

Assessing the Effect of Tumour Laterality on Lung Dose in Breast Cancer Radiotherapy

Muhammad Sohaib Nadeem, Sameed Hussain, Amjad Khan, Ujala Ali*, Noman Sadiq**

Department of Radiation Oncology, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan, *Department of Physiology, Army Medical College/National University of Medical Sciences (NUMS), Rawalpindi Pakistan, **Department of Physiology, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To explore the effects of laterality of breast cancer upon the irradiated lung dose.

Study Design: Retrospective observational study.

Place and Duration of Study: Tertiary care hospital Pakistan on patients treated between Jan to Jul 2023.

Methodology: The records of a total of 103 patients of breast cancers treated with curative intent radiotherapy were analysed. All had received an equivalent of 50 grays in 25 fractions or more of radiotherapy. The volume of lung irradiated in 95% isodose line was determined by central lung distance (CLD) and effect of laterality of tumour was seen on lung dose. The effect of presence of heart and its effect on potential reduction in lung dose in left sided breast cancer was determined and compared with the respective doses in right sided breast cancers.

Results: Among 103 patients, 57(45.3%) patients were having right sided breast cancer and 46(44.7%) were having left sided breast cancer. Mean CLD on right was 2.83 ± 0.63 cm and on left side was 2.32 ± 0.51 with a p -value of <0.001 .

Conclusion: In appropriately planned Intensity modulated radiotherapy (IMRT) of breast, presence of heart leads to cautious planning on left side and decreased ipsilateral lung doses, as compared with right sided tumours, so if similar cautious approach is used in right sided breast IMRT, dose and toxicity of right lung be decreased.

Keywords: Adjuvant Radiotherapy, Breast Cancer, Lung Toxicity, Tolerance Doses.

How to Cite This Article: Nadeem MS, Hussain S, Khan A, Ali U, Sadiq N. Assessing the Effect of Tumour Laterality on Lung Dose in Breast Cancer Radiotherapy. *Pak Armed Forces Med J* 2026; 76(5): 646-650. DOI: <https://doi.org/10.51253/pafmj.v76i5.11750>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Breast cancers accounting for 24.5% of all cancer cases in world and 28.7% in Pakistan. **Error! Reference source not found.**¹ Breast or chest wall radiotherapy can cause acute and late toxicities including lung toxicity.² Deep inspiratory breath hold (DIBH) is used to spare the heart, but it can lead to altered lung radiotherapy doses.³ Lung toxicity can be predicted by amount of lung volume irradiated or present in the treatment field. Most common field arrangements are tangential beams. Tangents can be medial or lateral tangents with intensity modulated radiotherapy (IMRT) by field in field technique. Total volume of lung radiated includes the portion of lung present in anterior supraclavicular beam as well.

We aimed to estimate the volume of lung in tangents alone with superior border at the level of lower medial end of clavicle. Central Lung Distance (CLD) is good surrogate of lung volume irradiated in tangents and is under use for very long time. It is the "perpendicular distance measured at the centre of the field, from the posterior part of the anterior chest wall to the posterior tangential field edge". While planning IMRT other very important organ at risk (OAR) is

heart.^{4,5} As radiotherapy to the heart can increase the risk of coronary artery disease,^{6,7} many methods have been devised to lessen the dose to the heart. The most used technique is DIBH.⁸⁻¹⁰ To determine the potential reduction in lung dose due to the effect of cardiac dose volume constraints in left sided radiotherapy, the plans of left sided breast carcinomas with those of right sided breast carcinomas were compared.

The purpose of this study was to evaluate the impact of laterality on lung volume irradiated, and if it is less on left side due to overcautious behaviour in treatment planning because of presence of heart, then suggest this cautious behaviour while planning the radiation of right side as well. This study was conducted to investigate the effect of laterality of breast cancer on the irradiated ipsilateral lung dose.

METHODOLOGY

It was a retrospective observational study including patients having breast cancers and given radiotherapy at Department of radiation oncology at a tertiary care Hospital. This study was performed in Aug 2023, on patients treated between January 2023 to 31 Jul 2023. Ethical review committee (ERC) / Institutional review board permission was sought (vide reference number 441) of the tertiary care hospital. This study included a total of 103 patients.

Correspondence: Dr Muhammad Sohaib Nadeem, Department of Radiation Oncology, Combined Military Hospital, Rawalpindi Pakistan
Received: 05 Mar 2024; revision received: 25 Sep 2024; accepted: 30 Dec 2024

The sample size was calculated by using WHO sample size calculator where the power of study was kept at 90%, alpha value was taken at 1%. Estimated difference in means was 12.4 “The ipsilateral lung V20 Gy reduced from 45.3 +/- 13.3% to 32.9”.¹¹ Calculated sample size was 66. We included a greater number of patients to improve study accuracy. Informed consent was attained from all the partakers of the study. A short history was taken prior to enrolment of the patients into the study.

Inclusion Criteria: We included the records of only female patients, between 20 to 80 years of age, having diagnosed breast cancer or ductal carcinoma in situ (DCIS), and undergone radiotherapy to chest wall or breast, to an equivalent of 50 Gray (Gy) in 25 fractions (Fx) or more. The most used dose fractionation was 40 Gy in 15 fractions. All patients received intensity modulated radiotherapy (IMRT) with tangential beams by field in field technique.

Exclusion Criteria: Records of 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.

The treatment plans for radiotherapy were assessed and CLD on 95% isodose line was calculated. Central Lung Distance (CLD) was the perpendicular distance measured at the centre of the radiation tangential field, from the posterior part of the anterior chest wall to its posterior field edge. Laterality (right sided versus left sided) was noted and CLD in each case was recorded. Statistical analysis was made using Statistical package for Social Sciences version 22.0. Frequencies were calculated for categorical variables like laterality. Mean and standard deviation was calculated for numerical variables. The difference in CLD in right sided cancers and left sided cancers was then analysed and ANOVA test was applied to determine the statistical significance in the difference of means. A *p*-value below and equal to 0.05 was considered as significant.

RESULTS

A total number of 103 patients undergoing radiation to chest wall or breast were analysed. All the patients were females. Out of total 103 patients, 57(55.3%) of the patients were having right sided breast cancer and 46(44.7%) were having left sided breast cancer (Figure-1).

Figure-2 shows that CLD had a normal distribution, so parametric tests were applied.

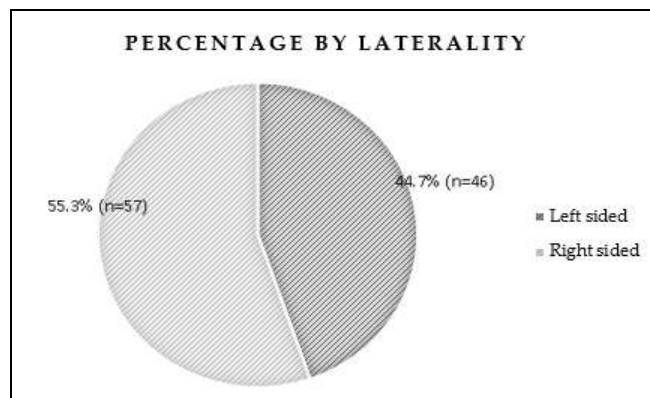


Figure-1: Distribution of patients by laterality (n=103)

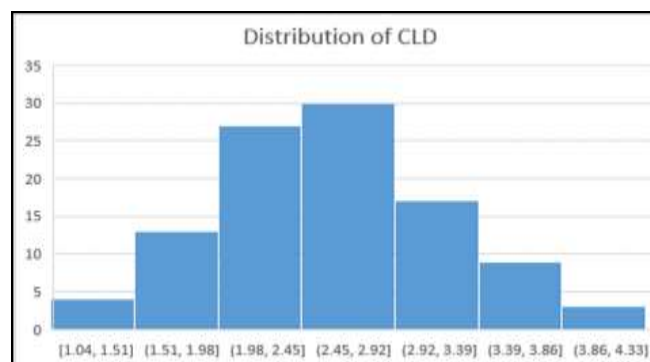


Figure-2: Distribution of Central Lung Distance in cm (n=103)

Table: Mean of Central Lung Distance and Laterality of Breast Cancer (n=103)

Parameter	Group-1 Right (n=57)	Group-2 Left (n=46)	p-value
Mean CLD (cm)	2.83±0.63	2.32±0.51	<0.001

Pearson correlation between laterality of the breast cancer and CLD was determined. Pearson's correlation coefficient (*r*) was -0.40, with a *p*-value of <0.001 which was statistically significant. Table shows the statistical analysis results applied to the data set. Means of the CLD of right sided tumours were compared with CLD of left sided tumours by applying ANOVA. Mean right sided CLD was 2.83±0.63 and left sided was 2.32±0.51, with a *p*-value of <0.001 showing a statistically significant difference.

DISCUSSION

Higher mean right sided CLD in our study signifies that heart has a protective role for the left lung. It cannot obstruct the radiation, and the attenuation effect may be minimal or negligible, due to high energy. But due to meticulous radiotherapy simulation on the left side, to protect heart, overall radiotherapy dose to the left lung decreases.

Radiation induced heart disease (RIHD) is a serious long-term complication of breast or chest wall

radiotherapy.¹² Radiotherapy to the heart can lead to many long-term side effects.¹³ Maximum heart volume in the field can be estimated by maximum heart distance (MHD).¹⁴ The radiation oncologists are meticulous while planning radiotherapy in left sided breast cancers.

Deep inspiratory breath hold (DIBH) can reduce the radiotherapy dose to heart. It is mostly employed in radiotherapy of breast cancers of left side.¹⁵ This technique was not available at our centre at the time of study. Later voluntary DIBH came into practice for left sided cancers when DIBH instruments are not available.¹⁶ DIBH also reduces the dose to liver and lung.^{17,18} We conducted this study, to determine the possibility of lung dose reduction in right sided tumors as well. Study done by Pandeli *et al*, on reduction of lung dose in radiotherapy right sided cancers suggests that DIBH should be used for right sided cancers.¹¹ Although it will prolong the treatment planning and delivery time and hence, lesser number of patients can be treated on a machine per day.¹⁹ Ultimately, quality comes with the investment of time and resources. However, there are conflicting and contrary findings. Some studies suggest the asymmetry between left and right-sided cases, while others indicate similarities in mean lung doses. So, we believe there is need for further research.

Several other factors can influence a lower radiation dose received by the left-sided lung as compared to the right-sided lung in ipsilateral breast cancer radiotherapy like individual anatomy, breast size, and lung volume play a role in lung dose variation. Similarly, a variation in radiotherapy techniques (e.g., tangential fields, breath-hold, IMRT) profoundly influence dose distribution to the lungs. But in this study, investigators have used a similar technique (field in field IMRT) for all patients. The choice of boost technique (sequential vs. simultaneous integrated boosts) might affect lung dosage in left-sided breast cancer radiotherapy.²⁰ Intra-operative radiotherapy can also be used to boost the tumor bed.²¹

While making a radiotherapy plan, use of multileaf collimators can help to reduce the dose to the underlying lung and heart. Their use should be done carefully, so that it does not shield the target volume. Field-in-field intensity modulation (IMRT) also helps to get uniform dose in the target volume. IMRT also helps to reduce the dose to the lung. For the difficult cases, where we cannot achieve our aimed target

volume doses and doses to the organs at risk are higher, use of volumetric arc therapy can help to achieve target volume uniformity and reduce the doses to organs at risk. VMAT can be used as a non-co-planer technique to achieve the desired results.²² These innovations in radiotherapy are helpful to get therapeutic gain and increase the therapeutic window of breast radiotherapy.

This study can be a milestone in therapeutic approach. The proven difference in radiation dose received by the left and right lungs during ipsilateral breast cancer radiotherapy has significant implications for treatment planning. Understanding factors that contribute to variability in lung exposure is crucial for minimizing the risk of radiation-induced pulmonary complications. It raises the possibility of refining treatment strategies to minimize lung toxicity without compromising therapeutic efficacy. Further investigations and larger study populations are necessary to authenticate these findings and provide more convincing evidence.

This highlights the need for further research to conduct studies with larger patient cohorts to better establish the heart's shielding effect in the context of diverse anatomical presentations. We need to promote standardization in radiotherapy techniques to allow for a more accurate comparison of lung doses across different studies. Authors also emphasize the importance of individualized treatment plans considering unique patient anatomy to optimize dose distribution and minimize lung exposure.

Further studies then should be conducted to find out the treatment planning factors which lead to reduced lung volume on left side and employ all those techniques while planning right sided radiotherapy as well. Attempts should be made not to take right lung for granted and rather attain its "as low as reasonably achievable" (ALARA) dose, and reduce right lung toxicity, without any added cost. This will help radiation/clinical oncologists and physicists to understand that they were not doing justice with the right lung.

LIMITATION OF STUDY

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

ACKNOWLEDGEMENT

Authors are thankful to the physics team for providing data and making calculations.

CONCLUSION

This study sheds light on the potential differences in lung radiation doses between right and left-sided breast cancer external beam radiotherapy. The presence of the heart plays a role in reducing ipsilateral lung doses in left-sided cancers because of cautious treatment planning on left sided cancers. Application of similar planning techniques in right sided carcinomas might decrease the lung toxicity in right side as well.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

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

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

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

NS: Conception, data acquisition, drafting the manuscript, 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.

REFERENCES

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. *CA Cancer J Clin* 2021; 71(1): 7-33. <https://doi.org/10.3322/caac.21708>
2. Corradini S, Krug D, Meattini I, Fastner G, Matuschek C, Cutuli B. Challenges in radiotherapy. *Breast Care* 2019; 14(3): 152-158. <https://doi.org/10.1159/000500847>
3. Simonetto C, Eidemuller M, Gaasch A, Pazos M, Schönecker S, Reitz D, et al. Does deep inspiration breath-hold prolong life? Individual risk estimates of ischaemic heart disease after breast cancer radiotherapy. *Radiother Oncol* 2019; 131: 202-207. <https://doi.org/10.1016/j.radonc.2018.07.024>
4. Finazzi T, Nguyen VT, Zimmermann F, Papachristofilou A. Impact of patient and treatment characteristics on heart and lung dose in adjuvant radiotherapy for left-sided breast cancer. *Radiat Oncol* 2019; 14(1): 153. <https://doi.org/10.1186/s13014-019-1364-3>
5. Corradini S, Ballhausen H, Weingandt H, Freisleder P, Schönecker S, Niyazi M, et al. Left-sided breast cancer and risks of secondary lung cancer and ischemic heart disease. *Strahlenther Onkol* 2018; 194(3): 196-205. <https://doi.org/10.1007/s00066-017-1213-y>
6. Milo ML, Thorsen LB, Johnsen SP, Nielsen KM, Valentin JB, Alsner J, et al. Risk of coronary artery disease after adjuvant radiotherapy in 29,662 early breast cancer patients: A population-based Danish Breast Cancer Group study. *Radiother Oncol* 2021; 157: 106-113. <https://doi.org/10.1016/j.radonc.2021.01.010>
7. Wennstig AK, Wadsten C, Garmo H, Fredriksson I, Blomqvist C, Holmberg L, et al. Long-term risk of ischemic heart disease after adjuvant radiotherapy in breast cancer: results from a large population-based cohort. *Breast Cancer Res* 2020; 22(1): 10. <https://doi.org/10.1186/s13058-020-1249-2>
8. Cao N, Kalet AM, Young LA, Fang LC, Kim JN, Mayr NA, et al. Predictors of cardiac and lung dose sparing in DIBH for left breast treatment. *Phys Med* 2019; 67: 27-33. <https://doi.org/10.1016/j.ejmp.2019.09.240>
9. Misra S, Mishra A, Lal P, Srivastava R, Verma M, Kumar SK, et al. Cardiac dose reduction using deep inspiratory breath hold (DIBH) in radiation treatment of left sided breast cancer patients with breast conservation surgery and modified radical mastectomy. *J Med Imaging Radiat Sci* 2021; 52(1): 57-67. <https://doi.org/10.1016/j.jmir.2020.12.004>
10. Herr DJ, Moncion A, Griffith KA, Marsh R, Grubb M, Bhatt A, et al. Factors associated with cardiac radiation dose reduction after hypofractionated radiation therapy for localized, left-sided breast cancer in a large statewide quality consortium. *Int J radiat oncol biol phys* 2024; 118(3): 632-638. <https://doi.org/10.1016/j.ijrobp.2023.09.013>
11. Pandeli C, Smyth LM, David S, See AW. Dose reduction to organs at risk with deep-inspiration breath-hold during right breast radiotherapy: a treatment planning study. *Radiat Oncol* 2019; 14: 223. <https://doi.org/10.1186/s13014-019-1430-x>
12. Qi WX, Cao L, Xu C, Cai G, Chen J. The optimal regional irradiation volume for breast cancer patients: A comprehensive systematic review and network meta-analysis of published studies. *Front Oncol* 2023; 13: 1081201. <https://doi.org/10.3389/fonc.2023.1081201>
13. Wei T, Cheng Y. The cardiac toxicity of radiotherapy—a review of characteristics, mechanisms, diagnosis, and prevention. *Int J Radiat Biol* 2021; 97(10): 1333-1340. <https://doi.org/10.1080/09553002.2021.1956007>
14. Wennstig AK, Wadsten C, Garmo H, Fredriksson I, Blomqvist C, Holmberg L, et al. Long-term risk of ischemic heart disease after adjuvant radiotherapy in breast cancer: results from a large population-based cohort. *Breast Cancer Res* 2020; 22: 1-9. <https://doi.org/10.1186/s13058-020-1249-2>
15. Ferdinand S, Mondal M, Mallik S, Goswami J, Das S, Manir KS, et al. Dosimetric analysis of Deep Inspiratory Breath-hold technique (DIBH) in left-sided breast cancer radiotherapy and evaluation of pre-treatment predictors of cardiac doses for guiding patient selection for DIBH. *Tech Innov Patient Supp Radiat Oncol* 2021; 17: 25-31. <https://doi.org/10.1016/j.tipsro.2021.02.006>
16. Lai J, Hu S, Luo Y, Zheng R, Zhu Q, Chen P, et al. Meta-analysis of deep inspiration breath hold (DIBH) versus free breathing (FB) in postoperative radiotherapy for left-side breast cancer. *Breast Cancer* 2020; 27: 299-307. <https://doi.org/10.1007/s12282-019-01023-9>
17. Vander Veken L, Van Ooteghem G, Razavi A, Quaresma SD, Longton E, Kirkove C, et al. Voluntary versus mechanically-induced deep inspiration breath-hold for left breast cancer: A randomized controlled trial. *Radiother Oncol* 2023; 183: 109598. <https://doi.org/10.1016/j.radonc.2023.109598>
18. Mader T, Pace R, da Silva RT, Adam LE, Näf G, Winter CC, et al. Deep inspirational breast hold (DIBH) for right breast irradiation: Improved sparing of liver and lung tissue. *Clin Transl Radiat Oncol* 2024; 45: 100731. <https://doi.org/10.1016/j.ctro.2024.100731>
19. Gaál S, Kahán Z, Paczona V, Kószó R, Drencsényi R, Szabó J, et al. Deep-inspirational breath-hold (DIBH) technique in left-sided breast cancer: various aspects of clinical utility. *Radiat Oncol* 2021; 16(1): 89. <https://doi.org/10.1186/s13014-021-01816-3>
20. Haussmann J, Corradini S, Nestle-Kraemling C, Bölke E, Njanang FJ, Tamaskovics B, et al. Recent advances in radiotherapy of breast cancer. *Radiat Oncol* 2020; 15(1): 71. <https://doi.org/10.1186/s13014-020-01501-x>

21. Stoian R, Exner JP, Gainey M, Erbes T, Gkika E, Popp I, et al. Comparison of intraoperative radiotherapy as a boost vs. simultaneously integrated boosts after breast-conserving therapy for breast cancer. *Front Oncol* 2023; 13: 1210879. <https://doi.org/10.3389/fonc.2023.1210879>
 22. Frengen J, Vikström J, Mjaaland I, Funderud M, Almberg SS, Dybvik KI, et al. Locoregional breast radiotherapy including IMN: optimizing the dose distribution using an automated non-coplanar VMAT-technique. *Acta Oncol* 2023; 62(10): 1169-1177. <https://doi.org/10.1080/0284186x.2023.2264488>
-