017.

Inclusion criteria were all locally advanced carcinoma breast patients who underwent MRM with or without adjuvant chemotherapy and had indications for PMRT. Exclusion criteria were patients having right sided breast cancer or bilateral breast cancer, patients requiring re irradiation or patients with prior radiotherapy to thoracic region, or patients having secondary malignancies.

Study design

All participants were included in this study after obtaining informed consent. Patients were immobilized and simulation was done using computed tomography (CT) scan with 3 mm thick slices. The planning CT data were then transferred to a Monaco treatment planning system. Contouring of target volumes (chest wall, axilla, supraclavicular fossa) was done according to RTOG breast cancer atlas.[10] Normal tissues including the heart, lung, spinal cord, right breast, were contoured as OARs. Clinical target volume (CTV) and planning target volumes (PTV) were delineated on axial CT images following International commission on radiation units and measurements (ICRU) report numbers 50 and 62.[11]

In this dosimetric study, we have generated 2 plans for each patient (both PB and EB plans) in the treatment planning system using simulation CT of the respective patients and compared the two plans in terms of target volume coverage and doses to OARs.

Three-dimensional conformal radiation therapy plans were generated using 6MV medial and lateral tangential beams with paired wedges and 0.5 cm bolus, multileaf collimators were used to shape the beams (Figure 1a). Electron-beam plans were generated with a single anterior oblique beam of energies from 6-12 MeV and 0.5-1 cm bolus to ensure adequate coverage to PTV (Figure 1b). A dose of 50 Gy was prescribed to PTV in 2 Gy per fraction, 25 fractions.

The plans were evaluated with the help of dose volume histogram (DVH). Qualitative evaluation was done by slice-by-slice evaluation of the dose conformity, and all hot and cold spots. Adequate PB plans to the chest wall was defined as 95% of the planned volume receiving at least 95% of the prescribed dose. In EB planning, for PTV to be covered by the 90% isodose line, electron energy of 6-12 MeV was chosen according to the depth of the PTV. We have not included the SCF and axilla coverage in the analysis.

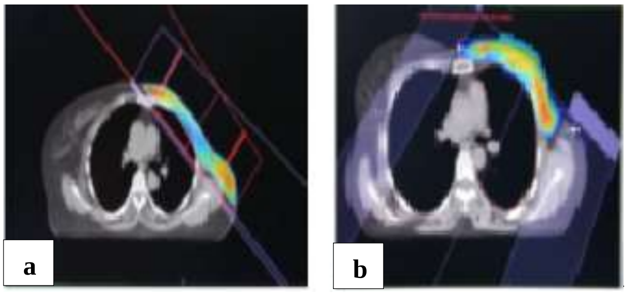

Figure 1: (a) 2 parallel opposed tangential photon beam arrangement for PMRT, and (b) single oblique electron beam arrangement for PMRT.

Dosimetric analysis

Target coverage was assessed by comparing the homogeneity index (HI) and conformity index (CI) of the plans.

HI was calculated using the formula [D2%-D98%]/D50%. Smaller HI values correspond to a more homogeneous dose distribution in the PTV. HI of zero corresponds to absolute homogeneity of dose.

CI is defined as the ratio of prescription isodose volume to PTV.

V_{RI}/TV (RI- reference isodose volume TV- treated volume). CI must be in between 1-2. CI of 0.9-1 and 2-2.5 indicates a minor violation.

OAR doses were evaluated by comparing the mean (D mean), as well as the dose-volume parameters such as V 20 Gy for lung and V 25 Gy, V 45 Gy for heart were also compared.

*V*20 Gy is percent volume of the lung receiving 20 Gy, *V*25 Gy is percent volume of the heart receiving 25 Gy; and *V*45 Gy is percent volume of the heart receiving 45 Gy.

Statistical analysis

Data was entered into Microsoft excel and analysed by IBM statistical package for the social sciences (SPSS) software version 20. Relevant statistical tests (t-test) were applied with considering p value <0.05 significant.

Ethical clearance

Institutional ethical committee clearance was obtained from GSL Medical College and General Hospital Rajahmundry, India.

RESULTS

The study was done in 22 left sided LABC who underwent MRM and PMRT at GSL Medical College between May to December 2017. 2 plans were generated (both PB and EB plans) in the treatment planning system using simulation CT of the respective patients and compared the two plans in terms of target volume coverage and doses to OARs.

Target coverage

The mean PTV (cc) for all patients was 583.28±198.42 (minimum 279.27 to maximum 974.7). As shown in Table 1 and Figures 2-4, the PTV coverage of PB plans was superior to that of EB plans. The PB plans provided superior CI (0.95±0.03), HI (1.11±0.05), and the difference mean between the groups was statistically significant (p<0.05).The difference in percentage volume of PTV receiving more than 95% of the prescribed dose (V95% of PTV=95.14±2.83) was also superior in the PB plan but was not found to be statistically significant (p>0.05).

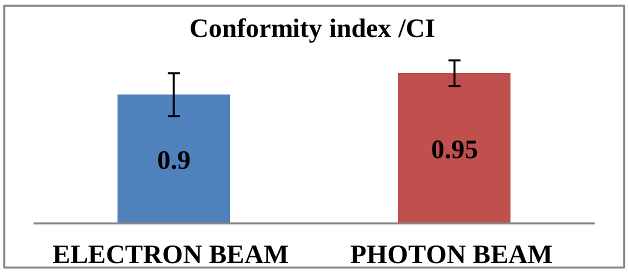

Figure 2: Conformity index (CI) of electron and photon beam plans.

Table 1: Target coverage comparison by electron and photon beams.

Index	Electron beam	Photon beam	P value
Conformity index	0.90±0.05	0.95±0.03	0.044
Homogeneity index	1.47±0.15	1.11±0.05	0.032
V 95% of PTV (Gy)	88.57±5.76	95.14±2.83	0.087
PTV (cc)	583.28+198.42		

In terms of lung dose, the PB plans had significantly more V20 Gy compared to the EB plans (p<0.05). D mean of the lung was more in the PB plans compared to EB plans but it was not found to be significant in lung dose (Table 2).

In terms of cardiac dose, the EB plans had significantly lesser D mean, V 25 Gy, and V 45 Gy compared to the PB plans (p<0.05). There was a significantly lesser mean contralateral breast dose (0.23±0.2) in EB plans (p<0.05) (Table 3).

Table 2: Doses to organs at risk – heart, lung and contralateral breast.

Volume	Index	Electron beam	Photon beam	P value
Lung	D mean (Gy)	15.22±8	16.26±3.24	0.24
	V 20 Gy	24.1±6.7	29.21±6.1	0.042
Heart	D mean (Gy)	4.4±2.9	9.3±4.8	0.0312
	V 25 Gy	9.4±5.4	19.4±22.8	0.029
	V 45 Gy	2.3±4.8	11.2±6	0.001
Contralateral breast	D mean (Gy)	0.23±0.2	2.12±0.75	0.0001

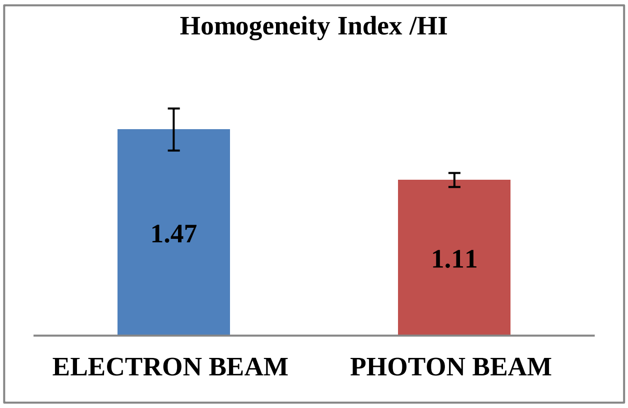

Figure 3: Homogeneity index (HI) of electron and photon beam plans.

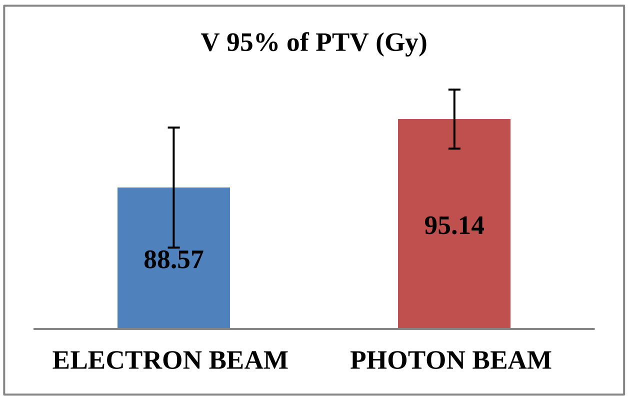

Figure 4: V 95% of PTV by electron and photon beam plans.

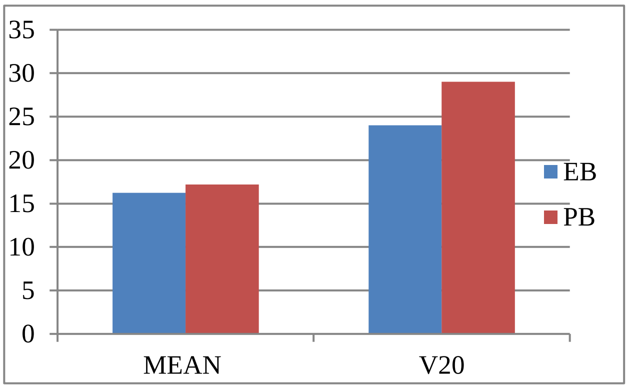

Figure 5: Mean and V20 of OAR-lung.

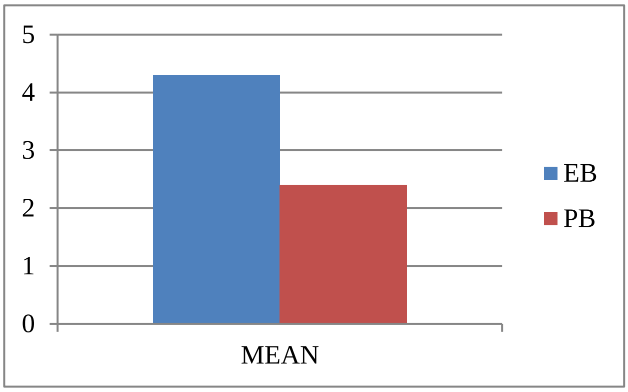

Figure 6: Mean dose to the OAR – heart.

DISCUSSION

The present study was a dosimetric analysis of two techniques of PMRT i.e. single enfaced EB and two parallel opposed tangential PBs. When CT based planning is used, it will be possible to assess and modify dose to target volume and also quantify and limit the amount of dose to OAR, which helps in predicting the risk of radiation toxicities.

Target coverage

In the present study, the PTV coverage of PB plans was superior in terms of both CI and HI when compared to EB plans. The difference in percentage volume of PTV receiving more than 95% of prescribed dose showed a trend towards significance for PB plans.

From physics point of view, EB is an attractive modality for irradiation of the chest wall as it is superficial, and require a limited depth dose, potential to decrease the dose to OARs- heart and ipsilateral lung compared with photon techniques.

The anatomy of the chest wall is a convex curvature, with varying depths across the target volumes, and irregular surface. This presents significant challenges in using EB. Mixed energy strips and customised bolus may increase the target coverage. But the multiple match lines are technically challenging and may lead to overdosed or underdosed regions.

Conformal radiotherapy with photons using multiple‑shaped fields, field in field technique, or with wedges for intensity modulation, yields good dose distributions in most of the patients.[12]

Electron-beam chest-wall irradiation in PMRT is as effective as photon-beam chest-wall irradiation in local and systemic control with disease-free and overall survival of 58% and 67% in 10 years and 50% and 55% in 20 years, respectively.[13]

Organs at risk

In the present study, there was no significant difference in mean lung dose by both the methods and there was a significant difference in favour of electron-beam plans for mean heart dose, V25 Gy of heart, V45 Gy of heart and V20 Gy of the left lung.

The risks of cardiac and pulmonary toxicities are highly dependent on technique of PMRT, field size and target volume sites. Appropriate risk estimate could aid radiation oncologist to decide the treatment field arrangements.

We have taken MLD and V20 of ipsilateral lung as predictor of radiation pneumonitis from the works done by Seppen-woolde et al and Graham et al.[14,15]

Ipsiateral lung V20<25% and MLD<15 Gy results in minimal or no RP. The risk of long term major cardiac complications linearly increased with mean heart dose and an estimated risk of 7.4% was found with every 1 Gy mean dose increment to the heart. And there was no significant cardiac complication if mean heart dose is <5 Gy.[5,16]

Hong et al reported a mean heart dose of 3.0 Gy±0.8 Gy, and V20 of 33.2±4.5% and V5 of 64.6±9.6% for ipsilateral lung when electrons were used for PMRT.[17]

Spierer et al treated 118 postmastectomy patients with CT-based EB therapy. They reported median heart V30 as 6.80% (range 1.29–22.98%) and ipsilateral lung V20 as 38.03% (range 21.68–59.55). In 64% of the patients, mixed energy EBs were used. 52 percent of the patients experienced RTOG grades 3 and 4 dermatitis.There were no rib fractures, brachial plexopathies, or symptoms of pneumonitis. The 5-year local control (LC) of 91% was reported in the study.[18]

In a similar study done by Vaiduriam et al, who compared electrons and tangential photons in PMRT reported that the doses to heart V30 were 1.4 percent and 5.7 percent (p=0.001) and D5 were 15.27 Gy and 31.76 Gy (p=0.001) was significantly reduced with electrons and there was appreciable chest wall coverage and no significant difference in V20 of the lung (26.5% and 24.7% (p=0.19).[19]

Ramgopal et al conducted another similar dosimetric study in 20 patients with left-sided breast cancer, comparing electrons to a standard tangential PB. V20 Gy of the left lung (p=0.001) and V45 Gy of the heart (p=0.017). There was no significant difference in mean cardiac dose (p=0.624) and V25 Gy (p=0.622). The difference in percent volume of PTVs receiving greater than 95% of the prescribed dose (p=0.077) trended towards significance.[20]

With 3D-conformal photon therapy techniques, mean cardiac dose varied from 4 Gy to 9 Gy. Techniques such as deep inspiration breath hold (DIBH), IMRT, VMAT, proton beam can be used to decrease heart and lung dose in adjuvant radiotherapy for breast cancer patients. Even with techniques like IMRT/VMAT, which can provide excellent target coverage and dose homogeneity, the mean heart dose is above 5 Gy. Proton therapy can achieve a heart mean dose of less than 1 Gy but it is very expensive and available in only a few centers.[21-24]

There was a significantly lesser mean contralateral breast dose (0.23 Gy±0.2) in EB plans (p<0.05) than in PB (2.12 Gy±0.75). The radiation dose received by the contralateral breast during PMRT is a concern because cancer induction may occur from low to moderate doses of radiation exposure.[25]

While the tangent beam photon plan and EB are simple and easy to deliver, many of the new techniques are complex, time consuming, difficult to implement in high volume centers. The resultant therapeutic advantage is often questioned as the associated long term radiation damage is a risk if not implemented properly.

CONCLUSION

Electron therapy cannot replace photons per se.

As per results from our study, electron-beam therapy reduced doses to the heart and lung significantly making it a preferred technique in left sided postmastectomy breast cancer patients. This may help oncologists tailor treatment for women who have long life expectation and who have pre-existing cardiac diseases.

However EB therapy has not gained much popularity due to limitations in applicator size, non-uniform dose distribution in target area due to convexity of chest wall and the tedious process of making customised bolus. And as this is a dosimetric study, there is a need for further research to evaluate the clinical benefit.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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