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Feasibility of Dose Reduction to the Left Anterior Descending Coronary Artery without Compromising Target Volume Coverage Using Tomotherapy Techniques

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Abstract

Background: Radiotherapy is associated with a high risk of heart disease in patients with left-sided breast cancer. Previously, the entire heart was considered an organ at risk during planning. Studies have shown that the effect of radiation therapy depends on the dose to specific heart substructures. However, the tolerance dose of the left anterior descending coronary artery (LAD), an important cardiac substructure, is yet to be determined. This study aims to verify the feasibility of reducing the LAD dose with appropriate dose-volume constraints for patients undergoing left whole-breast radiotherapy, without compromising the target dose coverage, using tomotherapy techniques.

Method: This retrospective study generated tomohelical and tomodirect plans initially without considering the LAD as an organ at risk (OAR) in the treatment planning. To reduce the LAD dose, plans were regenerated by including the LAD as an OAR with appropriate dose constraints. The dose-volume histogram parameters of these plans were compared with those of the initial plans of the respective types.

Results: Tomohelical plans showed a 4.4% reduction in maximum dose and a 3.8% reduction in V15 for LAD, while tomodirect plans registered a 3% reduction in V15, with the conformity index remaining constant. Based on the LAD dosimetric results, considering the LAD as an OAR is associated with lower LAD doses without compromising the target volume coverage.

Conclusion: It is feasible to reduce the LAD dose without compromising target volume coverage or affecting other OAR doses in patients with left breast cancer, using tomotherapy techniques.

Keywords: Heart diseases, Tomotherapy, Helical, Left-sided breast cancer, Coronary artery, LAD Dose reduction

Introduction

In breast cancer treatment, radiotherapy is effective in reducing the risk of recurrence and death. However, the benefits of radiotherapy are relatively consistent across different groups of women.¹ Among patients with left-sided breast cancer, radiotherapy is associated with a higher risk of heart disease compared with right-sided patients. This risk is particularly elevated when radiotherapy is combined with anthracycline-based chemotherapy.² Additionally, patients with a history of ischemic heart disease may face a higher risk compared with others.³ The exact cause of cardiac toxicity resulting from radiotherapy in breast cancer patients is not yet fully understood. It appears that the endothelial lining of the arteries is the target structure, leading to gradual functional alterations.⁴ Radiotherapy is believed to trigger continuous inflammatory processes, causing endothelial cell proliferation, formation of fibrin thrombus, and obstruction of the myocardial capillary lumen. This obstruction can lead to ischemia and cell death in the myocardium. As cardiac myocytes cannot divide, fibrotic tissue replaces the damaged cardiac tissue. Furthermore, radiation can induce an inflammatory process in the major arteries of the heart, accelerating the development of atherosclerosis.⁵

Previously, the entire heart was considered a single organ at risk during radiation therapy planning. However, studies have shown that the impact of radiation therapy depends on the dose received by specific substructures of the heart. As a result, dose constraints should be adjusted accordingly.⁶ Established dose constraints for the whole heart aim to reduce the risk of pericarditis and cardiovascular mortality. However, the tolerance dose for the left anterior descending coronary artery (LAD), a specific substructure of the heart, is yet to be determined.⁷ Existing evidence suggests that the LAD dose should be minimized to reduce the risk of radiation-induced

stenosis.⁸ In clinical practice, the LAD is not routinely delineated during breast radiotherapy due to difficulties in its delineation, and following the guidelines of the Radiation Therapy Oncology Group (RTOG) is deemed sufficient.⁹

In conventional radiation therapy, parallel-opposed tangential photon beams are used, which result in high radiation doses being delivered to the anterior of the heart and the proximal LAD. This technique lacks conformity to the target and is less advanced compared to other techniques, primarily due to the complex concave structure of the breast. On the other hand, intensity-modulated radiation therapy (IMRT) offers better target conformity and homogeneity for breast irradiation while sparing the anterior heart and ipsilateral lung from high radiation doses.

Tomotherapy refers to the delivery of intensity-modulated rotational radiation therapy using fan-beam delivery. It includes two IMRT treatment modalities: helical tomotherapy (tomohelical (TH)) and fixed-beam tomotherapy (tomodirect (TD)). TH involves rotational delivery of a fan beam and was the original beam delivery method used in the tomotherapy system. In contrast, TD provides a fixed-directional fan beam. When treating the chest wall without nodal irradiation, TH provides better sparing of the LAD. Conversely, TD plans are superior in terms of LAD sparing when irradiating the chest wall along with regional nodes.¹⁰ TH, using either the complete or directional block technique, is feasible for breast cancer treatment and achieves similar target volume coverage, homogeneity, and conformity, while better sparing the heart, LAD, and lungs compared with other techniques.¹¹ However, there is limited research evaluating LAD doses with TD and TH techniques in whole-breast radiotherapy without nodal irradiation. Therefore, our aim was to study the feasibility of helical and direct tomotherapy delivery techniques in reducing the LAD dose without compromising target coverage

for patients undergoing left whole-breast radiotherapy without nodal irradiation.

Material and Methods

A sample of 20 patients with left breast cancer who underwent adjuvant radiation therapy after breast-conserving surgery between February 2020 and February 2021 at Basavatarakam Indo American Cancer Hospital, Hyderabad, was considered for this retrospective study. Female patients aged 20–80 years with tumor stages I, II, and IIIA (T3N1M0) were included. All patients underwent a planned computed tomography (CT) scan with a 5-mm slice thickness using the Brilliance CT Big Bore (Philips Healthcare, Cleveland, OH, USA). During the scan and treatment time, patients were positioned with their heads turned toward the contralateral side, and both arms raised above their head in the supine position. The CT images were exported to the Eclipse treatment planning system, version 15.6.8 (Varian Medical System, USA), for contouring.

Ethical approval

This study was approved by the institutional ethics committee (IEC/2022/96.2). Informed consent was obtained from all the participants included in the study.

The target volume and organs at risk (OARs) were delineated according to the RTOG contouring guidelines.¹² LAD contouring was attempted on each CT image with contrast using the heart atlas proposed by Feng et al.⁶ 3D reconstruction of the entire LAD artery was performed using linear interpolation available in the treatment planning system when the artery was not contiguous owing to a lack of visibility on some slices. Figure 1 shows the LAD artery delineation. CT images, along with the structure set, were exported to the Tomoplanning station, version 5.1.1.6 (Accuray, Sunnyvale, CA), for treatment planning.

Initially, the TD and TH plans were generated without considering LAD as an OAR. TD plans were generated using two

to four tangential fields with the following plan parameters: pitch 0.5, modulation factor of 2, and a field width of 5.048 cm for all patients by providing a flash of three MLC (Multi-leaf collimator) leaves. A field width of 5.048 cm reduces the treatment delivery time, and a shorter treatment time can minimize intra-fractional error.¹³ Modulation factor is the ratio of maximum beamlet open time in sinogram to the average non-zero beamlets open time and limits the range of leaf open times allowed in the optimized plan. A smaller modulation factor creates very small leaf open times that can cause inaccuracies in the MLC latencies, and the plan becomes unachievable. At the same time, increasing modulation factors increase treatment times and may have hotspots that make the plan more complex and inefficient.¹⁴ Hence, the modulation factor of 2 was chosen in the present study. For both techniques, TomoEDGE dynamic jaws are used, which close and open around the target in a sliding window motion to improve the inferior/superior penumbra dose, thereby increasing the target coverage and reducing the OAR doses, as well as treatment time. The beam angles were slightly modified for each patient to appropriately cover the planning target volume (PTV) and reduce the OAR doses.

In the case of TH, plans were generated with the plan parameters of pitch 0.5, modulation factor 2, and a field width of 5.048 cm. The right lung and right breast were completely blocked to avoid the entrance dose and spinal cord directionally during the optimization process. Plan acceptance was based on the International Commission on Radiation Units and Measurements (ICRU) report number 83 guidelines.¹⁵

To reduce the dose of LAD, two plans, TD_{LAD} (TD with LAD as the OAR) and TH_{LAD} (TH with LAD as the OAR), were regenerated by considering LAD as the OAR and implementing appropriate dose-volume constraints. Throughout the optimization process, the dose volume

points for maximum dose (Dmax), V15, V20, and V30 were adjusted, and they were fixed once the PTV coverage deviated from the initial plans (which did not include LAD as an OAR), while keeping all other planning parameters constant. The dose constraints for LAD were set at 60% to 15% of the doses registered in the respective initial plans (TD IMRT and TH IMRT), with the low volume of LAD having a 60% dose constraint and the higher volume having a 15% dose constraint. During the optimization process, the priority given to LAD was the lowest among the other OARs.

The DVH parameters of the aforementioned plans were compared with the initial plans of the corresponding type (TD/TH), where no dose constraint was assigned for LAD. The plan quality was determined using quantities such as the ICRU-83 conformity index (CI) and homogeneity index (HI). The parameters compared for PTV dose coverage were CI and HI, while for LAD, the volumes receiving 15 Gy, 20 Gy, 30 Gy, and 40 Gy (V15, V20, V30, and V40, respectively), as well as the mean dose (Dmean), Dmax, and D0.1 cc (dose received by a 1cc volume), were considered. For the heart, the volumes receiving 10 Gy and 25 Gy (V10 and V25) and the mean dose (Dmean) were compared. The comparison for the ipsilateral lung included V5, V20, V30, and the mean dose. As for the contralateral lung and contralateral breast, only the mean dose was considered.

The normality of the data was determined using the Kolmogorov-Smirnov test. Depending on the distribution type, either Student's t-test or Mann-Whitney U test was used to assess the statistical significance of differences between treatment techniques. Differences were considered significant at a *P* value of less than 0.05.

Results

Table 1 presents the age and tumor characteristics of all patients included in the

present study. The patients had a median age of 50 years (range: 31–71 years). The most prevalent stage was stage IIA (50%), followed by stage IA (25%).

When comparing the LAD dose, there was a reduction in the LAD Dmax in TH_{LAD} compared to the TH plan (*P* < 0.001). The mean Dmax was reduced by 4.4%, and the mean D0.1cc was reduced by 8%. However, the LAD mean dose could only be reduced by 0.7% (*P* = 0.40). The V15 could be reduced by 3.8% (*P* = 0.01), and V20 reduced by 7.6% (*P* = 0.01). It is noteworthy that V30 could be considerably reduced by 22.7% (*P* = 0.01). Similarly, V40 also showed a reduction of 37.8%, but it was not statistically significant (*P* = 0.28). No significant change in heart dose during the process of sparing the LAD was observed in TH_{LAD}, but there was an 8.6% reduction in V25 dose. Similarly, for the ipsilateral lung, the change in dose was very low. The V5, V20, V30, and mean registered differences were 0.57%, 0.78%, 1.51%, and 0.28%, respectively. Similar results were observed for the contralateral lung and contralateral breast, where changes in mean doses were in the order of 0.89% and 3%, respectively. These results are summarized in table 2. The CI and HI of the target are represented in table 3, demonstrating no considerable change after considering LAD as an OAR. The isodose distributions of the TH_{LAD} and TH plans are shown in figure 2.

Similarly, when comparing TD_{LAD} and TD for LAD dose analysis, no significant reduction was observed in the LAD Dmax (*P* = 0.68). However, the dose to 0.1 cc was reduced by 4.02% (*P* = 0.2). In contrast to the Dmax, the LAD mean dose could be reduced by 4.1% (*P* = 0.05). There was no significant reduction in V15 and V20, but a reduction of 11.9% (*P* < 0.001) was observed for V30, as well as a reduction of 16.21% (*P* < 0.001) for V40. Similar to TH_{LAD}, TD_{LAD} also showed no significant change in the heart dose and the other OARs while sparing the LAD (Table 4). The CI and HI of the target are

represented in table 5. The isodose distribution for the TD_{LAD} and TD plans is shown in figure 3.

Discussion

In the present study, our aim was to evaluate the feasibility of tomotherapy techniques in reducing LAD dose while maintaining target coverage. This study is one of the few of its kind focusing on left breast cancer patients treated with tomotherapy techniques.

Significant reductions were observed in LAD mean dose, V30, and V40 when LAD was considered as an OAR in the TD technique. However, insignificant changes were noted in Dmax, D0.1cc, V15, and V20. This could be attributed to the lower priority assigned to LAD compared with other OARs during the plan optimization process, as well as the presence of small volumes consistently presented in the beam direction. The TH technique demonstrated decreased maximum LAD dose, V15, V20, and V30 when LAD was included as an OAR, owing to the freedom of gantry rotation in helical mode. However, further reductions in LAD doses may compromise target coverage.

In a study that accounted for baseline cardiac risk, Atkins et al. found that the volume of LAD receiving 15 Gy (V15Gy) was the most predictive factor for major adverse cardiac events in patients with locally advanced non-small-cell lung cancer.¹⁶ It was also noted as an independent predictor of major adverse cardiac events, while the mean heart dosage was insufficient in reliably predicting LAD V15Gy. These findings¹⁷ question the ongoing practice of using whole-heart limitations to reduce cardiac toxicity. In our study, considering LAD as an OAR in tomo helical IMRT significantly reduced V15.

Nieder et al. observed that LAD Dmax exhibited a stronger association with the onset of coronary artery calcification and LAD stenosis identified on CT angiography compared with the mean heart dose. IMRT techniques allow for the

creation of individualized dose distributions, sparing one ventricle and one of the coronary arteries.¹⁸ In our current investigation, Dmax was greatly decreased in tomo helical IMRT.

While the deep inspiratory breath-hold technique results in lower heart doses, tomotherapy can serve as an alternative technique for sparing the heart and coronary vessels, especially in patients who are unable to comply with the deep inspiratory breath-hold.¹⁹ According to a study by Aisling Barry et al.²⁰, post-mastectomy left-sided breast cancer patients were compared in terms of treatment plans using the free breathing technique and the active breathing control technique (ABC) plans generated through four-field IMRT. For LAD, Dmax values were 50.4 Gy and 31 Gy for the free breathing and ABC techniques, respectively, indicating superior results with the ABC technique for the remaining OARs as well. In comparison to our study, LAD Dmax performed better in ABC. This could be attributed to the fact that during deep inspiration breath-hold, LAD, being a substructure of the heart, moves away from the target, resulting in a significantly greater dose reduction using the ABC technique.

Anna M. Kirby et al.²¹ compared doses to LAD and other OARs using the supine and prone positions for whole-breast irradiation and partial breast irradiation by tangential IMRT. The study found that the supine position resulted in better achievement of LAD Dmax compared to the prone position for whole-breast irradiation. This difference could be attributed to the movement of the heart closer to the chest wall, resulting in greater exposure to the radiation field in the prone position. In this current study, all patients were treated in the supine position, and we aimed to further reduce Dmax, particularly in tomo helical IMRT, by considering the LAD during treatment planning.

Vayntraub A et al.²² conducted a study on prospective contouring and

avoidance of the LAD in patients receiving whole-breast radiotherapy without internal mammary nodes. They found that patients who underwent prospective contouring had lower unadjusted median maximum and median mean LAD doses compared with patients who were retrospectively contoured. The reductions were 39% and 27%, respectively. They also observed a significant reduction of 30% in the median Dmax for patients with internal mammary nodes cases, but no significant reduction in the median mean dose. In our study, the results for Dmax and mean dose for LAD with the TH technique were in good agreement with the above study, but with a smaller magnitude (less than 5%). However, TD did not result in any change in Dmax. This can be attributed to the adoption of an ABC during CT acquisition in their study.

Yeh H-P et al.¹¹ compared 5-field IMRT with six different helical tomotherapy plans that used a rectangular structure, complete directional complete block with different restricted angles, and the LAD as an OAR. They demonstrated that the mean dose to the LAD was effectively reduced by 30 to 55% without compromising PTV coverage using the TH technique compared to IMRT. They reported that TH plans with restricted angles of 10 and 20 degrees, while considering the LAD as an OAR along with other OARs, were superior techniques. In our current investigation, the mean dosage of LAD was reduced in TD IMRT, and a complete directional block was only used for the contralateral breast and contralateral lung. However, the TH IMRT technique did not achieve a significant reduction in the mean LAD dose, even after considering the importance of the LAD.

In our current investigation, there was negligible change in treatment time and the actual modulation factor for both techniques. This indicates that plan complexity remained the same while reducing the LAD dose. These findings confirm that LAD doses can be significantly reduced with tomotherapy

approaches without compromising target coverage, adhering to other OAR dose limitations, or increasing plan complexity. However, the present study has some limitations, including the failure to apply active breath control strategies, which could further help reduce LAD dosages.

Conclusion

Based on these findings, LAD can be considered as an OAR during breast radiotherapy planning, especially for patients with left breast cancer. It is feasible to reduce LAD doses using tomotherapy techniques without significantly impairing plan quality or increasing doses to other OARs.

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Conflict of Interest

None declared.

References

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;378(9804):1707-16. doi:10.1016/S0140-6736(11)61629-2.
2. Rehammar JC, Jensen MB, McGale P, Lorenzen EL, Taylor C, Darby SC, et al. Risk of heart disease in relation to radiotherapy and chemotherapy with anthracyclines among 19,464 breast cancer patients in Denmark, 1977-2005. *RadiotherOncol*. 2017;123(2):299-305. doi:10.1016/j.radonc.2017.03.012.
3. McGale P, Darby SC, Hall P, Adolfsson J, Bengtsson NO, Bennet AM, et al. Incidence of heart disease in 35,000 women

- treated with radiotherapy for breast cancer in Denmark and Sweden. *RadiotherOncol*. 2011;100(2):167-75. doi: 10.1016/j.radonc.2011.06.016.
4. Schultz-Hector S, Trott KR. Radiation-induced cardiovascular diseases: is the epidemiologic evidence compatible with the radiobiologic data? *Int J RadiatOncolBiol Phys*. 2007;67(1):10-8. doi: 10.1016/j.ijrobp.2006.08.071.
5. Sardaro A, Petruzzelli MF, D'Errico MP, Grimaldi L, Pili G, Portaluri M. Radiation-induced cardiac damage in early left breast cancer patients: risk factors, biological mechanisms, radiobiology, and dosimetric constraints. *RadiotherOncol*. 2012;103(2):133-42. doi: 10.1016/j.radonc.2012.02.008.
6. Feng M, Moran JM, Koelling T, Chughtai A, Chan JL, Freedman L, et al. Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer. *Int J RadiatOncolBiol Phys*. 2011;79(1):10-8. doi: 10.1016/j.ijrobp.2009.10.058.
7. Nilsson G, Witt Nyström P, Isacson U, Garmo H, Duvernoy O, Sjögren I, et al. Radiation dose distribution in coronary arteries in breast cancer radiotherapy. *ActaOncol*. 2016;55(8):959-63. doi: 10.1080/0284186X.2016.1182209.
8. Wennstig AK, Garmo H, Isacson U, Gagliardi G, Rintelä N, Lagerqvist B, et al. The relationship between radiation doses to coronary arteries and location of coronary stenosis requiring intervention in breast cancer survivors. *RadiatOncol*. 2019;14(1):40. doi: 10.1186/s13014-019-1242-z.
9. Shekel E, Levin D, Epstein D, Tova Y, Zalmanov-Faermann S, Pfeffer R. Is contouring the left anterior descending (LAD) artery necessary for left-breast patients?: A retrospective comparison between treated and revised plans. *International Journal of Radiation Oncology, Biology, Physics*. 2014;90(1):S265. doi:10.1016/j.ijrobp.2014.05.916.
10. Nobnop W, Phakoetsuk P, Chitapanarux I, Tippanya D, Khamchompoo D. Dosimetric comparison of TomoDirect, helical tomotherapy, and volumetric modulated arc therapy for postmastectomy treatment. *J ApplClin Med Phys*. 2020;21(9):155-62. doi: 10.1002/acm2.12989.
11. Yeh HP, Huang YC, Wang LY, Shueng PW, Tien HJ, Chang CH, et al. Helical tomotherapy with a complete-directional-complete block technique effectively reduces cardiac and lung dose for left-sided breast cancer. *Br J Radiol*. 2020;93(1108):20190792. doi: 10.1259/bjr.20190792.
12. Li XA, Tai A, Arthur DW, Buchholz TA, Macdonald S, Marks LB, et al. Variability of target and normal structure delineation for breast cancer radiotherapy: an RTOG Multi-Institutional and Multiobserver Study. *Int J RadiatOncolBiol Phys*. 2009;73(3):944-51. doi: 10.1016/j.ijrobp.2008.10.034.
13. Chiu ST, Wu PM, Cheng KF, Fok PH, Chiu G. Evaluation on dosimetric plan quality and treatment delivery time of dynamic jaw mode in TomoTherapy® for left-side breast cancer patients. *Journal of Radiotherapy in Practice*. 2021;1-8. doi:10.1017/s1460396921000522.
14. Binny D, Lancaster CM, Harris S, Sylvander SR. Effects of changing modulation and pitch parameters on tomotherapy delivery quality assurance plans. *J ApplClin Med Phys*. 2015;16(5):87-105. doi: 10.1120/jacmp.v16i5.5282.
15. Hodapp N. The ICRU Report 83: prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT). [Article in German] *Strahlenther Onkol*. 2012;188(1):97-9. doi: 10.1007/s00066-011-0015-x.
16. Atkins KM, Chaunzwa TL, Lamba N, Bitterman DS, Rawal B, Bredfeldt J, et al. Association of left anterior descending coronary artery radiation dose with major adverse cardiac events and mortality in patients with non-small cell lung cancer.

JAMA Oncol. 2021;7(2):206-19. doi: 10.1001/jamaoncol.2020.6332.

17. Atkins KM, Bitterman DS, Chaunzwa TL, Kozono DE, Baldini EH, Aerts HJWL, et al. Mean heart dose is an inadequate surrogate for left anterior descending coronary artery dose and the risk of major adverse cardiac events in lung cancer radiation therapy. *Int J RadiatOncolBiol Phys.* 2021;110(5):1473-9. doi: 10.1016/j.ijrobp.2021.03.005.

18. Nieder C, Schill S, Kneschaurek P, Molls M. Influence of different treatment techniques on radiation dose to the LAD coronary artery. *RadiatOncol.* 2007;2:20. doi: 10.1186/1748-717X-2-20.

19. Mathieu D, Bedwani S, Mascolo-Fortin J, Côté N, Bernard AA, Roberge D, et al. Cardiac sparing with personalized treatment planning for early-stage left breast cancer. *Cureus.* 2020;12(3):e7247. doi: 10.7759/cureus.7247.

20. Barry A, Rock K, Sole C, Rahman M, Pintilie M, Lee G, et al. The impact of active breathing control on internal mammary lymph node coverage and normal tissue exposure in breast cancer patients planned for left-sided postmastectomy radiation therapy. *PractRadiatOncol.* 2017;7(4):228-33. doi: 10.1016/j.prro.2016.11.010.

21. Kirby AM, Evans PM, Donovan EM, Convery HM, Haviland JS, Yarnold JR. Prone versus supine positioning for whole and partial-breast radiotherapy: a comparison of non-target tissue dosimetry. *RadiotherOncol.* 2010;96(2):178-84. doi: 10.1016/j.radonc.2010.05.014.

22. Vayntraub A, Quinn TJ, Thompson AB, Chen PY, Gustafson GS, Jawad MS, et al. Left anterior descending artery avoidance in patients receiving breast irradiation. *Med Dosim.* 2021;46(1):57-64. doi: 10.1016/j.meddos.2020.07.006.

Table 1. Patients' characteristics

| Parameter | Number of patients |
|-----------------------|--------------------|
| Age in years | |
| ≤ 50 | 10 |
| >50 | 10 |
| Stage grouping | |
| IA | 5 |
| IIA | 10 |
| IIB | 4 |
| IIIA | 1 |
| Tumour stage | |
| T1 | 7 |
| T2 | 11 |
| T3 | 2 |
| Nodal stage | |
| N0 | 14 |
| N1 | 6 |

Table 2. Helical tomotherapy dose-volume parameters for heart, LAD and other OARs

| Parameter | Tomohelical with LAD as OAR | | | | Tomohelical without LAD as OAR | | | | | |
|---------------------------------------|-----------------------------|--------|-------|--------|--------------------------------|--------|-------|-------|---------|---|
| | Mean | Median | SD | 95% CI | Mean | Median | SD | 95%CI | P value | % of variation with respect to LAD as OAR |
| Heart | | | | | | | | | | |
| Mean (Gy) | 9.22 | 8.88 | 1.86 | 0.87 | 9.22 | 8.93 | 1.85 | 0.87 | 0.98 | -0.01 |
| V10 (%) | 37.44 | 36.25 | 9.81 | 4.59 | 37.95 | 36.00 | 8.64 | 4.05 | 0.98 | 1.34 |
| V25 (%) | 4.81 | 3.70 | 4.37 | 2.04 | 5.26 | 4.00 | 4.50 | 2.11 | 0.73 | 8.61 |
| LAD Coronary Artery | | | | | | | | | | |
| Mean (Gy) | 22.95 | 22.04 | 5.44 | 2.54 | 23.12 | 23.28 | 7.09 | 3.32 | 0.40 | 0.74 |
| D max (Gy) | 37.94 | 38.75 | 6.81 | 3.19 | 39.69 | 40.55 | 7.04 | 3.29 | 0.00 | 4.43 |
| D0.1cc (Gy) | 31.88 | 34.1 | 6.0 | 3.19 | 34.64 | 36.8 | 4.04 | 5.1 | 0.014* | 7.97 |
| V15 (%) | 77.67 | 86.00 | 23.40 | 10.95 | 80.79 | 87.00 | 22.45 | 10.51 | 0.01* | 3.86 |
| V20 (%) | 57.92 | 58.80 | 21.24 | 9.94 | 62.71 | 63.50 | 19.67 | 9.20 | 0.01* | 7.63 |
| V30 (%) | 23.81 | 14.95 | 21.87 | 10.23 | 30.80 | 30.00 | 20.75 | 9.71 | 0.01* | 22.71 |
| V40 (%) | 3.44 | 0.00 | 8.47 | 3.96 | 5.53 | 0.30 | 9.96 | 4.66 | 0.28 | 37.83 |
| Ipsilateral Lung | | | | | | | | | | |
| Mean (Gy) | 17.64 | 17.70 | 1.80 | 2.23 | 17.69 | 17.66 | 1.69 | 2.10 | 0.44 | 0.28 |
| V5 (%) | 92.84 | 97.00 | 8.61 | 10.69 | 93.37 | 97.40 | 7.40 | 9.19 | 0.41 | 0.57 |
| V20 (%) | 35.42 | 35.00 | 5.09 | 6.32 | 35.70 | 35.20 | 4.94 | 6.13 | 0.04* | 0.78 |
| V30 (%) | 11.76 | 12.00 | 2.93 | 3.64 | 11.94 | 12.30 | 2.90 | 3.60 | 0.09* | 1.51 |
| Contralateral lung mean (Gy) | 0.67 | 0.70 | 0.09 | 0.12 | 0.67 | 0.70 | 0.09 | 0.11 | 0.37 | 0.89 |
| Contralateral breast mean (Gy) | 0.38 | 0.40 | 0.04 | 0.05 | 0.39 | 0.40 | 0.04 | 0.04 | 0.11 | 3.08 |

SD: Standard deviation; CI: Confidence interval; LAD: Left anterior descending coronary artery; V10: Volume receiving 10 Gy; V15: Volume receiving 15 Gy; V20: Volume receiving 20 Gy; V25: Volume receiving 25 Gy; V30: Volume receiving 30 Gy; V40: Volume receiving 40 Gy; D0.1cc: Dose received by 0.1cc volume; "*" highlights the significant P value; OAR: Organ at risk

Table 3. Target volume parameters for tomohelical technique

| Parameter | Tomohelical with LAD as OAR | | | | Tomohelical without LAD as OAR | | | | P value | % of variation with respect to LAD as without OAR |
|------------|-----------------------------|--------|------|--------|--------------------------------|--------|------|--------|---------|---|
| | Mean | Median | SD | 95% CI | Mean | Median | SD | 95% CI | | |
| PTV | | | | | | | | | | |
| D2 (Gy) | 52.58 | 52.60 | 0.08 | 0.10 | 52.6 | 52.6 | 0.34 | 0.16 | 0.37 | 0.04 |
| D98 (Gy) | 44.82 | 44.60 | 0.54 | 0.68 | 45.2 | 44.8 | 1.55 | 0.73 | 0.21 | 0.36 |
| D50 (Gy) | 49.91 | 49.90 | 0.07 | 0.08 | 50.13 | 50.1 | 0.12 | 0.06 | 0.06 | 0.52 |
| CI | 1.05 | 1.05 | 0.01 | 0.02 | 1.06 | 1.05 | 0.06 | 0.03 | 0.42 | -1.28 |
| HI | 0.16 | 0.16 | 0.01 | 0.01 | 0.15 | 0.16 | 0.04 | 0.02 | 0.23 | -2.46 |

D2: Dose received by 2% volume; D98: Dose received by 98% volume; D50: Dose received by 50% volume; CI: Conformity index; HI: Homogeneity index; 95% CI: 95% confidence interval; SD: Standard deviation; OAR: Organs at risk; LAD: Left anterior descending coronary artery; PTV: Planning target volume

Table 4. Tomo direct dose-volume parameters for heart, LAD and other OARS

| Parameter | Tomodirect with LAD as OAR | | | | Tomodirect without LAD as OAR | | | | | |
|--------------------------------|----------------------------|--------|-------|----------|-------------------------------|--------|-------|----------|---------|---|
| | Mean | Median | SD | 95.0% CI | Mean | Median | SD | CI 95.0% | P Value | % Of variation with respect to LAD as without OAR |
| Heart | | | | | | | | | | |
| Mean (Gy) | 4.87 | 4.85 | 1.14 | 0.53 | 5.00 | 4.76 | 1.27 | 0.60 | 0.79 | 2.5 |
| V10 (%) | 13.08 | 12.35 | 3.87 | 1.81 | 13.31 | 12.30 | 4.22 | 1.98 | 0.91 | 1.7 |
| V25 (%) | 6.21 | 6.55 | 1.82 | 0.85 | 6.31 | 6.20 | 2.01 | 0.94 | 0.99 | 1.6 |
| LAD Coronary Artery | | | | | | | | | | |
| Mean (Gy) | 21.22 | 22.36 | 6.65 | 3.11 | 22.14 | 24.07 | 7.36 | 3.45 | 0.05 | 4.1 |
| Dmax (Gy) | 44.53 | 47.08 | 10.51 | 4.92 | 44.65 | 46.94 | 10.48 | 4.91 | 0.68 | 0.3 |
| D0.1cc (Gy) | 41.54 | 43.4 | 5.83 | 7.23 | 43.28 | 45.5 | 3.79 | 4.71 | 0.27 | 4.02 |
| V15 (%) | 56.81 | 59.40 | 17.58 | 8.23 | 58.62 | 61.50 | 17.36 | 8.12 | 0.55 | 3.1 |
| V20 (%) | 52.83 | 55.00 | 17.30 | 8.09 | 55.49 | 56.20 | 16.93 | 7.92 | 0.44 | 4.8 |
| V30 (%) | 39.03 | 43.75 | 17.25 | 8.07 | 44.29 | 48.40 | 18.82 | 8.81 | <0.001* | 11.9 |
| V40 (%) | 16.21 | 13.10 | 13.95 | 6.53 | 24.08 | 26.65 | 14.93 | 6.99 | <0.001* | 32.7 |
| Ipsilateral Lung | | | | | | | | | | |
| Mean (Gy) | 8.786 | 8.7 | 1.61 | 2.00 | 8.936 | 9.34 | 1.67 | 2.08 | 0.38 | 1.68 |
| V5 (%) | 28.98 | 29.6 | 5.48 | 6.80 | 29.24 | 29.5 | 5.63 | 6.99 | 0.23 | 0.89 |
| V20 (%) | 18.2 | 18.4 | 3.37 | 4.19 | 18.64 | 19.5 | 3.79 | 4.70 | 0.39 | 2.36 |
| V30 (%) | 12.74 | 11.3 | 3.00 | 3.73 | 13.28 | 13.9 | 2.88 | 3.58 | 0.35 | 4.07 |
| Contralateral lung mean (Gy) | 0.304 | 0.3 | 0.03 | 0.04 | 0.33 | 0.34 | 0.04 | 0.05 | 0.17 | 7.88 |
| Contralateral breast mean (Gy) | 0.356 | 0.36 | 0.06 | 0.07 | 0.37 | 0.37 | 0.05 | 0.06 | 0.38 | 3.78 |

SD: Standard deviation; CI: Confidence interval; LAD: Left anterior descending coronary artery; V10: Volume receiving 10 Gy; V15: Volume receiving 15 Gy; V20: Volume receiving 20 Gy; V25: Volume receiving 25 Gy; V30: Volume receiving 30 Gy; V40: Volume receiving 40 Gy; D0.1cc: Dose received by 0.1cc volume; "*" highlights the significant P value; OAR: Organs at risk

Table 5. Target volume parameters for tomodirect technique

| Parameter | Tomodirect with LAD as OAR | | | | Tomodirect without LAD as OAR | | | | P value | % of variation with respect to LAD as without OAR |
|------------|----------------------------|--------|------|--------|-------------------------------|--------|------|--------|---------|---|
| | Mean | Median | SD | 95% CI | Mean | Median | SD | 95% CI | | |
| PTV | | | | | | | | | | |
| D2 (Gy) | 51.30 | 51.30 | 0.31 | 0.38 | 51.2 | 51.2 | 0.26 | 0.12 | 0.60 | 0.00 |
| D98 (Gy) | 46.54 | 46.70 | 0.72 | 0.90 | 46.3 | 46.5 | 0.93 | 0.44 | 0.24 | 0.26 |
| D50 (Gy) | 49.84 | 49.80 | 0.11 | 0.14 | 50.07 | 50.1 | 0.05 | 0.03 | 0.03 | 0.40 |
| CI | 1.13 | 1.10 | 0.06 | 0.08 | 1.1 | 1.1 | 0.06 | 0.03 | 0.16 | 0.81 |
| HI | 0.10 | 0.09 | 0.02 | 0.03 | 0.1 | 0.09 | 0.02 | 0.01 | 0.44 | -3.04 |

D2: Dose received by 2% volume; D98: Dose received by 98% volume; D50: Dose received by 50% volume; CI: Conformity index; HI: Homogeneity index; 95% CI: 95% confidence interval; SD: Standard deviation; OAR: Organ at risk; PTV: Planning target volume

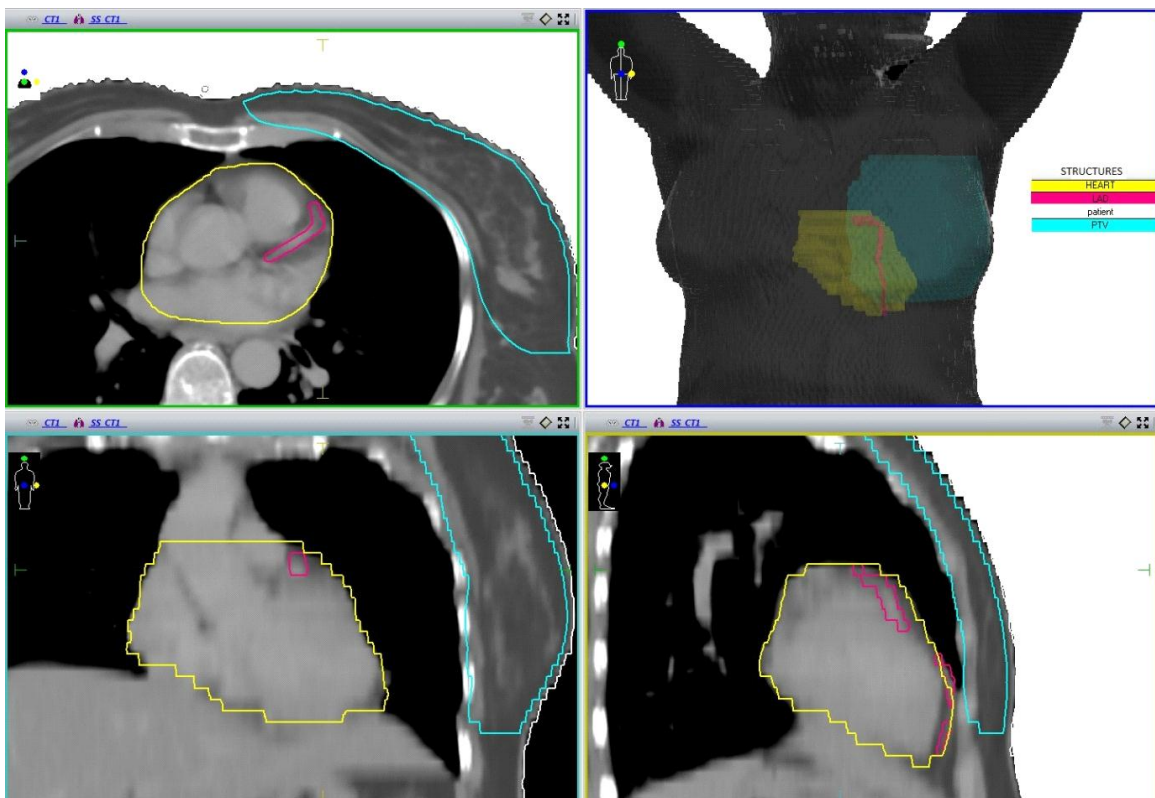


Figure 1. This figure shows the delineation of the left anterior descending coronary artery on computed tomography images with contrast.

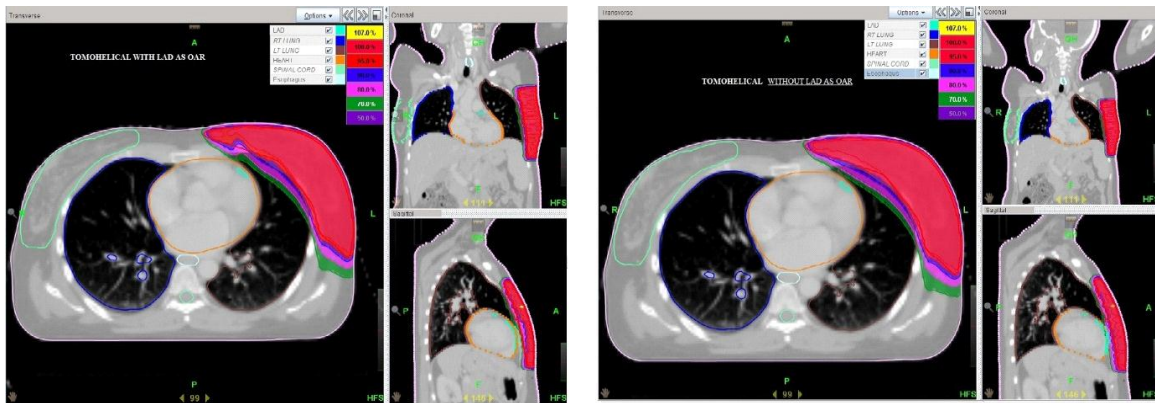


Figure 2. This figure illustrates the comparison of dose distribution for the tomohelical intensity-modulated radiation therapy technique.

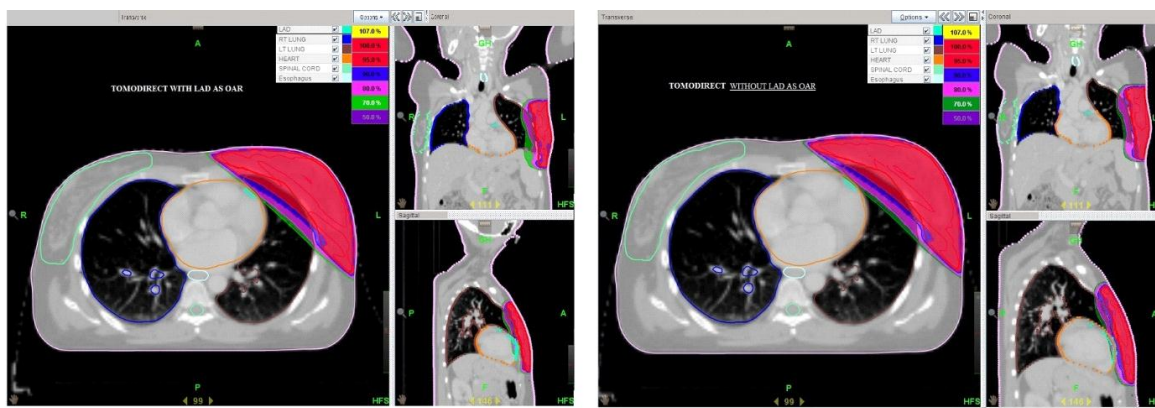


Figure 3. This figure demonstrates the comparison of dose distribution for the tomodirect intensity-modulated radiation therapy technique.