QUANTIFICATION OF CARDIAC DOSE FROM BREAST CANCER RADIOTHERAPY USING COMPUTED TOMOGRAPHY BASED DOSIMETRY METHOD

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ABSTRACT Aim: In breast cancer, chest wall and breast irradiation invariably result in some radiation exposure to the heart and coronary vessels, especially in left-sided disease. The purpose of this study is to quantify the dose received by the heart and the Left Anterior Descending artery in left-sided breast cancer patients treated in our institution. **Methods and Materials:** Patients with breast cancer who had undergone mastectomy or Breast Conservation Surgery and who had indications for post-operative radiotherapy were subjected to a fractionation schedule of 50Gy in 25 fractions to the chest wall or breast using Three Dimensional Conformal Radiotherapy. Dose Volume Histogram for the heart and the Left Anterior Descending artery were generated. **Results:** The average mean and maximum dose received by the heart was 14.12 Gy and 53.29 Gy, respectively. The average mean and maximum dose received by the Left Anterior Descending artery was 46.6 Gy and 52.5 Gy, respectively. **Findings:** The mean and maximum dose received by the heart and Left Anterior Descending artery are high in this study. This could be due to differences in target volume delineation and the higher percentage of mastectomy patients in our study. This study highlights the importance of delineating the heart and the Left Anterior Descending artery as organs at risk and the benefit of using cardiac sparing techniques for protecting the heart and coronary vessels.

KEYWORDS Breast Cancer, Radiation, Cardiotoxicity, Heart, LAD

Introduction

Breast cancer represents the most common female malignancy in both the developing and developed world and is the primary cause of death in women globally[1].

Radiotherapy plays an integral role in the management of breast cancer. The use of RT after mastectomy or lumpectomy has shown to improve local control, breast cancer-specific survival and overall survival[2]. Breast cancer is becoming an increasingly survivable disease with advances in diagnosis and treatment. Thus the focus has shifted to long term treatment-related toxicity. It has been postulated that the moderate protection offered by radiotherapy may be counterbalanced by a moderate increase in the risk of death. The 'Early Breast Cancer Trialists' Collaborative Group' reported excessive mortality from heart disease in patients receiving radiation therapy2. Cardiac mortality is reported to be higher in left-sided breast cancer patients than in right-sided breast cancer patients because higher cardiac radiation doses were delivered.

This study aims to assess the approximate radiation dose received by the heart and major coronary vessels in left-sided breast cancer patients treated with chest wall irradiation in our institute so that the likely cardiac morbidity and mortality for these patients may be predicted by comparing with the doses received by patients irradiated in the trials mentioned above for which the risks are known in patients with left-sided breast cancer [3].

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Aims and objectives

To quantify the radiation dose received by the heart and the left anterior descending artery in left-sided breast cancer radiation.

To determine whether there is a correlation between the type of surgery and the dose received by the Heart and the Left anterior descending artery.

Materials and Methods

Study population

Patients with Carcinoma Left Breast registered in the Department of Radiotherapy, Government Medical College Hospital, Kozhikode, from January 2014 to July 2015 who had undergone either breast-conserving surgery or mastectomy and who had indications for post-operative radiotherapy. This study was conducted after obtaining ethical clearance from the Institutional Ethical Committee. Patients were enrolled after obtaining written informed consent. All patients were treated with a tumour dose of 50Gy to the isocenter in 25 fractions, five days per week. The dose distribution was calculated with full three dimensional CT density information, including lung correction, using the Anisotropic Analytical Algorithm (AAA).

Simulation

The patient was placed in the supine position with both the arms flexed and abducted to more than 90 degrees. Both hands were made to hold the handgrip placed on the board above the head. The arms were held in position by arm supports attached to the board, and the head was turned to the right. A headrest and a hip rest were also used to aid in patient reproducibility.

Target delineation

The tangential field borders were determined clinically and marked by radio-opaque wires. The medial border was 1cm from the mid-line or the medial end of the mastectomy scar. The superior border was at the caudal border of the clavicular head. The inferior border was 1 cm below the inframammary fold, and the lateral border was at the mid-axillary line. A contrast-enhanced CT scan was taken with the patient in the treatment position from the level of the C6 vertebra to below the level of the diaphragm. The chest wall or breast CTV, the regional lymphatics and the supraclavicular field (when indicated) were contoured according to the RTOG guidelines, and the reference radio-opaque wires placed. The organs at risk assessed were the heart and the Left Anterior Descending Artery (LAD). The heart and the LAD were contoured with the aid of a heart contouring atlas, "Development and Validation of a Heart Atlas to study Cardiac exposure to Radiation following treatment for Breast Cancer"[4]. For each treatment plan, dose-volume histograms (DVHs) for the heart and the LAD were generated with a 1-cm radial margin. The superior limit of the heart included the right and left atria and excluded the pulmonary trunk, ascending aorta, and superior vena cava. The caudal border of the myocardium was taken as the inferior limit of the heart. Because of its short length, the left main coronary artery was assessed with the LAD artery. The location of the LAD artery was also identified using the course of the anterior interventricular groove. A radial margin of 1 cm was added to the left anterior descending artery contour to allow for uncertainty in the identification of arterial position, respiratory movement and the beating movement of the heart. For each organ at risk, the mean and maximum dose was assessed for each patient. For each of these quantities, the average value over all assessed patients (referred to as "average mean" or "average maximum") was calculated together with its standard deviation (SD). (Figure 1)

Treatment planning

Computerised Tomography data was exported to a computerised treatment planning system (Eclipse, Version11). Beam weights and wedges were optimised based on the dose distribution for the central axis plane. All patients were planned with either 6MV or 15MV photons. Field borders were not modified to reduce or avoid cardiac irradiation, and cardiac shielding was not used. All patients were treated with a tumour dose of 50Gy to the isocenter in 25 fractions, five days per week. The dose distribution was calculated with three dimensional CT density information, including lung correction using the AAA. (Figure 2)

Statistical analysis

Data were entered in Microsoft Excel & analysis was done using the SPSS version 20.0 software and analysed with the help of descriptive statistics such as mean, standard deviation, percentage and statistical tests such as Independent T-test were applied appropriately.

Results

Twenty-seven patients had participated in our study, with the mean age being 47.6 years. Ten patients (37%) in our study presented with locally advanced disease. These patients had to undergo neoadjuvant chemotherapy before surgery. The majority of the patients in our study (66.6%) had T2 disease. Only four patients (15%) had negative nodes on axillary staging. The majority of the patients (55%) had N1 disease. Only four patients (15%) had undergone breast-conserving surgery (BCS), while 23 patients (85%) had undergone mastectomy (MRM).

Quantification of Radiation Dose to the heart and the LAD:

The average mean dose received by the heart was found to be 1401.4 Gy (SD 434.8) which accounted for 28% of the total dose. A correlation was found between the mean dose received by the heart and the type of surgery. The average mean dose received by the heart in patients who had undergone mastectomy was 1484.3cGy (SD 383.6), and in BCS patients were 869.4 cGy (SD 288.2). The average mean dose received by the heart was higher in mastectomy patients when compared to BCS patients. The correlation was statistically significant. ($p=0.005$) (Bar Graph 1) The average maximum dose received by the heart in our study was 5334.2cGy (154) which accounted for 106% of the total dose. The mean percentage of the heart volume in the treatment field was found to be 24%. A correlation was found between the percentage of heart volume in the field and the type of surgery. The mean percentage of heart volume in the treatment field was 25.8% for mastectomy patients, while that for BCS patients was 13.7%. So the volume of the heart receiving more than 25 Gy was higher for mastectomy patients than in BCS patients, and this correlation was found to be statistically significant ($p=0.009$). The average mean dose received by the LAD was 4629 cGy (SD 591.7) which accounted for 93% of the total dose.

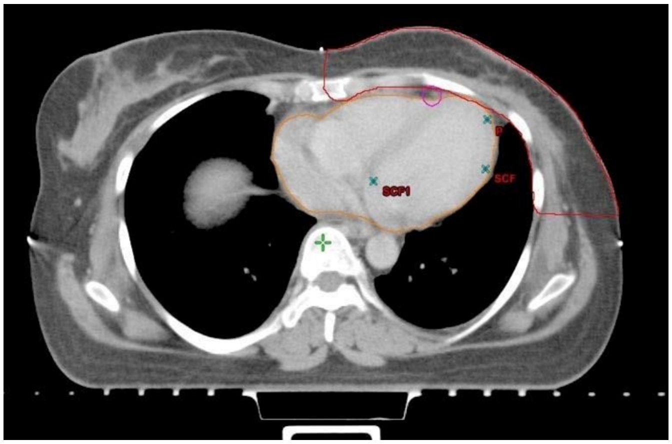


Figure 1: Contour of CTV and organs at risk.

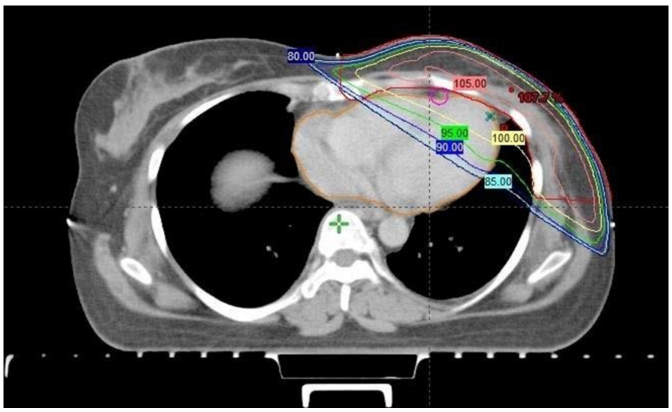


Figure 2: 3DCRT plan.

A correlation was also found between the mean dose to the LAD and the type of surgery. The average mean dose received by the LAD in mastectomy patients was 4814cGy (SD 322), and in BCS patients were 3560cGy (SD 699.6). The mean LAD doses were more significant for patients who have undergone mastectomy when compared to breast-conserving surgery, and this correlation was statistically significant (p<0.001). (Bar Graph 2)

The average maximum dose received by the LAD was 5242 cGy (SD 188.1) which accounted for 105% of the total dose. The average percentage of the volume of the LAD in the treatment field (that is, receiving more than 25 Gy) was 91.7% (11.8). A correlation was also found between the volume of the LAD in the treatment field and the type of surgery. The average percentage of LAD volumes in mastectomy patients was 95.1%, and for BCS patients were 72.5%. Greater volumes of LAD was in the treatment field for mastectomy patients when compared to BCS patients, and this difference was found to be statistically significant (p=0<0.001).

Discussion

Radiotherapy has played an important role in preventing breast cancer deaths while increasing the risk of cardiovascular mortality. Radiation-induced heart disease, the most common being pericarditis, started becoming a significant problem when large volumes of the heart were exposed to >40Gy[5]. Another manifestation was cardiomyopathy [5-7]. Late manifestation of radiation-induced heart disease includes an unexpectedly high incidence of ischemic heart disease[8,9]. Left-sided breast cancer

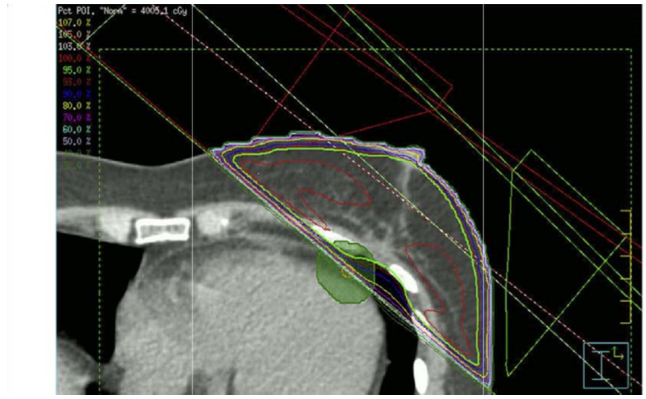


Figure 3: The Contour CTV image for the study by Bartlett et al, 2010 [13].

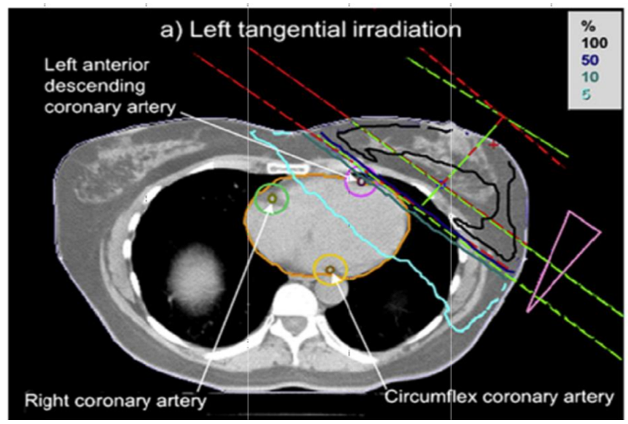


Figure 4: Contour for CTV, heart and the LAD in the Taylor et al study, 2006 [12].

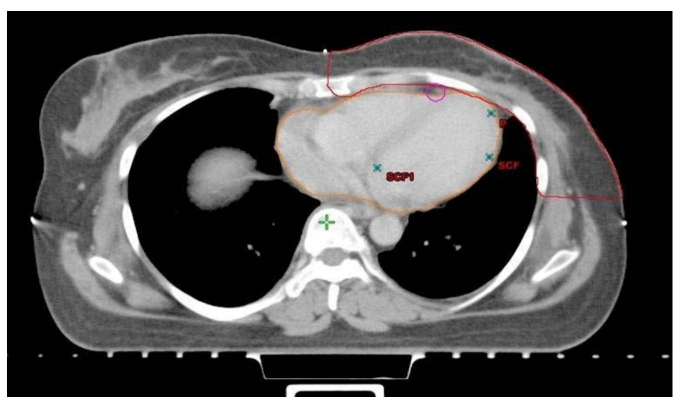


Figure 5: Contouring image of a mastectomy patient in our study.

Table 1 Comparison of Mean Dose received by the Heart in different studies.

Study	Mean Dose received by the heart
1970s[11]	13.3Gy
1990s[11]	4.7 Gy
2006[12]	2.3 Gy
2010[13]	0.8 Gy
Present Study	14.12 Gy

Table 2 Comparison of Mean Dose received by the LAD in different studies

Study	Mean Dose received by the LAD
1970s[11]	31.8 Gy
1990s[11]	21.9 Gy
2006[12]	7.6 Gy
2010[13]	6.7 Gy
Present Study	46.2 Gy

Table 3 Comparison of the maximum dose received by the LAD in different studies

Study	Maximum LAD dose
1970s[11]	52 Gy
1990s[11]	51.5 Gy
2006[12]	35.2 Gy
2010[13]	40.3 Gy
Present Study	52.5 Gy

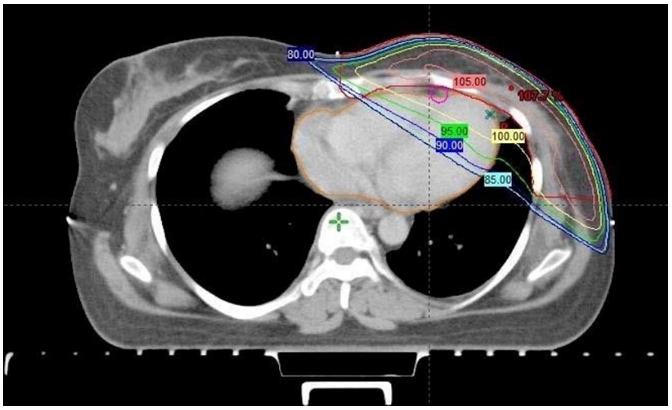
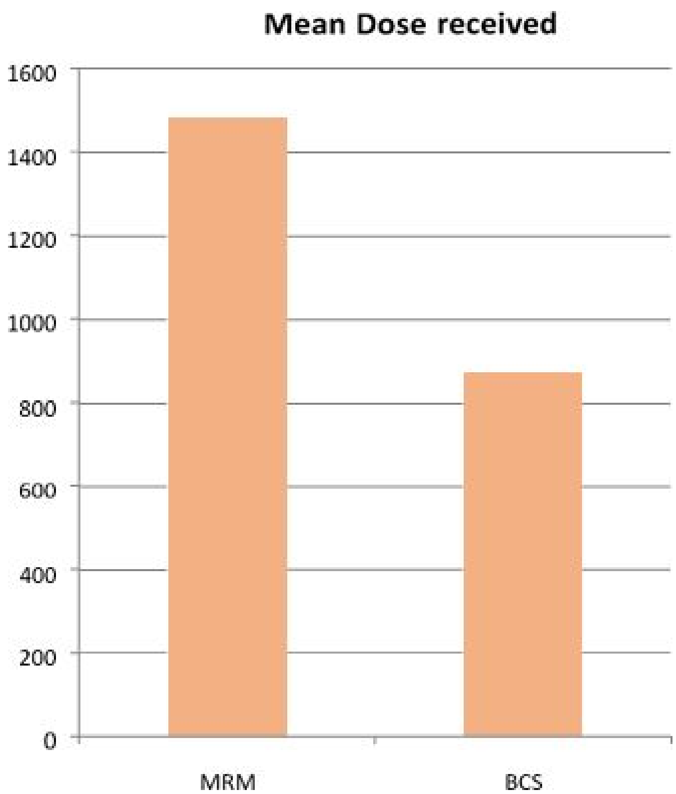
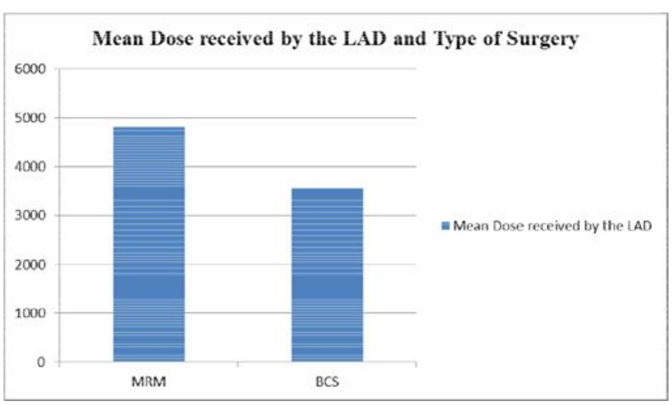


Figure 6: Treatment Plan for the same patient.



Graph 1: Mean dose received by the heart for MRM patients versus BCS patients.



Graph 2: Mean dose received by the LAD for MRM patients versus BCS patients.

has been associated with higher mortality due to ischemic heart disease than the right [10]. A population-based case-control study of major coronary events in women who underwent radiation for breast cancer showed that the major coronary events increased linearly with mean dose to heart by 7.4% per grey with no apparent threshold [10].

In our study, the average mean dose received by the heart was found to be 1401.4 Gy (SD 434.8) which accounted for 28% of the total dose. This was high when compared to western data. (Table 1) A correlation was found between mean dose received by the heart, percentage of heart in the field, and type of surgery. These were higher in mastectomy patients when compared to BCS patients, and the correlation was statistically significant. The average mean dose received by the LAD was 4629 cGy (SD 591.7) which accounted for 93% of the total dose. This value was also found to be high when compared to available data. (Table 2)

An association was also found between the mean dose to the LAD and the type of surgery. The mean LAD doses were greater for patients who have undergone mastectomy (4814cGy) when compared to breast-conserving surgery (3560cGy), and this correlation was found to be statistically significant ($p<0.001$). This was also seen in a study by Bartlett et al. in which he found that the mean LAD NTDmean and LADmax in Gray were significantly greater for patients who underwent mastectomy: 5.9 (SD 3.6) versus 8.7 (SD 5.3), $p=0.004$ and 38.2 (SD 11.3) versus 45.5(SD 3.6), $p<0.01$ [13]. The average maximum dose received by the LAD was 5242 cGy (SD 188.1) which accounted for 105% of the total dose. (Table 3) The average percentage of the volume of the LAD in the treatment field (that is, receiving more than 25 Gy) was 91.7% (11.8). In the Taylor et al. study, the volume of the LAD in the treatment field was 13%. Greater volumes of LAD was in the treatment field for mastectomy patients (95.1%) when compared to BCS patients (72.5%), and this difference was found to be statistically significant ($p=0<0.001$).

In this single-institution study, the mean radiation dose to the heart and the LAD, the maximum dose to the heart, and the LAD were high when compared to similar studies conducted in the West. The volume of the heart and the LAD in the treatment field were also found to be higher.

The probable reasons why the heart and the LAD received a high dose in our study could be due to a higher percentage of mastectomy patients in our study when compared to Western data, where they studied more BCS patients. It has already been shown that mastectomy patients received more radiation dose than BCS patients.

Another reason for the difference may be due to differences in target volume delineation. We had taken the medial end of the CTV to be the medial end of the mastectomy scar, which extended up to the midline in most patients. Also, the field borders were not modified to reduce the cardiac dose. The lateral border was taken as the midaxillary line as recommended by the RTOG guidelines.

In the studies available in the literature, the contoured images show that the medial and the lateral borders of the CTV did not reach up to the recommended anatomical landmarks. So the heart and the LAD were almost outside the field. This may explain the wide disparity seen between the present study and Western data. (Figure 3-6)

Conclusion

This study highlights the importance of contouring the heart and the LAD as organs at risk in breast cancer radiation, especially in left-sided disease and the importance of adopting cardiac sparing techniques. A more planned surgery limiting the medial and lateral extent of the mastectomy scar might prevent larger fields from being included in the CTV, which in turn may reduce the radiation dose to the heart and the LAD. The choice of breast conservation surgery may be encouraged as the preferred option in patients in whom there is no contraindication, so that the radiation dose received by the heart and the LAD may be reduced. This study is limited by the small number of patients studied and the smaller proportion of BCS patients.

Abbreviation

- AAA: Anisotropic Analytical Algorithm
- BCS: Breast Conservation Surgery
- CTV: Clinical Target Volume
- LAD: Left Anterior Descending Artery
- MRM: Modified Radical Mastectomy

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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