

Assessing the Effect of Surgical Procedure on Radiotherapy Dose to Lung in Breast Carcinomas

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ABSTRACT

Objective: To investigate the effect of surgical procedure, mastectomy versus breast conservation surgery (BCS) on radiotherapy dose to the lung, in patients of breast cancer treated with adjuvant radiotherapy (RT).

Study Design: Retrospective longitudinal study.

Place and Duration of Study: Combined Military Hospital Rawalpindi, Pakistan over a period of 8 months, on patients treated between Jan 2023 - Aug 2023.

Methodology: A total of 103 female breast cancer patients receiving an equivalent of 50 Gray in 25 fractions or more (upto 16 gray in 8 fractions or equivalent) of adjuvant radiotherapy to breast after breast conservation surgery (BCS) or chest wall (after mastectomy) were studied. All received field in field intensity modulated radiotherapy (IMRT) with tangential beams. Their lung doses were estimated by measuring the central lung distance (CLD), as a surrogate to volumetric lung dose. Data was analyzed by SPSS version 22. Pearson correlation was checked. Mean CLD between the two surgical groups was compared.

Results: Of total 103 patients, 72(69.9%) had modified radical mastectomy (MRM) and 31(30.1%) had breast conservation surgery (BCS). Surgical procedure mastectomy versus breast conservation surgery has a significant correlation with CLD ($r = -0.27$, p -value 0.005). Mean CLD after MRM was 2.71 ± 0.63 cm and after BCS was 2.34 ± 0.49 cm with a statistically significant difference (p -value - 0.005).

Conclusion: Breast conservation surgery (BCS) not only spares the organ but also reduces the radiation toxicity due to lower effective doses to the underlying lung, leading to decreased side effects. All cases where BCS is possible, mastectomy should be avoided.

Keywords: Breast-conserving therapy, Breast radiotherapy. Mastectomy, Lung radiation dose, organ at risk doses.

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INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy among the female and second leading cause of death.¹ Surgery is the basic treatment of breast cancers and is done in all breast cancer cases if possible.² Either breast conservation with wide local excision of primary tumor (called breast conservation surgery - BCS) is considered or mastectomy, depending upon site, size, number of lesions, age, possibility of adjuvant radiation, cosmesis after surgery. Treatment of breast cancer usually includes radiotherapy to either breast or chest wall, mostly given after surgery (adjuvant settings).³ After mastectomy radiation is not given to some low-risk cases like if the size is less than 5 cm, but after BCS, all cases receive radiation to reduce the risk of local recurrence. Nodal irradiation is done in addition to primary site irradiation in high-risk patients for nodal relapse.⁴ Radiation to breast or mastectomy bed is usually given by medial and lateral tangent beams.

Dose inhomogeneity is corrected by field in field intensity modulated radiotherapy (IMRT).⁵ There is always some portion of ipsilateral lung, irradiated in the field which leads to acute, sub-acute or late toxicity of lung. Lung volume irradiated can be estimated by central lung distance (CLD), measured at beam center.⁶ CLD is surrogate of lung volume irradiated.⁷ There should be different volume of lung irradiated after mastectomy versus after breast conservation surgery. This may be due to pendulous nature of breast, heavy breasts, over/under contouring of breast tissue in intact breast, closeness of target volume to lung after mastectomy, and thinking fat as breast tissue in fatty patients.⁸ These factors may lead to increased volume of lung (organ at risk - OAR) irradiated, increased lung radiation dose and hence increased early and delayed lung toxicity.⁹

The rationale of this study is to find out the surgical group with increased lung toxicity. Although surgical techniques are standard but percentage of surgical procedure leading to less radiation to lung, can be increased, and radiotherapy techniques can be modified in the increased lung dose group. This study

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will lead to further research on the topic and to find out reasons of increased lung dose in a particular group of patients. This will also help to search for further strategies to reduce the lung dose and mitigate the side effects of radiotherapy.

METHODOLOGY

It was a retrospective longitudinal study which included patients having invasive breast cancers and given radiotherapy at Department of radiation oncology of Combined Military Hospital (CMH) Rawalpindi, Pakistan. This study was performed between Sep 2023 to Dec 2023, on patients treated between January 2023 to Aug 2023. Institutional review board permission was obtained (via reference number 440 of CMH Rawalpindi). This study included a total of 103 patients. The sample size was calculated by online calculator by select statistics of United Kingdom where the power of study was kept at 80%, alpha value was taken at 5%. Estimated difference in means in CLD between the two surgical procedures was 12.4 mm.¹⁰ Calculated sample size was 103. Written informed consent was gotten from all the partakers of the study. Short history was taken before enrollment into study.

Inclusion Criteria: Female patients, between 20 to 80 years of age, having diagnosed invasive breast cancer and undergone radiotherapy to chest wall or breast, to an equivalent of 50 Gray (Gy) in 25 fractions (Fx) or more. Most of the patients received 40 Gy in 15 Fx protocol. All patients received intensity modulated radiotherapy with tangential beams by field in field technique were included.

Exclusion Criteria: All patients with age <20 years or >80 years were excluded. We also excluded patients receiving <50 Gy or equivalent dose. Patients planned by volumetric arc therapy (VMAT) were also excluded. Males were not included.

Radiotherapy treatment plans of 103 consecutive breast cancer patients, on our treatment planning system, were assessed and central lung distance (CLD) on 95% isodose line for two groups of surgical procedure carried out (mastectomy versus breast conservation surgery) was calculated and recorded. Statistical analysis was made using statistical package for social sciences (SPSS) version 22. Frequencies were calculated for categorical variables like type of surgical procedure used. Mean and standard deviation was calculated for numerical variables like central lung distance. The CLD amongst radiotherapy plans of post mastectomy patients with CLD after breast

conservation surgery was compared by applying independent sample t-test for comparison of their means. Pearson’s correlation coefficient (r) was used to find the correlation between CLD of mastectomy and BCS. The p-value below 0.05 was to be considered as significant.

RESULTS

A total number of 103 patients were analyzed. All participants were females. Out of total 103 patients, 72(69.9%) had mastectomy and 31(30.1%) had breast conservation surgery (Figure).



Figure: Distribution of Patients by Surgical Procedure =103)

Data of surgical procedure was uniformly distributed. Mean CLD for all patients was 2.61±0.63. Correlation between CLD of different types of surgical procedures was carried out. Pearson’s correlation coefficient (r) was -0.27 with a p-value of 0.005 indicating a strong correlation between CLD of mastectomy and BCS. Means of the CLD after modified radical mastectomy (MRM) was compared with CLD after breast conserving surgery (BCS) by applying independent sample t-test. Mean CLD after MRM was 2.71±0.63 and after BCS was 2.34±0.56 with a p-value of 0.005 showing a statistically significant difference, as summarized in Table.

Table: Study Parameters Comparing Means of Central Lung Distance as per surgical procedure (n=103)

Parameter	Group-1 MRM (n=72)	Group-2 BCS (n=31)	p-value
Mean CLD (cm)	2.71±0.63	2.34±0.56	0.005

MRM: Modified Radical Mastectomy BCS: Breast Conservation Surgery

DISCUSSION

Breast conservation rate in our population was 30.1% of patients. BCS rates are increasing in the world and hence in Pakistan as well. For example, in

New Zealand between 2000 to 2014 only 14.4% had BCS. There was no significant statistical difference in BCS group and surgery group in terms of overall survival (OS) or invasive disease-free survival (iDFS).¹¹ This led to increasing confidence in the procedure and the rate of BCS in New Zealand increased to 55.3 % for invasive breast cancer in 2018–2019.¹² Few patients of mastectomy group may not require adjuvant radiotherapy, so mastectomy number may be a little higher and underestimated.

BCS rates are also increasing in Pakistan. A study conducted in Peshawar (Pakistan) from January 2015 to December 2021, had 33.3% BCS rate,¹³ which is almost similar to our study (30.1%). Another study is planned in Peshawar (Pakistan) for BCS versus mastectomy in developing countries.¹⁴ The increase in BCS rates is due to increase in the breast cancer awareness campaigns, early acquiring the treatment, improved diagnostic facilities, higher confidence in BCS with longer experience of surgeons, increasing health awareness amongst masses, increased awareness in general practitioners and social media impact. Other factors leading to increased BCS rates in Pakistan include easy availability of specialists in private clinics, if someone has money, even poor can go to the radiologists, surgeons and oncologists working in public sector hospitals easily without appointment, increasing trust of surgeons in breast conservation and increasing number of radiation machines.

Recently, oncoplastic breast surgery is being adopted in Pakistan. For all eligible patients for breast conservation, between 2016-2021 at two leading cancer centers in Karachi routine BCS rate was 42.4% and 57.4 percent had oncoplastic surgery,¹⁵ so cosmesis is also being looked after now. The breast surgeons are getting training in oncoplasty and plastic surgeons are also doing oncoplastic surgeries. Number of trained breast surgeons is increasing with introduction of fellowship in breast surgery by College of Physicians and surgeon (CPSP) in Pakistan. So BCS rate is expected to increase in coming years in our setups.

Several studies have stated that the CLD is an unsurpassed indicator of ipsilateral irradiated lung volume during two-field tangential breast radiotherapy.¹⁶ For example, a trial showed on univariate linear regression that CLD ($B=0.28$, $p=0.008$) was one of the influencing factors of lung volume irradiated (V20). Similarly, CLD ($B=0.28$, $p=0.018$) attained a significant statistical difference in

left sided lung dose, on the multiple linear regression.¹⁷ This study has used CLD as an indicator to lung doses.

In our study, mean CLD after MRM was 2.71 (SD=0.63) and after BCS was 2.34 (SD=0.49). So CLD after mastectomy was higher in our study, meaning that higher volume of lung is irradiated after mastectomy as compared to the intact breast. It may be due to the shape of radiation target volume and proximity of target volume to the lung. Post BCS, target volume is breast tissue, which is away from lung but post mastectomy, the target volume is chest wall which is encasing the lung in a horseshoe shape and is just adjacent to the lung. A study conducted by Fadavi *et al.*, in 2022 showed mean lung dose in BCS group was 0.314 gray versus 0.414 gray in MRM group which is in line with the results in our study, where CLD was higher in mastectomy group.⁸

The radiation dose to lung is crucial because chance of secondary cancer to the lung ($p=0.0007$) and contralateral breast ($p=0.002$) is also higher in women receiving radiation therapy to the contralateral breast, that's why we contour contralateral breast and try to decrease its radiation dose. Similarly, there was a higher incidence of mortality from non-breast cancer causes like heart diseases and lung ailments, which are the long-term side effects of radiotherapy.¹⁸⁻¹⁹ Reducing the radiation dose to lung has long term survival implications,²⁰⁻²¹ for the patient, suggesting the significance of our study.

CONCLUSIONS

Surgical procedure of breast can affect the dose of radiotherapy to the underlying lung. Mastectomy leads to higher dose, because after mastectomy target volume is just the remaining chest wall which is encircling the lung.

LIMITATIONS OF STUDY

This study was done on a lesser sample size and at a single institution. Multicentric studies on treatment planning systems from different institutions and more number of patients are proposed.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MSN & UA: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZAA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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