

INVESTIGATION OF FREE BREATHING TECHNIQUE
IMPLICATION TOWARDS CARDIAC STRUCTURE
DOSE IN LEFT BREAST RADIOTHERAPY:
RETROSPECTIVE STUDY

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RETROSPECTIVE STUDY

by

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Dissertation submitted in partial fulfillment
of the requirements for the degree of
Bachelor of Medical Radiation (Honours)

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CERTIFICATE

This is to certify that the dissertation entitled Investigation of Free Breathing Technique Implication Towards Cardiac Structure Dose in Left Breast Radiotherapy: Retrospective Study is the bona fide record of research work done by Ms Nur Syahmina Binti Shahari during the period from October 2024 to July 2025 under my supervision. I have read this dissertation and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation to be submitted in partial fulfillment for the degree of Bachelor of Medical Radiation (Honours).

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated and duly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research and promotional purposes.

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LIST OF ABBREVIATIONS

LAD	Left Anterior Descending
D _{mean}	Mean Dose
D _{mas}	Maximum Dose
FB	Free Breathing
CT	Computed Tomography
RTOG	Radiation Therapy Oncology Group
DEGRO	German Society for Radiation Oncology
OAR	Organ at Risk
CAD	Coronary Artery Disease
HPUSM	Hospital Pakar Universiti Sains Malaysia
DIBH	Deep Inspiration Breath Hold
3D- CRT	Three-Dimensional Conformal Radiation Therapy
IMRT	Intensity Modulated Radiation Therapy
VMAT	Volumetric Modulated Arc Therapy
DICOM	Digital Imaging and Communications in Medicine
LV	Left ventricle

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**PENYIASATAN IMPLIKASI TEKNIKPERNAFASAN BEBAS
TERHADAP DOSSTRUKTUR JANTUNG DI PAYUDARA KIRI
RADIOTERAPI: KAJIAN RETROSPEKTIF**

ABSTRAK

Kajian ini bertujuan untuk menilai secara menyeluruh parameter dosimetri struktur jantung, menilai korelasi dosimetri volumetrik, dan menyiasat hubungan antara dos global jantung dan dosimetri khusus arteri “Left Anterior Descending” (LAD) dalam pelan radioterapi payudara kiri. Objektifnya adalah untuk memastikan pematuhan kepada tahap toleransi yang disyorkan dan mengenal pasti parameter kritikal untuk perlindungan jantung. Analisis retrospektif telah dijalankan ke atas 35 pesakit kanser payudara kiri yang dirawat dengan pelan teknik “3D-CRT” di Hospital Pakar Universiti Sains Malaysia (HPUSM) dari Januari hingga Disember 2024, menerima dos yang ditetapkan sebanyak 40 Gy dalam 15 pecahan. Tiada data selepas Disember 2024 dimasukkan dalam kajian ini, dan tempoh penyelidikan tidak melebihi Julai 2025. Kelulusan etika telah diperoleh, dan pengambilan sampel secara purposif telah digunakan. Simulasi CT dilakukan dalam keadaan bernafas bebas. Organ berisiko (OARs), termasuk jantung, menjalani “auto-contouring”, manakala LAD dilukis secara manual oleh seorang ahli fizik perubatan disebabkan strukturnya yang rumit seperti yang dilihat dalam imej CT. Parameter dosimetri dinilai berdasarkan garis panduan toleransi RTOG 0617 dan DEGRO. Analisis korelasi Spearman's rho digunakan untuk menentukan hubungan antara volum jantung/LAD dan dosnya masing-masing, serta antara dos jantung purata dan dos khusus LAD, selepas ujian normaliti awal. Analisis

menunjukkan tiada korelasi yang signifikan secara statistik antara isipadu jantung dan dos purata jantung ($r = 0.018$, $p = 0.917$), mahupun antara isipadu LAD dan parameter dosimetrianya (LAD D_{mean} : $r = -0.077$, $p = 0.659$; LAD V_{40} : $r = 0.162$, $p = 0.353$). Satu korelasi positif sederhana yang signifikan secara statistik telah dikenalpasti antara dos purata jantung dan dos purata LAD ($r = 0.442$, $p = 0.008$). Sebaliknya, korelasi antara dos purata jantung dan LAD V_{40} (%) tidak signifikan secara statistik ($r = 0.240$, $p = 0.165$). Parameter volumetrik jantung dan LAD tidak dapat meramalkan dos radiasi kepada struktur-struktur ini dengan tepat. Walaupun terdapat korelasi antara dos jantung purata dan dos LAD purata, metrik dos jantung global tidak mencukupi untuk sepenuhnya menangkap kawasan dos tinggi kritikal dalam LAD. Oleh itu, untuk perlindungan jantung yang berkesan dalam radioterapi payudara kiri, perancangan masa depan memerlukan pemantauan teliti terhadap kedua-dua dos purata jantung keseluruhan dan, yang penting, parameter khusus LAD, terutamanya LAD V_{40} (%), untuk memastikan perlindungan jantung yang menyeluruh dan mengurangkan kardiotoxikisiti jangka panjang. Penyelidikan masa depan harus melibatkan kohort yang lebih besar untuk mengesahkan penemuan ini dan meneroka kesan klinikal daripada kelebihan LAD V_{40} .

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ABSTRACT

This study aimed to comprehensively evaluate the dosimetric parameters of cardiac structures, assess volumetric-dosimetric correlations, and investigate the relationship between heart dose and LAD specific dosimetry in left breast radiotherapy plans. The objective was to ascertain adherence to recommended tolerance levels and identify critical parameters for cardiac sparing. A retrospective analysis was conducted on 35 left breast cancer patients treated with 3D-CRT at Hospital Pakar Universiti Sains Malaysia (HPUSM) from January to December 2024, receiving a prescribed dose of 40 Gy in 15 fractions. No data beyond December 2024 was included in this study, and the research period did not extend beyond July 2025. Ethical clearance was secured, and purposive sampling was employed. CT simulation was performed under free breathing conditions. Organs at risk (OARs), including the heart, underwent auto-contouring, while the LAD was manually delineated by a medical physicist due to its complicated structure visualized in the CT images. Dosimetric parameters were assessed against RTOG 0617 and DEGRO tolerance guidelines. Spearman's rho correlation analysis was utilized to determine relationships between heart/LAD volumes and their respective doses, as well as between heart mean dose and LAD-specific doses, following preliminary normality testing. The analysis revealed no statistically significant correlation between heart volume and heart mean dose ($r = 0.018$, p

=0.917), nor between LAD volume and its dosimetric parameters (LAD D_{mean} : $r = -0.077$, $p = 0.659$; LAD V_{40} : $r = 0.162$, $p = 0.353$). A moderate, statistically significant positive correlation was identified between heart mean dose and mean LAD dose ($r = 0.442$, $p = 0.008$). Conversely, the correlation between heart mean dose and LAD V_{40} (%) was not statistically significant ($r = 0.240$, $p = 0.165$). Volumetric parameters of the heart and LAD do not reliably predict radiation dose to these structures. While a correlation exists between heart mean dose and mean LAD dose, global heart dose metrics are insufficient to fully capture critical high-dose regions within the LAD. Consequently, for effective cardiac sparing in left breast radiotherapy, future planning necessitates meticulous monitoring of both the overall heart mean dose and, crucially, LAD-specific parameters, particularly LAD V_{40} (%), to ensure comprehensive cardiac protection and mitigate long-term cardiotoxicity. Future investigations should involve larger cohorts to confirm these findings and explore the clinical impact of LAD V_{40} exceedance.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Breast cancer is a major global health concern and remains the most prevalent cancer among women in Malaysia. According to the Ministry of Health Malaysia, breast cancer accounted for 17.7% of all cancer cases diagnosed between 2017 and 2021, establishing it as the leading cancer type in the country (*Management of Breast Cancer (Third Edition)*, 2019). This shows how important it is to discover safe and effective ways to treat the condition that not only control it but also reduce side effects.

At Hospital Pakar Universiti Sains Malaysia (HPUSM), breast cancer is the most commonly treated condition within the Radiotherapy Department. Patients undergo a comprehensive treatment strategy involving surgery, chemotherapy, and radiotherapy. Radiotherapy is essential in controlling tumor growth, decreasing recurrence rates, and enhancing overall survival rates. However, delivering radiotherapy precisely to the tumor while sparing surrounding healthy tissues remains a significant challenge.

For left-sided breast cancer patients, the proximity of critical organs such as the heart and the Left Anterior Descending (LAD) to the radiation field increases the risk of radiation-induced cardiac toxicity. The left main coronary artery and proximal LAD are frequently affected by radiation-induced coronary artery disease (CAD) because they are anterior and centrally positioned, meaning they receive larger radiation doses, according to a 2020 case report and review. Even in patients without conventional risk factors, this damage causes accelerated CAD, raising the possibility of serious cardiac events (Dogra et al., 2020).

Therefore, accurate delineation and dose assessment of the LAD are essential during radiotherapy planning.

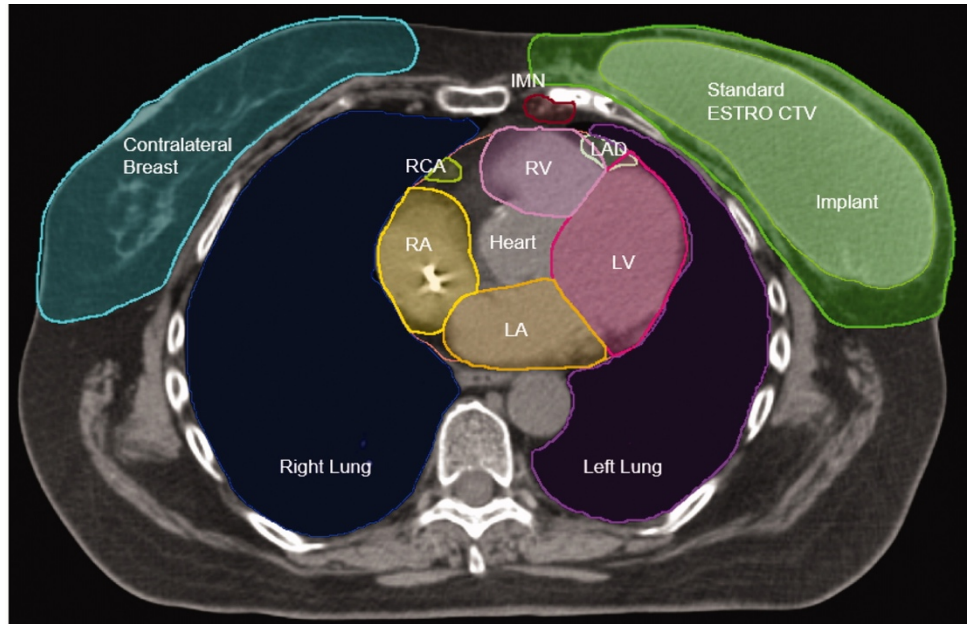


Figure 1.1: Transverse CT image showing LAD contouring (Milligan et al., 2021)

To enhance the precision of radiation delivery, HPUSM employs MV- orthogonal imaging for verification in breast cancer cases. This technique utilizes bony landmarks such as the rib cage and sternum for patient alignment, helping to reduce positioning errors and improve clinical outcomes. However, while MV-orthogonal imaging assists with setup accuracy, it does not provide real time tumor tracking or account for soft tissue movement. This limitation becomes particularly relevant in FB techniques, where respiratory motion can cause significant shifts in the position of critical structures such as the heart and the LAD, thereby increasing the risk of unintended radiation exposure.

A 2023 study by Taylor et al. demonstrated that both respiratory and cardiac motions influence the radiation dose received by the LAD, which is a well-established independent

predictor of major cardiac events. Furthermore, MV imaging alone is insufficient for ensuring precise dose delivery, as it lacks the ability to visualize and track soft tissue structures like the LAD in real time. This limitation was highlighted in a study by (Zhang et al. (2023) which introduced ionizing radiation acoustic imaging a real-time 3D dose mapping system. Their findings emphasized that relying solely on static bony landmarks, as in conventional MV imaging, fails to account for internal organ motion and anatomical variations, ultimately leading to dose delivery inaccuracies. Despite its limitations, MV-orthogonal imaging remains a standard tool in radiotherapy due to its practicality, availability, and ability to provide consistent anatomical reference points based on bony landmarks.

Therefore, the challenges posed by respiratory motion and the critical proximity of cardiac structures, especially the LAD artery, necessitate ongoing efforts to optimize radiotherapy techniques. Understanding the dosimetric impact of free breathing and enhancing LAD dose assessment are vital steps toward improving the long-term cardiac safety and overall outcomes for left breast cancer patients treated at HPUSM and similar centers.

1.2 Problem Statement

Although radiotherapy is essential for treating left-sided breast cancer and reducing recurrence, the heart's close proximity to the treatment area exposes it to incidental radiation, increasing the risk of late cardiac toxicity, a major cause of morbidity and mortality among survivors.

Standard radiotherapy planning typically treats the heart as a single OAR because contouring the entire heart on CT scans is relatively straightforward. However, relying solely on heart mean dose inadequately reflects the true risk of radiation-induced cardiac events, as it averages dose over the whole heart and overlooks dose heterogeneity within critical substructures (Hoppe et al., 2018).

Among these, the LAD is particularly vulnerable due to its anatomical position and vital role in myocardial perfusion. Emerging evidence shows that radiation dose to the LAD correlates more strongly with major adverse cardiac events than heart mean dose, largely because of its anterior location and critical function in supplying blood to the heart muscle (nurlu, 2022).

However, LAD contouring remains challenging in clinical practice due to its small size, complex course, and poor visibility on non-contrast CT scans. This difficulty, combined with the assumption that following general heart dose guidelines suffices, means the LAD is often not contoured or specifically assessed.

This lack of consistent LAD delineation and dose evaluation represents a significant gap in current radiotherapy planning, limiting accurate cardiac risk prediction and optimization of treatment to minimize long-term cardiovascular harm in breast cancer survivors. Addressing this gap is critical to improve cardiac safety in left breast radiotherapy.

1.3 Research Question(s)

1. Do the dosimetric parameters of tumor and cardiac structure in the left breast radiotherapy plans of the 35 patients meet the recommended tolerance levels as outlined in RTOG 0617 and DEGRO guidelines?
2. Is there a correlation between anatomical volumes (heart volume and LAD volume) and their respective dosimetric parameters (Heart D_{mean} , LAD D_{mean} , and LAD V_{40}) in left breast radiotherapy?
3. What is the correlation between the heart mean dose and LAD-specific dosimetric parameters (LAD D_{mean} and LAD V_{40})?

1.4 Study Objective

1.4.1 General Objective

To evaluate the dosimetric impact of free breathing left breast radiotherapy on the cardiac structures in Hospital Pakar Universiti Sains Malaysia (HPUSM).

1.4.2 Specific Objective

1. To evaluate the dosimetric parameters of the tumor and cardiac structure (heart and LAD) for left breast planning technique using RTOG 0617 and DEGRO tolerance
2. To assess the correlations between anatomical volumes (heart volume and LAD volume) and their respective dosimetric parameters (Heart D_{mean} , LAD D_{mean} , and LAD V_{40}) in left breast radiotherapy.
3. To correlate the heart mean dose and LAD specific dosimetric parameters (LAD D_{mean} and LAD V_{40}).

1.5 Significance of Study

Radiotherapy is vital for left-sided breast cancer treatment but poses a risk of radiation-induced cardiac toxicity, especially to the LAD, a critical vessel near the treatment area. While advanced techniques like DIBH reduce heart doses, FB radiotherapy remains common due to its simplicity, though it may increase variability in LAD dose exposure and cardiac risk.

This study focuses on assessing the dosimetric impact of FB left breast radiotherapy on the heart and LAD, addressing the gap in routine LAD dose evaluation despite evidence linking LAD dose parameters to cardiac morbidity. By comparing dosimetric data with established guidelines, the research aims to improve cardiac risk prediction and inform treatment optimization, ultimately enhancing cardiac protection in clinical practice at HPUSM and similar centers.

CHAPTER 2

LITERATURE REVIEW

2.1 Clinical Significance of Protecting Organs at Risk in Left Breast Radiotherapy

Radiotherapy is an essential component of breast cancer management, particularly after breast-conserving surgery or mastectomy for left-sided disease. However, the anatomical proximity of the heart, left lung, and LAD to the left breast introduces a persistent challenge on how to deliver an effective tumoricidal dose while minimizing exposure to these critical organs at risk (OARs). The clinical significance of this challenge has grown as breast cancer survival rates improve, making long-term treatment-related morbidity an increasingly important consideration.

Among these, the heart is especially vulnerable during left breast radiotherapy. Multiple large cohort studies have documented a clear dose-response relationship between mean heart dose and subsequent cardiac morbidity and mortality, demonstrating that even modest increases in heart dose correlate with a heightened risk of major coronary events. For instance, Hussein et al. (2025) reported a mean heart dose of 6.4 Gy during FB radiotherapy in a cohort of 60 patients. Although this dose falls within some recommended guidelines, it remains associated with a non-negligible risk of late cardiac toxicity. Notably, the mean LAD dose in the same cohort was reported at 20.5 Gy a dose of particular concern given the LAD's crucial role supplying the anterior myocardium and its documented sensitivity to radiation-induced atherosclerosis.

As breast cancer survival rates continue to improve, awareness of the long latency period of radiation-induced heart disease which can manifest a decade, or more post-treatment further underscores the clinical imperative to minimize cardiac exposure. Late cardiac sequelae, including ischemic heart disease, pericarditis, and arrhythmias, exhibit a dose-dependent incidence, motivating efforts to optimize radiotherapy planning.

2.2 Clinical and Dosimetric Implications of LAD Exposure

Building upon the established significance of overall cardiac dose, growing evidence identifies the LAD artery as a particularly sensitive and clinically relevant OAR. Its anterior anatomical position often places it directly within tangential radiation fields used for breast irradiation, exposing it to potentially higher doses compared to whole heart dose metrics.

Clinical investigations have consistently demonstrated a dose-response relationship linking LAD radiation exposure to increased risks of coronary artery stenosis, myocardial ischemia, and major adverse cardiac events. For example, (Hoppe et al., 2018) reported that patients receiving LAD doses exceeding 20 Gy experienced a fivefold increased risk of radiation-induced coronary stenosis and higher rates of coronary interventions. Prospective LAD delineation and dose optimization protocols have been shown to significantly reduce radiation doses to the artery without compromising tumor coverage one such study by Vayntraub et al. (2021) demonstrated statistically significant reductions in median mean and maximum LAD doses through prospective LAD contouring.

Given these findings, routine LAD contouring should be incorporated into clinical radiotherapy planning. Accurate LAD delineation allows precise dosimetric evaluation, enabling optimization strategies such as advanced beam arrangements and intensity modulation to more effectively spare the LAD while maintaining sufficient tumor coverage.

2.3 Factors Contributing to High Dose of LAD in Free Breathing Left Breast Radiotherapy

Respiratory motion is a primary contributor to the variability and elevation of LAD dose in FB radiotherapy. The heart and LAD artery move dynamically during the breathing cycle, causing shifts in their position relative to the radiation fields. This motion leads to fluctuating dose distributions that static planning CT scans may not fully capture, resulting in underestimation of the true LAD dose (Poitevin-Chacón et al., 2018). The displacement of the LAD during free breathing can be several millimeters, which is significant given the artery's small size and proximity to the chest wall.

The LAD artery lies immediately adjacent to the anterior chest wall and often overlaps with the tangential fields used in left breast radiotherapy. Tumor location, breast size, and shape influence the spatial relationship between the LAD and the radiation field. Larger breast volumes or tumors located medially or deeply increase the likelihood of the LAD receiving higher doses (Diremsizoglu et al., 2025). This proximity makes the LAD vulnerable to incidental radiation, especially when respiratory motion is not controlled.

The LAD is a small, narrow, and elongated structure, with typical volumes ranging from approximately 1.5 to 3.0 cm³ (Rao et al., 2024). Its small size makes it highly sensitive to contouring variability and imaging resolution. Minor differences in delineation or CT slice

thickness can significantly affect dose calculations. Additionally, the small volume means that high doses to even a limited segment of the LAD can have clinically significant consequences, as focal damage to the artery can precipitate symptomatic coronary artery disease (Wennstig et al., 2019)

The choice of radiotherapy technique and planning parameters also impacts LAD dose. Plans that do not explicitly include the LAD as an OAR may deliver higher doses to the artery. Advanced planning techniques such as volumetric modulated arc therapy (VMAT) with LAD and left ventricle (LV) sparing have been shown to significantly reduce cardiac doses without compromising tumor coverage (Diremsizoglu et al., 2025). However, centers relying solely on FB without motion management or LAD-specific constraints may face challenges in adequately sparing the LAD.

Recent clinical data highlight the importance of volume-based dose metrics such as LAD V_{15} Gy and LAD V_{40} Gy. The German Society for Radiation Oncology (DEGRO) recommends LAD $V_{40} < 1\%$ to minimize coronary artery disease risk (Piroth et al., 2019). These metrics capture the extent of high-dose exposure within the LAD, which is more predictive of cardiac toxicity than mean dose alone.

2.4 Clinical Findings on Correlation of Heart Dose and LAD Dose

Multiple clinical studies have consistently demonstrated that radiation dose to the LAD correlates more strongly with cardiac morbidity and mortality than heart mean dose alone. This distinction is critical because patients whose heart mean dose values fall within accepted constraints may still receive clinically significant doses to the LAD, thereby increasing their risk of radiation-induced cardiac events.

Tagami et al. (2021) performed a large-scale screening of 6,593 breast cancer patients treated with radiotherapy using coronary computed tomography angiography (CCTA). They found that patients with left-sided breast cancer had significantly higher rates of CAD in the LAD (76%) compared to right-sided cases (31%, $p < 0.001$). Importantly, mean LAD radiation dose and heart mean dose were strongly correlated with the incidence of CAD, with a 21% higher incidence of disease specifically in the LAD territory among those receiving higher doses.

The study by Garg and Kumar (2022) provides important clinical insights into the dosimetric differences between the whole heart and the left anterior descending (LAD) artery in patients with left-sided breast cancer undergoing radiotherapy. Their comparison of three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) revealed that while both techniques aim to minimize cardiac exposure, the LAD artery often receives a higher and more heterogeneous dose than the heart mean dose suggests.

In the reanalysis of the NRG Oncology/RTOG 0617 trial, it was demonstrated that a left anterior descending (LAD) coronary artery volume receiving 15 Gy or more (LAD V15 Gy $\geq 10\%$) is independently associated with an increased risk of all-cause mortality. Specifically, patients with LAD V15 Gy $\geq 10\%$ had a hazard ratio of 1.43 (95% CI, 1.02–1.99; $P = .037$) for all-cause mortality compared to those with LAD V15 Gy $< 10\%$. In contrast, mean heart dose (MHD) ≥ 10 Gy was not significantly associated with mortality risk (adjusted HR, 1.12; 95% CI, 0.88–1.43; $P = .36$). The median overall survival was shorter for patients with higher LAD doses (20.2 months) compared to those with lower doses (25.1 months), with 2-year survival estimates of 47% versus 67%, respectively ($P = .004$). These

findings emphasize the critical importance of incorporating cardiac substructure dose constraints, particularly for the LAD artery, into radiotherapy planning to improve cardiac risk stratification and patient outcomes (McKenzie et al., 2023).

2.5 RTOG 0617 Protocol and DEGRO Recommendations for Cardiac Dose Constraints

The Radiation Therapy Oncology Group (RTOG) 0617 trial, initially designed for locally advanced non-small cell lung cancer (NSCLC), has become a pivotal reference for cardiac dose constraints in thoracic radiotherapy, including applications in left breast cancer radiotherapy. The trial demonstrated a significant association between cardiac radiation dose and overall survival, underscoring the critical importance of minimizing heart exposure during treatment to improve patient outcomes.

2.5.1 Heart Dose Constraints

RTOG 0617 established key dose-volume constraints for the whole heart aimed at reducing cardiac toxicity and enhancing survival. Specifically, the volume of the heart receiving at least 5 Gy (V_5) and 30 Gy (V_{30}) were found to correlate significantly with overall survival, with higher volumes linked to worse outcomes. The protocol recommended limiting the heart V_{30} to less than 100%, with subsequent protocols applying even more stringent constraints. Additionally, heart mean dose was identified as a critical factor, with evidence showing that each 1 Gy increase in mean heart dose raises the risk of major adverse cardiac events by approximately 7.4% (Chun et al., 2017). These constraints, while developed for

lung cancer, are also applicable to left breast cancer radiotherapy due to similar concerns regarding cardiac exposure.

2.5.2 LAD Dose Considerations

Although RTOG 0617 primarily focused on whole heart dose, reanalysis of the trial data revealed that doses to cardiac substructures, particularly the LAD, are more predictive of cardiac outcomes than mean heart dose alone. Elevated LAD doses have been independently associated with increased all-cause mortality and cardiac events. Specifically, a LAD volume receiving 15 Gy or more (LAD V15 Gy) of 10% or greater was linked to poorer survival outcomes (McKenzie et al., 2023). This finding highlights that even when heart mean dose constraints are met, elevated LAD doses can still confer significant cardiac risk, emphasizing the necessity of LAD-specific dose constraints in treatment planning.

Complementing RTOG 0617, the German Society for Radiation Oncology (DEGRO) provides specific and stringent dose constraints for the LAD artery to minimize radiation-induced coronary artery disease, particularly relevant in breast cancer radiotherapy. DEGRO recommends that the volume of the LAD receiving 40 Gy or more (LAD V₄₀) should be kept below 1% to reduce the risk of coronary artery stenosis and subsequent cardiac morbidity (Piroth et al., 2019). This constraint focuses on limiting high-dose exposure to small volumes of the LAD, which is critical given the artery's small size and vulnerability. Volume-based metrics like LAD V₄₀ are considered more predictive of cardiac toxicity than mean dose alone.

CHAPTER 3

METHODOLOGY

3.1 Research Tools

3.1.1 Eclipse Treatment Planning System

The treatment planning process for this study was conducted using the Eclipse Treatment Planning System (TPS), version 14. Developed by Varian Medical Systems, Palo Alto, California, USA. Eclipse TPS in Figure 3.1 is a widely utilized, clinically validated software platform designed for comprehensive radiotherapy treatment planning. It supports various external beam modalities, including three- dimensional conformal radiotherapy (3D-CRT), intensity- modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and stereotactic body radiation therapy (SBRT).

For this research, Eclipse was employed specifically for the generation and evaluation of 3D- CRT plans in left- sided breast cancer patients. The systems integrate advanced dose calculation algorithms, image registration capabilities, and detailed anatomical modeling to ensure accurate and reproducible treatment planning. In this study, Anisotropic Analytical Algorithm (AAA) was utilized for dose calculations due to its proven accuracy in heterogeneous tissues, which is essential in breast cancer where anatomical variations can significantly influence dose distribution.

The planning process began with the importation of computed tomography (CT) simulation images into Eclipse. These images were used for contouring of the target volume and OAR (OARs), which were delineated in accordance with the guideline set forth by the

Radiation Therapy Oncology Group (RTOG) and institutional protocols. The clinical target volume (CTV), planning target volume (PTV) and critical structures such as the heart, ipsilateral lung, contralateral breast, and spinal cord were carefully outlined.

Eclipse provides a suite of optimization tools and dose visualization features, allowing for iterative refinement of beam configurations, gantry angles, field arrangements, and multi- leaf collimator (MLC) shapes. For each patient, treatment plans were generated using tangential photon beams, with beam energy typically 6 MV. This system enabled evaluation of dosimetric parameter including dose- volume histogram (DVH), conformity index (CI), homogeneity index (HI), and coverage statistics.

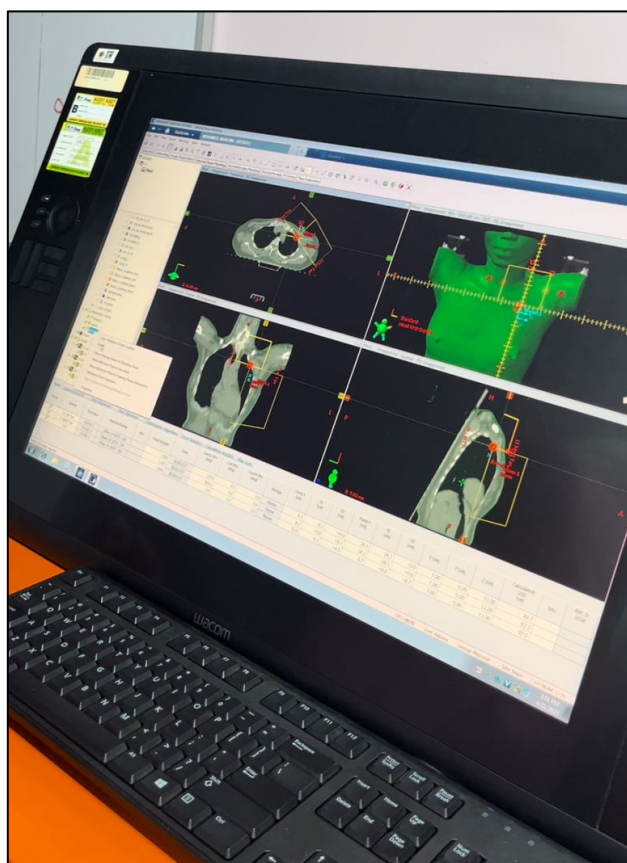


Figure 3.1: Eclipse TPS (V. 14) (Varian Medical Systems, Inc. Palo Alto CA, USA)

3.1.2 IBM Statistical Package for the Social Sciences SPSS Statistics (SPSS) Statistics

This study used IBM (International Business Machine) SPSS (Statistical Package for the Social Sciences) Statistics (Version 27) as shown in the Figure 3.2 for further descriptive and statistical analysis. This software analysed all selected data that passed the inclusion and exclusion criteria. The spreadsheet of raw data is as in (Appendix B). The selected data were imported from the Excel datasheet into the SPSS. The descriptive and statistical analysis was performed for dosimetric parameters of cardiac structure.



Figure 3.2: IBM SPSS Statistics Interface (V. 27)

3.2 Methodology

3.2.1 Ethical Clearance

This retrospective study was involved the secondary data of 3- D CRT treatment planning of stage I, II and III left breast cancer patients that had been treated at HPUSM from January 2024 to December 2024. The data were collected at Department of Nuclear Medicine, Radiotherapy and Oncology at HPUSM. Ethical clearance in (appendix A) was obtained as a condition for research that proposes to involve human participants as sources of data by submitting the Research Ethics Clearance (REC) application forms electronically with a follow- up softcopy that reflects the necessary signature to the Human Research Ethics Committee USM (JEPeM). This clearance form was submitted about three to six months earlier before starting the research to get the granted ethical clearance and statement from the ethical committee. The granted date was from 12th February 2025 to 11th February 2026.

3.2.2 Patient's Data Selection

Purposive sampling method was used in the process of the patient's data selection as it is one of the most cost- effective and timesaving sampling methods as it is requiring less fieldwork. The total number of left breast cancer cases at HPUSM form January 2024 to December 2024 was approximately 120 patients. However, only 35 patients met the inclusion and exclusion criteria. In this study, the registration number (RN) of 35 left breast cancer patients that had been diagnosed with stage I to III and using 3D- CRT treatment planning technique at HPUSM from January 2024 to December 2024 were listed and their treatment planning were assessed. The inclusion and exclusion criteria of this study as stated below:

- i) The inclusion criteria
 - a) The prescription dose should be 40 Gy per 15 fractions
 - b) Patients who received supraclavicular fossa (SCF) irradiation, alongside those who did not.

- ii) The exclusion criteria

Patients with incomplete dosimetric data, including those lacking left anterior descending artery (LAD) delineation in the treatment planning system, were excluded from the analysis to ensure consistency and accuracy in the evaluation of organ-at-risk dose parameters.

3.2.3 CT Simulation Procedure

All patients underwent CT simulation in the supine position using a breast board immobilization system to ensure accurate and reproducible positioning. Prior to the procedure, the patient's identity was verified using name and registration number (RN). The patient was briefed by the radiation therapist about the simulation process, and informed consent was obtained after addressing any concerns. The patient was instructed to remove all metal objects from the chest region and change into a hospital gown to avoid imaging artefacts.

During setup, the breast board (Figure 3.3) was placed on the CT couch, with adjustments made to optimize chest exposure and patient comfort. The patient was positioned lying on their back, with both arms raised above the head and supported using arm rests to

adequately expose the chest wall and axillary region. The left breast was allowed to fall naturally, avoiding any skin folds or compression that might affect dose accuracy. Room lasers were used to align the patient with external anatomical landmarks, and temporary markers were placed on the midline and lateral chest to assist in accurate positioning. Ball bearings (BBs) were also placed externally on the skin to provide visible reference points on the CT images, which are important for verifying the isocenter and assisting with accurate patient setup during treatment planning and delivery.



Figure 3.3: Breastboard (MT-350) (CIVCO Radiotherapy, USA)

An anterior scanogram was acquired to verify the patient's alignment and define the appropriate scan range. The CT scan was then conducted under free breathing conditions, where the patient was instructed to breathe normally throughout the procedure. Once image quality and positioning were confirmed, skin tattoos were applied at superior, inferior,

medial, and both lateral regions using black ink injected into the skin with a sterile needle, serving as semi-permanent reference marks for daily treatment setup. A CT simulation chart was completed to document all relevant positioning information. Finally, the acquired DICOM images were transferred to the RayStation Treatment Planning System (TPS) for contouring of organs-at-risk.

3.2.4 Treatment Planning for Left Breast Cancer

3.2.4 (a) Contouring Procedure using RayStation TPS

Following CT simulation, all image datasets were transferred to the RayStation TPS (Figure 3.4) for structure delineation and preparation for treatment planning.

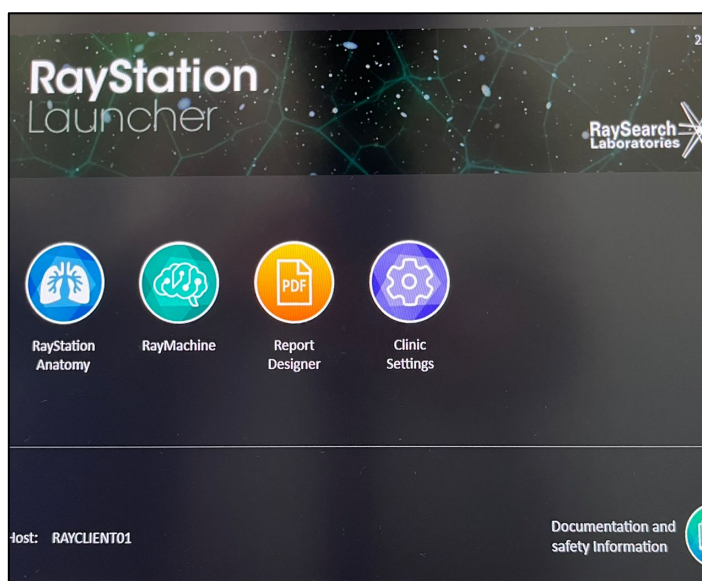


Figure 3.4: RayStation TPS (V. 2024B) (RaySearch Laboratories, Sweden)

The radiation therapist was contouring the majority of organs at risk (OARs), including the heart, ipsilateral lung, contralateral lung, spinal cord, and external body contour, using the system's deep learning auto-segmentation tool. This tool leverages artificial intelligence algorithms to provide rapid and standardized anatomical segmentation, thereby improving efficiency and reducing inter-observer variability.

However, it is important to note that not all OARs are available in the system's auto-contouring library. Specifically, the left anterior descending artery (LAD) was not auto-contoured and therefore required manual delineation by the medical physicist after the dataset was imported into the Eclipse Treatment Planning System (TPS). LAD contouring was performed using anatomical landmarks on CT images and based on standardized reference guidelines, as accurate delineation of the LAD is critical for evaluating potential cardiac toxicity, particularly in left-sided breast radiotherapy.

All auto-generated contours were thoroughly reviewed for accuracy and clinical appropriateness. In particular, the external body contour often included non-patient structures such as the breast board, which appeared on the CT scan. This necessitated manual editing to exclude the breast board and retain only the true anatomical outline of the patient, ensuring precise dose calculation. Additional discrepancies such as contour misalignment, incomplete boundaries, or structural overlap were corrected manually in accordance with institutional contouring protocols.

Once all required structures were reviewed and finalized, the contours were imported into the Eclipse TPS, where target volumes were manually delineated by the radiation oncologist based on clinical judgment and standard breast radiotherapy guidelines. The

finalized dataset was then used by the medical physicist for treatment planning and dosimetric evaluation.

3.2.4 (b) Treatment Planning using Eclipse TPS

Treatment planning was conducted using the Eclipse Treatment Planning System (Version 14, Varian Medical Systems) for all left breast cancer patients in this study. The process began with beam arrangement and field setup, which included the creation of two opposing tangential fields medial and lateral to cover the entire left breast. These tangential fields were angled obliquely from anterior directions to conform to the chest wall while minimizing radiation exposure to the heart, contralateral breast, and ipsilateral lung. Beam borders were opened according to patient-specific anatomy. For the breast tangents, the superior border was placed just below the inferior edge of the clavicle. The inferior border extended 2 cm below the inframammary fold to ensure adequate coverage of the inferior breast tissue. The lateral border extended just 2 cm of the opening air from the nearest breast tissue to the field.

For patients requiring supraclavicular fossa (SCF) irradiation, an additional anterior SCF field was created. The superior border of this field was aligned at the level of the thyrocricoid groove, while the inferior border matched the superior border of the breast tangents. The medial border was placed at midline near to the spine, and the lateral border extended to the tip of the lateral edge of the humeral head. To avoid beam divergence at the junction between the SCF and breast fields, the half-beam block technique was used. In this setup, the SCF field was blocked inferiorly, and the medial breast field was blocked

superiorly, using asymmetric jaws or non-divergent collimation. This ensured a seamless match between the fields and prevented overdose or underdose at the junction.

For breast-only treatments, the isocenter was positioned centrally within the breast volume, typically at the midpoint between the medial and lateral tangents. This allowed symmetric setup of tangential fields and ensured balanced dose distribution across the breast.

For breast with SCF plans, the isocenter was placed at the junction (match line) between the breast and SCF fields. This strategic positioning enabled the application of the half-beam block technique, ensuring non-divergent field edges at the superior aspect of the tangents and inferior edge of the SCF field, thus avoiding dose overlap or cold spots.

A normalization point was then selected within the PTV, ideally located in a region of homogeneous tissue, avoiding build-up regions or lung interfaces. The plan was normalized such that 100% of the prescribed dose 40 Gy in 15 fractions (2.67 Gy per fraction) corresponded to this point. This hypofractionated schedule aligns with national and international protocols for early-stage breast cancer.

To enhance dose uniformity and improve target coverage, multileaf collimators (MLCs) were manually adjusted to match the PTV shape while sparing nearby organs-at-risk (OARs). Field-in-field (FIF) segments were added to modulate the dose in high-dose regions and eliminate hotspots. Dose calculation was performed, then each plan was rigorously evaluated.

3.2.4 (c) Dosimetry Analysis

Following dose calculation, each treatment plan underwent comprehensive evaluation to ensure it met both target coverage goals and organ-at-risk (OAR) sparing criteria. For target volume assessment, it was required that at least 95% of the Planning Target Volume (PTV) received a minimum of 95% of the prescribed dose, ensuring adequate and uniform dose distribution throughout the breast. The maximum dose ($D_{\max}$) was also reviewed, with the acceptable limit set at no more than 107%–110% of the prescribed dose. Attention was given to regions prone to dose inhomogeneity, particularly areas influenced by tissue density variation or overlapping field-in-field (FIF) segments.

A Dose-Volume Histogram (DVH) analysis was conducted (Figure 3.5) to assess dose distribution across both the PTV and surrounding OARs. Specific dosimetric parameters were evaluated against established constraints to minimize potential treatment-related toxicity. For the heart, D_{mean} was ideally kept below 20 Gy to reduce the risk of late cardiac complications. The LAD, a critical substructure of the heart, was closely monitored, with the $D_{\max}$ aimed to be under 40 Gy, and volume-based constraints such as LAD V_{40} were kept as low as possible preferably <1% to reduce the risk of coronary artery damage based on DEGRO. These dosimetric evaluations were guided by institutional protocols and tolerance limits recommended by international guidelines such as RTOG and DEGRO, ensuring both effective tumor control and optimal protection of normal tissues.