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Assessment of radiation doses for cardiac and left anterior descending coronary artery in patients undergoing Left breast radiation therapy in Palestine

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Assessment of radiation doses for cardiac and left anterior descending coronary artery in patients undergoing Left breast radiation therapy in Palestine

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Dedication

I would like to present this work to my little Angel for giving me all the inspiration and support I need.

To all of those around me, who have always been with their support and love.

A special thanks for all of the world's patients who suffer from radiotherapy sessions and post-treatment complications, who inspired me and other to provide like this studies.

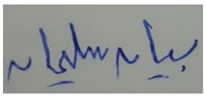
Bayan Suliman

Declaration

I hereby declare that this thesis represents my own work which has been done after registration for the degree of Master degree at Al-Quds University, and has not been previously included in a thesis or dissertation submitted to this or any other institution for a degree, diploma or other qualifications in Palestine.

This research, obtained the relevant ethical approval by the scientific Committee of Augusta Victoria Hospital, and acknowledged my obligations and the rights of the participants**.**

Bayan Saleh Ali Suliman

Signed: 

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Bayan Suliman

Assessment of radiation doses for cardiac and left anterior descending coronary artery in patients undergoing Left breast radiation therapy in Palestine

Abstract

Purpose: To evaluate radiation doses in cardiac radiotherapy planning in left breast cancer patients using 3D conformal radiotherapy planning technique based on computed tomography (CT) dose planning.

Methods: Data was retrospectively collected from archived Computed Tomography (CT) images, whole heart and left anterior descending coronary artery (LAD) radiation doses at Augusta Victoria Hospital (AVH) between 2017-2019. Data composed of 176 breast cancer radiotherapy cases; 70 chest wall irradiated mastectomies patients, and 106 breast irradiated lumpectomies patients.

Individual dose volume histograms for the whole heart and for LAD were obtained, in addition to the calculated mean, median and maximum volume percentage (V10%, V25%, V30%) of these structures for the study sample which represents the percentage of heart volume receiving (x) Gy or higher, then compared to the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) guidelines and previous studies for dose assessment of heart and LAD.

Represents the percentage of an organ's volume receiving (x) Gy or higher

Results: Results showed the whole mean heart dose (MHD) and the mean dose of LAD were 2.2 Gy and 13.94 Gy, respectively. In which, 4.5% of patients received MHD ≥ 4Gy, all subjects received V25% less than 10cm expect one V25% ≥ 10. 11 % of patients received LAD maximum dose ≥ 45 Gy. In spite of the dose variations found in both MHD and LAD in this study, and the dose differences noticed when compared to studies that used other radiotherapeutic techniques such as Deep Inspiration Breath Hold technique (DIPTH), MHD and LAD dose assessments were equivalent to those of the compared previous studies and Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) guidelines.

Conclusions: Dose assessments of adjuvant CT-based radiotherapy of subjects with left breast cancer demonstrated similar MHD but higher LAD doses when compared to previous studies and QUANTEC guidelines used to predict cardiac toxicities in most patients in the study sample.

Since there is no worldwide standardized protocol or heart dose constrains in left breast radiotherapy, this study suggests maintaining the lowest received dose and volume of the heart or organ at risk included in the treatment plan, as well as using advanced techniques

as DIPH to reduce the latent effects on radiotherapy patients, especially the heart complications that could occur.

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List of Abbreviations and Units

Abbreviation	Meaning
APBI	Accelerated partial breast irradiation
BED	Biological effective dose
CAD	Coronary artery disease
CT	Computed tomography
CTV	Clinical target volume
3D-CRT	Three-Dimensional ConFormal Radiotherapy
DIBH	Deep inspiration breathing hold technique
D_{mean}	The average dose delivered to an organ
DVH	Dose volume histograms
FB	Free breathing
Gy	Gray the SI unit of absorbed radiation
IM	Internal mammary
IMN	Internal mammary lymph nodes
IMRT	Intensity modulated radiotherapy
LAD	Left anterior descending coronary artery
LV	Left ventricle
MHD	Mean Heart Dose
MV	Mega volts
NTCP	Normal Tissue Complication Probability
OAR	Organ at risk
PTV	Planning target volume
QUANTEC	Quantitative Analyses of Normal Tissue Effects in the Clinic
RRHD	Radiation related heart disease
RT	Radiotherapy
SC	Supraclavicular
s-IMRT	Simple IMRT
TPS	Treatment planning system
$V_{(xGy)}$	Represents the percentage of an organ’s volume receiving (x) Gy or higher.

Chapter One:
Introduction

1.1 Introduction

Breast cancer is the most common cancer among women worldwide and the second leading cause of cancer death **(Ghoncheh et al. 2016, Rojas et al. 2016, Torre et al.2015).**

The breast radiotherapy treatment (RT), combined with breast surgery have shown to be the most adequate treatment used today for treating ssubjects with breast cancer. RT has a major role in the management of breast cancer by reducing the rates of recurrence, and the death from breast cancer. It also improves the overall survival rate for both early stage breast cancer after breast conserving surgery and locally advanced disease after mastectomy **(Carmel at al. 1976, Kivanc et al. 2019).**

Although most breast cancer patients can be cured of their disease, there is a risk of long term hazards of RT, which needs to be under focus. Especially, the irradiation of the heart and lung in left-sided breast RT, which are linked with an increased risk of cardiac events, pneumonitis, lung fibrosis and secondary lung cancer **(Darby et al. 2010, Finazzi et al. 2019, Taylor et al.2017)**. One of the most difficulties and challenges that face radiation oncology, is the unavoidable risk to the normal and surrounding tissues, which needs special attention when irradiating the breast, such as the chest wall (CW) and regional lymphatics including supraclavicular (SC), axillary, and internal mammary (IM) lymph nodes to the doses of organ at risk (OAR) surrounding the tumor, as the lungs, heart, and the opposite breast tissue.

The history of recognizing heart damages caused by radiation doses appeared in the 1960s. Previously, the heart was considered a radio-resistant organ that would be unaffected by cardiac doses below ~30 Gy. However, since then, many studies of breast cancer patients who received mean cardiac doses of 3–17 Gy when given radiotherapy of Hodgkin lymphoma, and studies on atomic bomb survivors in Japan, who received doses of up to 4 Gy, showed that radiation-related heart disease (RRHD) can occur following lower doses.

At higher RT doses, the RRHD may occur within a year or two or above 10 years of exposure,

meaning the risk increases with younger age at irradiation in addition to the presence of conventional risk factors, while latent period is much longer at lower RT doses. Additionally, the RRHD includes many conditions of pathological expressions such;

pericarditis, pericardial fibrosis, diffuse myocardial fibrosis, and coronary artery disease (CAD). Today the RRHD (as pericardial and myocardial diseases) are less common due to the development of techniques and modifications in breast RT, while the frequency of CAD is of the highest (**Carmel at al. 1976, Darby et al. 2010**). In the history of left breast RT, the range of heart doses received recently are generally lower resulting from the related developments of techniques, energy beam, target doses, different volumes, and contouring modalities, yet the heart in most women still receives doses of 1 to 5 Gy. Some trials suggested that exposures at this level can cause ischemic heart disease, but at any given dose, there were uncertainties of the magnitude of risk to the heart. Moreover, it could be to developed at a younger age and often in patients without risk factors (**Whelan et al.2015, Henson et al. 2013**).

The damages related to RRHD can occur following therapeutic irradiation, which can cause a microvascular and macrovascular damage through indirect secondary effects; including acute and delayed pericarditis, pancarditis with both pericardial and myocardial fibrosis, CAD, and valvular disease. Although it is not known whether a high radiation dose to a small volume, or the lower average dose to the whole heart is responsible for cardiovascular effects, the risk of cardiac events in early RT-treated breast cancer patients is related to both dose and irradiated heart volume.

In breast irradiation, for the purpose of curative or palliative treatment, 80% of cancer patients need radiotherapy at some time or other (**Taylor et al. 2007**). Cardiac damage relates to the heart absorbed dose, therefore, the optimum results of radiotherapy treatment requires a judicious balance between the total dose of radiotherapy delivered and the threshold limit of the surrounding normal critical tissues, hence, normal tissues should be protected against radiation injury, especially the critical and sensitive organs that may exist surrounding the target. This reinforces the need to understand the biological effects caused by radiation to cancer and normal cells, also the expected complications after radiation treatment. During breast irradiation, there is a risk of pneumonitis, lymphedema, cardiac disease, and late secondary neoplasms from the radiation therapy especially for women with left-sided breast cancer.

Many studies have shown a difference in cardiac damage between the right and left breast radiation therapy, as It was greater in left breast RT. Also, it was shown that cardiac mortality was 16% higher in women with left-sided breast cancer compared with women with right sided breast cancer. The current average mean heart dose is likely to be around

2–7 Gy for left-sided, and around 1.5 Gy for right-sided breast cancer radiotherapy (**Henson et al. 2013,Taylor et al.2008**). Moreover, some trials compared the outcomes of treatment between the irradiation of whole-breast alone and in addition to the regional lymph node, which shows that the irradiation of whole-breast with regional node may increase the risks of pneumonitis, lymphedema, cardiac disease (**Henson et al. 2015**). There are many uncertainties remain regarding the region of the heart most important for RT-induced toxicity. Studies focused on radiation-induced abnormalities of the heart show the most significant radiation-induced damages are coronary and myocardial. In this context, several recent studies segment the heart focusing on some arteries to evaluate the dose distribution and occurring damages as in the left ventricle and the left anterior descending artery (LAD).

Notably, numbers of trials have shown different segments of heart differ in their radiational absorption rate due to inhomogeneous of heart structures in distributions and of beam heterogeneity. Moreover, there is a lack in radiotherapy guidelines of heart structures segment doses, and the sensitivity of each segment to radiation, raising the need to follow the safest possible strategy to minimize dosages to all segments. Similarly, Some studies focused on the estimates of cardiac exposure demonstrated the greatest radiation doses were received by the anterior part of the heart and the left anterior descending coronary artery, which are common sites of atherosclerosis causing myocardial infarction. Irradiation of these structures might have contributed to the excess risk of death from heart disease. As a result, recommendations have been made determining segmental and regional RT doses to the left ventricle to help in guiding the focus in diagnostic cardiology in the post radiotherapy settings (**Whelan et al.2015**, **Walston et al.2017**).

The Modern techniques of treatment focuses on reducing the heart volume and coronary vessels included in the treatment volume. Still, it is difficult to completely avoid cardiac irradiation and the segment of LAD coronary artery within the treatment volume, which are frequently included **(Stewart et al.2010, Sardaro et al.2012).**

Recently, many attempts and strategies were used to mitigate radiation-induced heart damage, to focus on reducing the cardiac volume in the radiation field. With the development in the fields of radiation physics and radiation technology, several new techniques have been developed to better cover the breast and internal mammary lymph nodes (IMN) drainage area, or reduce exposure dose to heart without compromising radiation dose to the breast, which optimizes target coverage and reduction of exposure dose to heart are major challenges for patient care.

Also, Radiotherapy techniques have changed. In comparison to the previous decade's irradiation of the breast or chest wall, the recent irradiated volume of the heart decreased from 87% for older radiotherapy to 41% for more recent radiotherapy (**Henson et al.2013**). At the same time, many studies discussed the comparisons between techniques most commonly used in current breast cancer radiotherapy, such as breath hold techniques, prone positioning, intensity-modulated radiation therapy(IMRT), and accelerated partial breast irradiation (APBI), as well as techniques to improve traditional three-dimensional conformal radiation therapy (3D-CRT) (**Yorke et al.2017**).

Several research centers discussed the different clinical techniques, in which the anatomical position of the breast and chest wall are kept stable so that therapeutic effects are guaranteed. Currently, tangential radiotherapy is the standard of breast cancer radiotherapy techniques in most radiotherapy centers, in which most women are irradiated for breast cancer using tangential radiotherapy after breast surgery, this method of treatment is considered of little harm on treated women.

However, in some countries, left tangential radiotherapy still delivers higher heart doses of several Gray (Gy) with a chance of increasing in the future. Recent studies show that the survival rate of breast cancer will increase by including internal mammary lymph node (IMN) to the irradiated region, even though it is difficult to irradiate IMN without incidentally irradiating the heart. The differences of thoracic anatomy among women gives additional unavoidable radiation dose received by the heart. As a result, it is difficult to achieve full tumor dose coverage without exposing the heart during breast irradiation, as well as other tumor types laying close to the heart; such as: lymphoma, lung cancer, and esophageal cancer (**Zhang et al.2015, Taylor et al. 2018**).

The deep inspiration breath-hold (DIBH) technique is one of strategies that are used recently during breast RT. This technique decreases the heart dose by reducing the heart volume which receives a significant radiation dose, through increasing the distance from the target volume to the heart. This is accomplished by using an active breathing control (ABC) device that moderates the breathing cycle by controlling the lung volume. Furthermore, this technique and prone positioning nearly reduced mean heart dose to less than 2 Gy, regardless of breast volume **(Tang et al. 2019, Mulliez et al. 2015).** However, DIBH was not favorable in some cases as it needs a team training on ABC usage, additional imaging, and longer procedural time in the treatment unit. Moreover, it requires patient-staff coordination and high patient tolerance. The BH technique should prove being dosimetrically beneficial compared to the standard technique, since in some cases, the body habitus and thoracic geometry may be moving toward a small amount of cardiac radiation dose with standard tangential photon beams.

While generalized decreased cardiac function has been generally reported, some studies in this review have specifically shown decreased left ventricular or (LAD) function or perfusion after radiation **(Taylor et al. 2018, Meattini et al. 2017).**

Based on foregoing, the purpose of this work is to assess the radiation doses delivered to the heart and the LAD during left sided breast cancer patients treated with tangential breast radiotherapy, especially since there is a lack of similar studies in this filed in Palestine.

1.2 Problems Statement

There is increasing incidences of side effects related to RT of the left breast, especially the cardiac disease. Even though there is a variety of radiation therapy techniques and modalities used for left breast RT, there is an increasing trend in heart diseases as a side effect for left breast RT. Radiation oncologist not only worry about survival rate following breast RT, but also from its consequences in the coming latent period **(Chang et al.2019, Lee et al.2017).**

It can be stated that there is a lack of radiation dose assessment for patients undergoing left breast radiotherapy and subsequent effects on the heart in Palestine. Therefore, this study was carried out to evaluate the cardiac dose during left breast radiotherapy and to propose an amendment on treatment policy in cases where the heart could receive a considerable high radiation dose during treatment planning.

1.3 Objectives

This study aims at evaluating the heart doses received during left breast irradiation using 3-DCRT for young patients with breast cancer. Additionally, it will assess the techniques utilized in breast irradiation and cardiac doses by estimating the risks through following the applied protocols in relationship to the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) guidelines, that focus on dose volume estimates of the heart to evaluate the cardiac toxicities.

1.4 Motivation of the Study

This research was motivated by the lack of radiotherapy treating hospitals in Palestine, as well as the observation of the lack of standardized dosages exposed to oncology patients. Augusta Victoria Hospital (AVH), the only radiotherapy hospital in the area, generously made their resources available to fulfil my interested in radiation dose assessment for oncology patients. The research started with an evaluation of the heart radiation dose estimation for left breast RT patients, and there is a plan to follow up with those patients for the latent period in 10 years, to construct an observational study on cardiac effects such as radiation morbidity, in order to inspect the strength of guidelines that followed in this study ,after a period of time.

Chapter Two:

Literature Review

The literature review for this study reviews published studies and analyses of the cardiac dose during RT, especially left breast irradiation, and studies regarding the optimal techniques used in left breast RT.

2.1 Introduction

RT treatment play an important therapeutic tool for the treatment of different types of cancers, for more than 100 years. Which used high energy rays or radioactive materials, to destroyed the cancers cells. Unfortunately, the normal tissues in the area of tumor cells also affected by radiation. But with the development of RT techniques, thus can be limited by focusing of RT treatment beam on tumor and use

fractioning the total dose of irradiation, to allowing the normal tissue recovering and repairing itself **(Tward et al. 2012).**

In view of the history of cardiac dose in breast irradiation, there were a reduction of exposure to the heart over time. However, the radiation-induced cardiac death occurs in higher frequency after treatment**.** For example, **(Henson et al. 2013)** assess the radiation related mortality from heart diseases and lung cancer, reported that the risk for women irradiated for breast cancer is unknown today depending on the dose to heart and lung. Also, their study reported that the radiation-related risks are seen more in the third decade after exposure than during the first two decades.

Many randomized studies have given an indication of the extent to which radiotherapy has increased cardiac risk of left side compared to right side (16% higher in left breast), as reported in a study of **(Taylor et al. 2008).**

Many studies compared between techniques used in breast RT. Zhang et al 2015 study compared the three-dimensional conformal RT (3D-CRT), intensity-modulated radiotherapy (IMRT), and simple IMRT (s-IMRT), to evaluate the physical and biologically effective doses (BED) received by the heart and cardiac substructures in each technique. The study reported that the cardiac Normal Tissue Complication Probability (NTCP) in IMRT technique is significantly lower than that in 3D-CRT. Also, the 3DCRT can reduce the volume of heart and LV receiving lower doses compered to IMRT, however, the dose coverage for target area and the dose uniformity is better with IMRT and s-IMRT. In the same context, **(Schubert et al. 2011)** reported that all of these techniques (3DCRT, forward planned IMRT, inverse-planned IMRT, helical tomotherapy, and topotherapy) used in RT provide adequate coverage of the intact breast, but there were differences of the doses received by the target and normal tissue, and their homogeneity.

2.2 Previous Studies

Because of the uncertainty of the newer techniques of radiotherapy in reducing heart risk, in addition to the uncertainty of which anatomical regions of the heart is more important in inducing toxicities, a latent interval between the radiation exposure and the development of cardiac complications is needed. An excess of 10 years is preferred to obtain a fulfilled result.

Some studies suggests the injury to LAD plays a significant role, while others suggest the volume of left ventricle (LV) in treatment filed, which gives a predictor for development of short term myocardial perfusion defects after treatment. For example, for patients irradiated with left tangential radiotherapy, it was found that a small part of the anterior heart (usually included the LAD coronary artery) received doses of about more than 20 Gy for half of patients treated **(Taylor,et al. 2008)**.

Based on the absence of evidence for a threshold dose for cardiac morbidity and mortality, the procedures needed for heart protection should be considered to minimize both the dose delivered to the heart and the volume of heart irradiated as well as the dose delivered to the LAD. Recently, several studies described a deep inspiration breath hold technique (DIBH), which reduces the heart and LAD doses by displacing the breast and chest wall away from the heart during treatment. For instance, (**Hayden et al. 2012)** found that the average mean heart dose was reduced from 6.9 Gy to 3.9 Gy with breath-hold treatment compared to free breathing (FB) treatment. Also, in this context, **(Simonetto et al. 2019)** found that when using of DIBH compared to FB technique in 3D-CRT the mean heart doses were reduced by 35%. On a recent study **(Duma et al. 2019)**, the DIPH technique recommended by the breast cancer expert of the German Society of Radiation Oncology as the best heart sparing technique compare to various heart-sparing radiotherapy techniques as prone position, IMRT, VMAT, and partial breast irradiation(PBI).

Many studies reported on the factors that should be focused on that increase the heart risk in RT. **(Taylor et al 2017)** reported that numerous factors can contribute to the relationship between the heart dose as previous heart disease and smoking. For healthy nonsmokers, the estimated risks of lung cancer or cardiac mortality from radiotherapy was much smaller than the benefit from radiotherapy. Another studies discussed the relationship between the heart dose in left breast RT and the region included to be radiated such as lymph nodes and supraclavicular joint. As **(Finazzi et al. 2019)** reported, there is an association between the increase in heart and lung doses when the lymph nodes are included. **Deraby et al. 2013** demonstrated a fundamental role in finding a linear relationship between the radiation dose without a threshold and the major coronary events. It demonstrated that all patients received a similar relative effect of radiation, but the absolute effects differed largely based on prior cardiac risk factors and age. In another study, the distribution of individually determined radiation dose to the heart was analyzed to find difference in dose distribution through the cardiac sub-structures, and the cardiac dose affected by the tumor location and the treatment choices **(Wollschläger et al. 2016).**

Chapter Three:
Methods

This chapter provides the framework of the study, including an evaluation of the cardiac dose, techniques used in treatment of left breast RT, carried out in AVH for evaluating the cardiac dose, and statistical analysis of the data using Microsoft Excel version 2016, with P-value of $P \leq 0.05$ considered statistically significant. All related and required data were taken from the Department of Oncology – Medical Physics in Augusta Victoria Hospital, Jerusalem- Palestine

3.1 Study Design and Sources of Data

A retrospective study was carried out using data of patients treated with external beam RT between 2017 and 2019, at Augusta Victoria Hospital (AVH) - department of Oncology-Medical physics. Main data for cardiac dose received during left breast RT were taken from the treatment planning system (TPS) based on CT images and from dose volume histograms (DVH) of every patient.

3.2 Study Population

The study target in this study are all female patients (22-52 years) with left breast cancer (BC) treated by RT between 2017 and 2019.

3.3 Study Sample

The sample consists of 176 young female patients (22-52 years), randomly selected with unilateral BC, and were treated with planned conformal 3D external beam radiotherapy (3D-CRT) following breast-conserving surgery.

3.4 Inclusion Criteria

Female patients with left side breast cancer treated with postoperative RT with or without chemotherapy after breast-conserving surgery (lumpectomy or mastectomy), and referred for tangential left breast radiotherapy between 2017-2019, at Augusta Victoria Hospital.

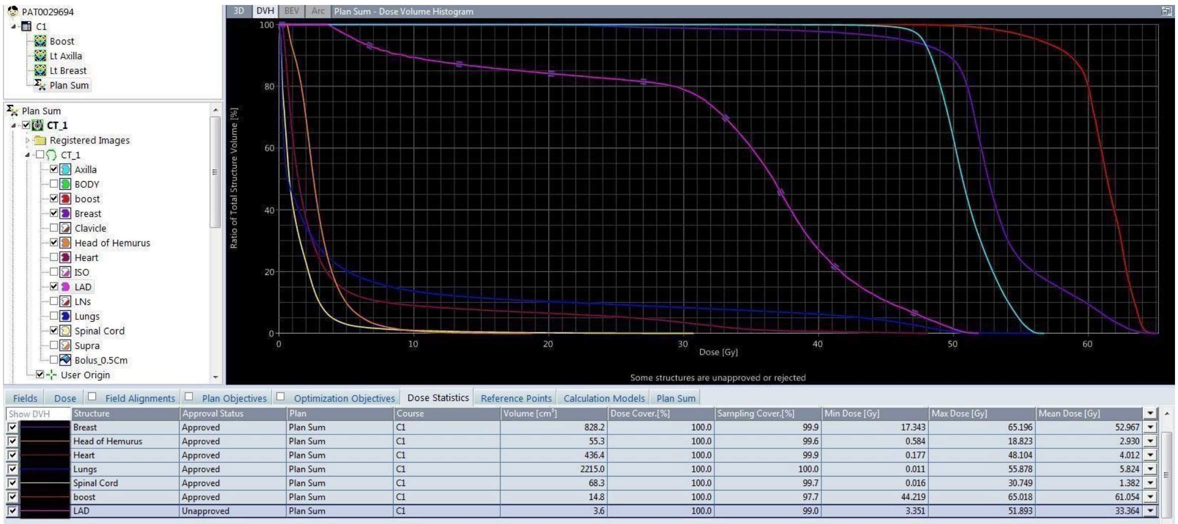
3.5 Exclusion Criteria

- Male patients.
- Patients with previous irradiation history for left breast cancer or other cancer types. - Patients treated with non-adjuvant therapies, such as the palliative treatment, partial breast irradiation, and uncommon fractionation (single doses other than 1.8–2.67 Gy).
- Patients with ages greater than 52 years.
- Patients with bilateral breast CA.

3.6 Data Collection, Dose Description and Treatment Plane

After institutional research ethics approval by AVH, the data of heart doses between 2017-2019 were retrospectively collected. Collected data include demographic information such as; patient number, date of treatment, and age. However, there was a lack in data related to previous or existing cardiac complications, treatments, or previous chemotherapy.

Also, the treatment information included; the type of technique, RT dose, fractionations, dose received by the heart, LAD, and breast. Based on CT imaging and treatment plan for each patient, the minimum, mean, and maximum point doses, and volume of target area (breast/chest wall), LAD, and heart, in addition to the dose volume histogram (DVH) for each patient were extracted. The DVH of sample for one patient is shown in **Fig. (3.1).**



Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
	Breast	Approved	Plan Sum	C1	828.2	100.0	99.9	17.343	65.196	52.967
	Head of Hemurus	Approved	Plan Sum	C1	55.3	100.0	99.6	0.584	18.823	2.930
	Heart	Approved	Plan Sum	C1	436.4	100.0	99.9	0.177	48.104	4.012
	Lungs	Approved	Plan Sum	C1	2215.0	100.0	100.0	0.011	55.878	5.824
	Spinal Cord	Approved	Plan Sum	C1	68.3	100.0	99.7	0.016	30.749	1.382
	boost	Approved	Plan Sum	C1	14.8	100.0	97.7	44.219	65.018	61.054
	LAD	Unapproved	Plan Sum	C1	3.6	100.0	99.0	3.351	51.893	33.364

Fig 3.1: Example of a treatment plan which includes the DVH and dose statistic for many structures and OAR surrounding the target.

All treatment plans were completed in three-dimensional conformal radiation therapy (3DCRT) system **(Brilliance Big Bore, Philips).** Treatment plans were made and modified based on patient and tumor related factors, then approved by a radiation oncologist prior to treatment sessions. The most frequent mean dose to the target volumes was 42.72 Gy given in
1.8 Gy fractions (40-52Gy).

Some patients also received an additional boost dose at the physician's discretion to either the lumpectomy cavity or chest wall with a median dose of 10 Gy (8–16 Gy). Conventional photon beams of 6 MV, were used for dose delivery.

Such treatment planning was conformal with the recommendations of the National Comprehensive Cancer Network (NCCN) guidelines, stating that a whole 50 Gy irradiation should be given in 25 fractions to the whole breast, followed by 8-16 Gy given in 4-8 fractions to the tumor bed.

The breast and heart were contoured by the oncologists according to the contouring guidelines. While the left anterior descending coronary artery (LAD) was not included in the contouring that previously existed in this study, the radiation oncologists were asked to contour and delineate the LAD following the heart atlas, as can be seen in **Fig.(3.2).**

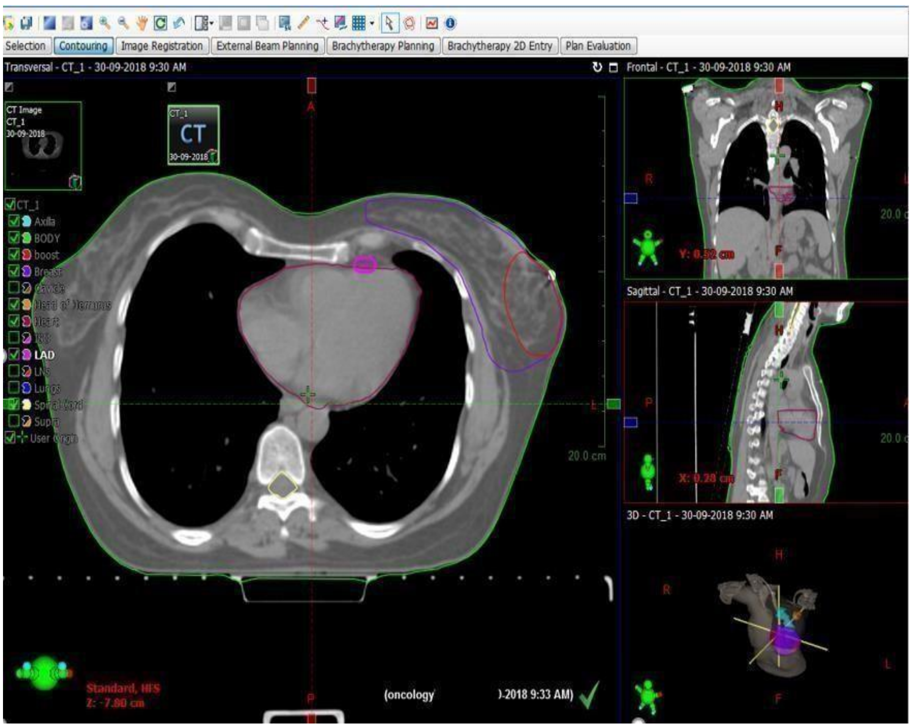


Fig 3.2 Example of contouring process of LAD, with the assistance of radiation oncologists of AVH.

For each patient, dose volume histograms (DVHs) for the whole heart and for the delineated LAD were obtained from the treatment planning module supplemented by the individual mean, median, and maximum doses. Furthermore, the volume percentage of the respective structure receiving 25 Gy or more (V25Gy) was assessed, as well as the V10 and V30. Patient data and treatment characteristics are shown in **table (3.1).**

Table 3.1-a: Patient and treatment characteristics.

Characteristic	**Numbers**
Number of patients Chest Wall Breast	176 105 71
Age- Median Mean Range	 34.5 42.2 22-52
Total Dose (Gy) (min-max)	42.72 (39.37-66) Gy
Heart volume (cm^3) Mean (min-max) V10 % V25 % V30 %	 457.5(239.9-786.8) 3.2 (0-30.5) 1.5 (0-21.34) 0.77 (0-18.89)
Heart Dose (Gy) Mean (min-max) Max Min	 2.2 (.157-13.721) 38.62 (0.469-64.228) 0.2 (0-1.002)
Mean LAD Volume (cm^3) (min-max)	2.42(0.8-5.3)
LAD Dose (Gy) (min-max) LAD Mean LAD Min LAD Max	 13.94 (.116-55.07) 3.82 (0-29.012) 32.15 (.287-65.61)
Breast-Chest Wall Volume (cm^3) (minmax) Mean Breast volume Mean Chest-wall volume	 942.5 (165.4-8319) 419.5 (120-1399.6)

Table 3.1-b: Patient and treatment characteristics.

Characteristic	Numbers
Breast-Chest Wall Dose (Gy) (min-max)	
Breast-Min	24.5 (2.37-57.69)
Breast- Max	58.15 (42.142-74.36)
Breast-Mean	37.77 (3.41-59.87)
Chest Wall-Min	19.23 (.067-51.5)
Chest Wall - Max	51.47(24.1-70.63)
Chest Wall –Mean	36.94 (1.94-61.72)
Number of Non-Boost	83(Total)
Breast without boost	19
Chest Wall without boost	64
Boost Dose (Gy)	
Min	38.74 (8.9-62.49)
Max	60.02 (42.02-74.36)
Mean	56.66 (40.25-70.223)

Abbreviations: B=Breast; Ch=Chest Wall; LAD = left anterior descending artery; Gy: gray; V: volume; D: dose; V25 Gy= Volume receiving 25Gy or more; V30 Gy= Volume receiving 30Gy or more; V10= Volume receiving 10Gy or more.

3.7 Predicting the risk

Clinical pericarditis and long-term cardiac mortality are the two most relevant cardiac toxicities. There are several protocols and groups with focused work on dose-volume estimates for the heart. As reviewed by the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC), it was predicted and summarized that a V25 <10% of the heart will be associated with a <1% probability of cardiac mortality at 15 years after radiotherapy (Emami et al. 2013). Whereas, for predicting of the Pericarditis, the Mean

Heart Dose < 26 Gy and V30 $<46\%$.Therefore, the data from this study were analyzed and compared to QUANTEC guidelines.

3.8 Statistical Analysis

Collected data was analyzed using Microsoft Excel version 2016, and $P \leq 0.05$ were considered statistically significant.

3.9 Obtained Approval

Approvals were taken by formal letters from Al-Quds University to the AVH.
The AVH approved the study in the Department of radiation Physics-Radiation oncology.
AVH ethical committee approval letter can be found in Appendix.

3.10 Contribution of the study

It is intended that the findings of this research will be used by local and regional authorities to assess and evaluate the doses for heart during left breast radiotherapy and to gain a knowledge about the national treatment and levels pertaining to radiotherapy procedures. These findings could be used for correction and development of the current RT techniques in Palestine. In addition, to use the outcomes of this study in the future to examine the QUANTEC guidelines in predicting the cardiac toxicities.

Chapter Four:
Results and Discussion

The dose assessment and evaluation for patients undergoing left breast irradiation are consider to be of persistent need due to the presence of heart complications associated with radiotherapy treatments.

This chapter displays and discusses the results of the dose assessments of the heart during left breast RT.

4.1 Patients, Cardiac dosimetric parameters

This study evaluated the risk of cardiac dose for patients treated with 3-DCRT. The dosimetric analyses of CT-based RT plans were available for 176 cases. Selection was done after excluding the right breast irradiation and bilateral breast irradiation, as well as the patients who underwent previous radiotherapies **(Appendix 1**). The study included all patients who underwent RT to the left breast alone with free breathing (FB) technique, and treated with a hypo-fractionated regimen of 42.72 Gy in 16 fractions and 50 Gy in 25 fractions. Also, 93 patients of the sample received a boost to the surgical cavity of 10-16 Gy in five fractions within 1 week using a photon or electron beams according to tumor depth on the breast. As shown in (**Fig (4.1)** there is a linear correlation between dose used in treatment plan and the dose received to the heart .

Most of DVHs fell well within the QUANTEC guideline V_{25} <10% for all patients except one.

And MHD of less than 4 Gy for all patients except 8 patients (4.5%). With a of MHD and V25% (**Fig (4.2), Table (4.1)).** The risk of cardiac mortality was less than 1% for most patients. Also, all of patients received heart dose <26 Gy and V30% <46%, meaning the predicting of pericarditis <1%, with cases overall receiving low radiation doses to the heart.

The LAD was irradiated to more than 25 Gy on at least one axial slice in 69% of cases and to more than 40 Gy in 37% of cases. Only 11% of cases had >1 cm of continuous circumferential dose to the LAD of >46 Gy.

According to QUANTEC guidelines, one of all patients has a V25% more than 10%, in which the probability of cardiac mortality at 15 years after RT is more than 1% (**Fig. 4.3)** demonstrated a linear correlation of MHD and V25%). For predicting of the Pericarditis

<1% for all patients, in which the mean Heart Dose < 26 Gy and V30 <46%, however, the overall LAD doses are slightly high.

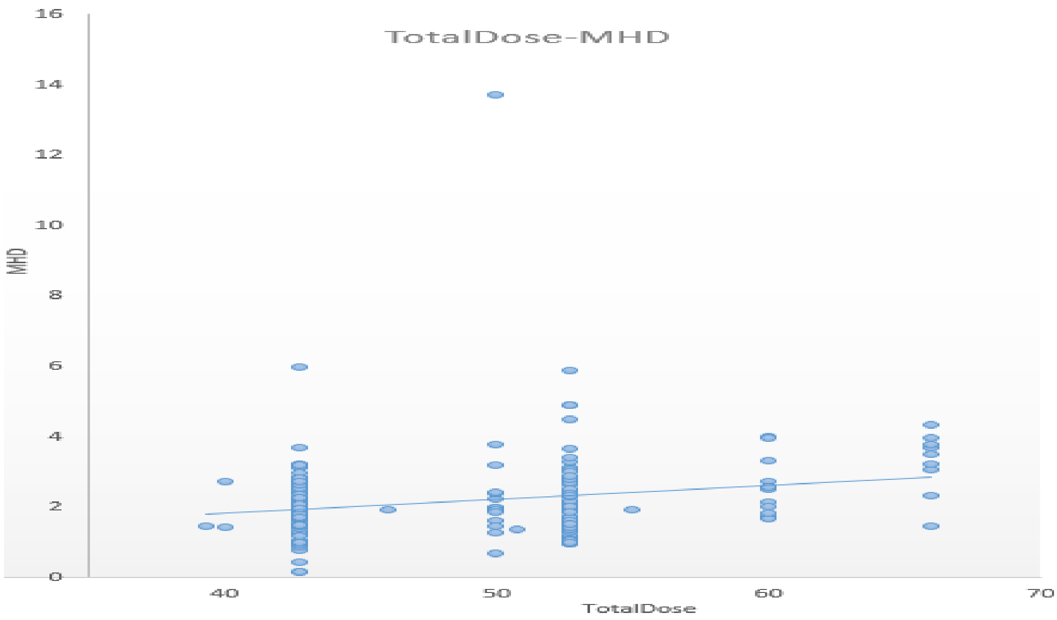
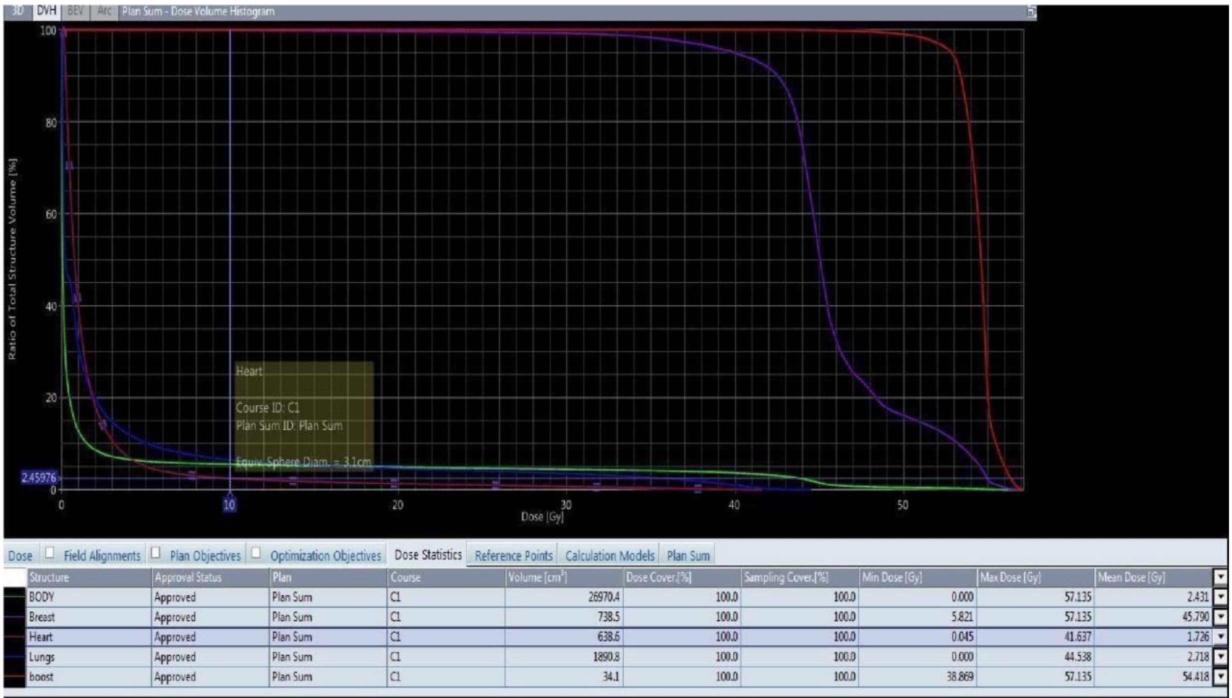


Figure (4.1) Correlation of MHD and Total Dose used.



Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
BODY	Approved	Plan Sum	C1	26970.4	100.0	100.0	0.000	57.135	2.431
Breast	Approved	Plan Sum	C1	738.5	100.0	100.0	5.821	57.135	45.790
Heart	Approved	Plan Sum	C1	638.6	100.0	100.0	0.045	41.637	1.726
Lungs	Approved	Plan Sum	C1	1890.8	100.0	100.0	0.000	44.538	2.718
boost	Approved	Plan Sum	C1	34.1	100.0	100.0	38.869	57.135	54.418

Fig 4.2 A dose statistic and DVH for patient No. 31, which the left breast irradiation with using a boost in tumor site. The DVH showed that 2.45 % of heart volume received less than 10 Gy

Table 4.1 Baseline patient and treatment characteristics for all patients (n =176)

Characteristic	All Patients
Age – mean ± SD	**34.5 ± 14.85**
Breast –chest wall Volume (cm^3) – mean ± SD	**734.4 ± 5715.3**
MHD (Gy) – mean ± SD	**2.2 ± 0.154**
MHD (Gy) – n (%) < 1.7 Gy ≥ 1.7 Gy MHD <4 Gy MHD≥4 Gy	 **35.8%** **64.2%** **95.45%** **4.5%**
Heart Volume (cm^3) – mean ± SD Heart V25 Gy (cm^3) – mean ± SD	**457.5 ± 175** **1.5 (0-21.34) ±.5315**
Heart V25 Gy (cm^3) – n (%) < 10 cm^3 ≥ 10 cm^3	 **99.43%** **0.569 %**
Maximum LAD Dose (Gy) – mean ± SD	**32.15 ± 0.2468**
LAD >20 Gy	**44 patients (25%)**
LAD % >45 Gy	**11.93 %**

Abbreviations: SD=Standard Deviation; MHD=Mean Heart Dose; V25 Gy= Represents the percentage of *Heart* volume receiving (25) Gy or higher.

LAD = left anterior descending artery 3D-CRT: three-dimensional conformal radiotherapy; Gy: gray; V: volume; D: dose.

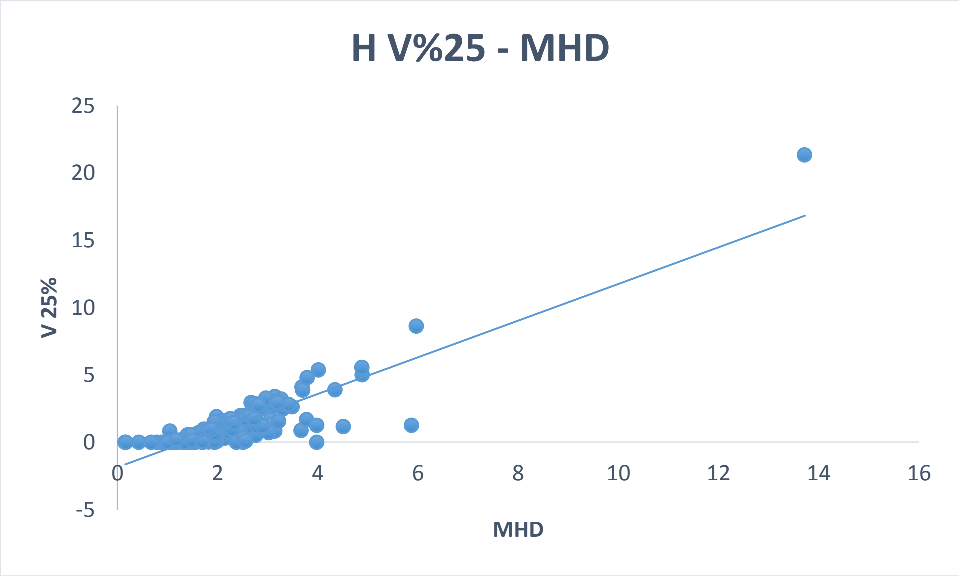


Figure (4.3) Relationship of MHD and heart V25% for all patients.

The heart is considered as the organ at risk in compliance with the QUANTEC guidelines in prediction of cardiac toxicity. However, there was a differentiation of occurrence of toxicity for each of anatomical region of the heart as the majority of cardiac mortality cases are related to coronary vascular disease and the major arteries supplying the right and left ventricle. Moreover, when the small volume of heart receives a large dose, no guidelines were available to keep cardiac mortality at low risk, meaning, to guide the planning objectives, there is no clear data about dose-response data of dose volume-sensitive point of the heart.

The delineation of the sub-regions of the heart is challenging because of their structural definition through the device used in treatment planning as; CT, MRI, or other modalities, in which it's difficult to differentiate the heart sub-structures in most of imaging modalities. In addition, the anatomical-functional complexities, the interaction between structures, and their overlaying anatomy, gives uncertainty of contouring the specific structures of the heart. Thus, affects the determination of the heart region most important in RT-induced toxicities, especially, breast radiotherapy doesn't usually use contrast media. It becomes more challenging when countering the vessels, as the LAD. An example of the delineated anatomy of 3D-CRT for three different patients demonstrating the LAD location in breast, chest wall irradiation, and a boost in tumor bed (**Fig. 4.4**).

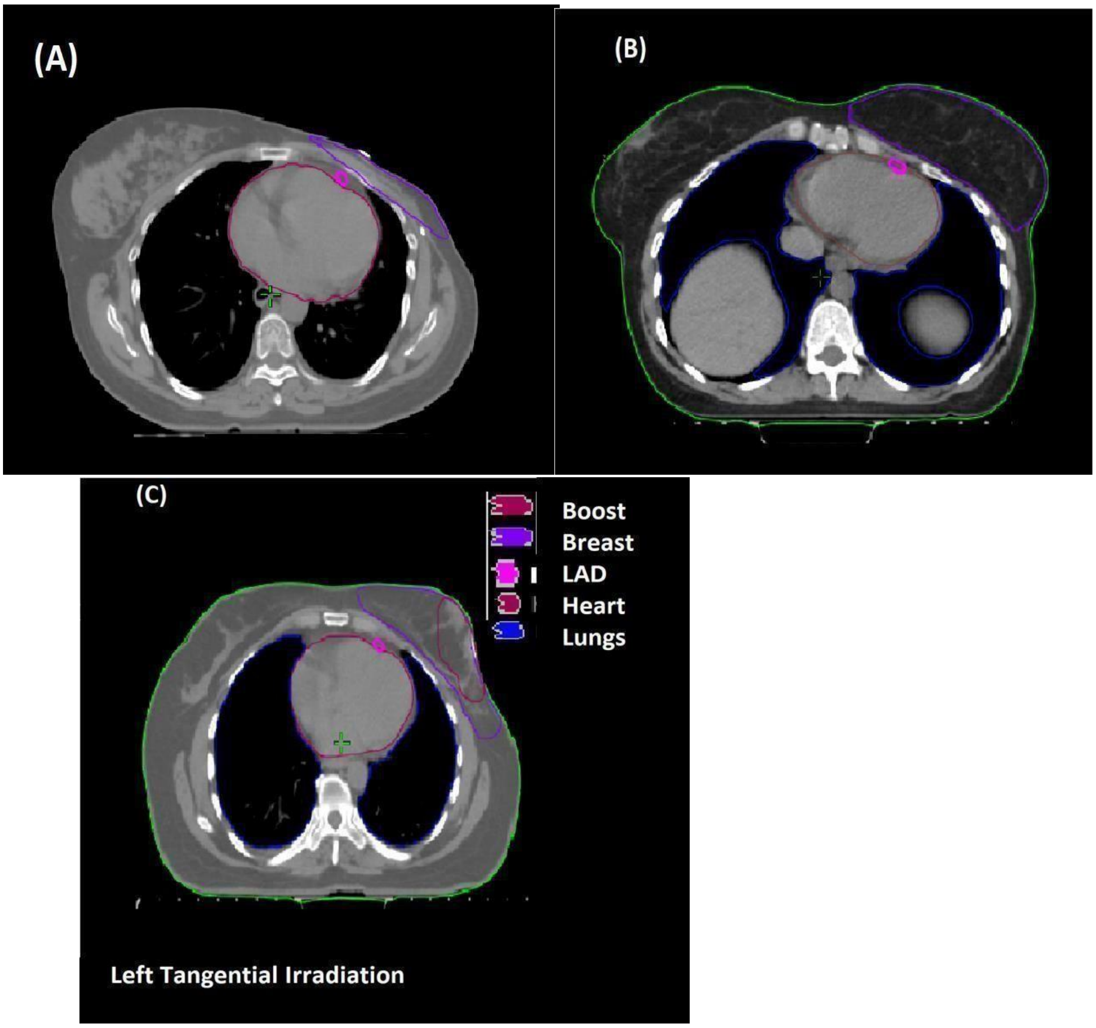


Fig. 4.4 The delineated anatomy of 3D-CRT for three different patients demonstrating the LAD location (A) Demonstrates the tangential irradiation to the left chest wall (B) Irradiation to the left breast, (C) Irradiation to the left breast with a boost in tumor bed.

The analysis by Derby et al demonstrated for each 1 Gy in MHD, increasing 7.4% the rate of major coronary events. In which, modelled a threshold of MHD over 3 Gy will increasing the risk. In this study, 29 patients (16% of Total patients) exceeded 3 Gy MHD. Moreover, the MHD comparison between patients with breast irradiation and chest wall irradiation indicated that breast irradiation had more cases 18.8%, while chest wall irradiation were 10% of the cases. This may be related to the use of boost technique more for patients with breast irradiation, which increases the MHD. In addition, A lack of contouring uniformity was noticed across patient treatment plans. For example, some patient plans included the supraclavicular joint, or infra-lymph node …etc. This is related to the customized treatment plans for each patient. This may contribute to increasing

MHD. Also, Darby et al showed that MHD was a better predictor of coronary events than mean dose to the LAD. However, this study showed a correlation between the MHD and mean LAD dose, but with high radiation dose received in LAD. Patients with the highest mean heart dose (13.7 Gy) also had the highest LAD dose (55.06 Gy). **(Fig. 4.5) (Table 4.2).** In this context, many dosimetry studies have shown that high mean radiation dose received in LAD during left breast irradiation are due to its location and the larger longitudinal section of LAD laying in the RT field **(Table 4.3)**.

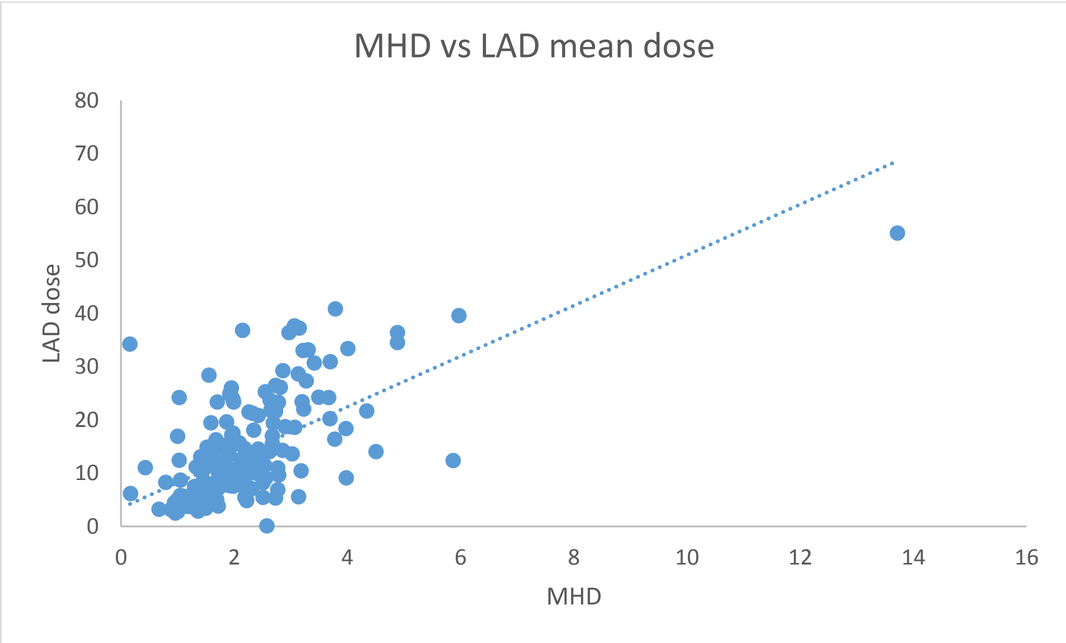


Figure (4.5) correlation of the mean heart dose and mean LAD dose of all patients.

Table 4.2 Dosimetric parameters of organ at risk(OAR) including heart and LAD.

OAR	PARAMETERS	MEAN	SD
Heart	Mean dose (Gy)	2.2	0.1514
	Max dose (Gy)	38.62	6.564
	V30 % (cm^3)	0.77	0.3359
	V25 % (cm^3)	1.5	0.5315
	V10 % (cm^3)	3.2	0.7737
LAD	Dmax (Gy)	32.15	0.2468

Abbreviations: SD=Standard Deviation; MHD=Mean Heart Dose; V25 Gy= Volume receiving 25Gy or more; LAD = left anterior descending artery 3D-CRT: threedimensional conformal radiotherapy; Gy: gray; V: volume; D: dose.

Table 4.3 Dosimetric analysis of heart doses in breast and chest-wall irradiation

Dosimetric characteristic	Breast irradiation N=106	Chest-wall irradiation N= 70	p-value
Patients with V25 Gy> 10% N (%)	0 (0%)	1 (1.4%)	
Patients with V25 Gy > 5% N (%)	3 (2.8%)	2 (2.8%)	0.04
Mean Heart dose (Gy): Median (25th-75th percentile)	1.98 (1.48-2.74)	1.95 (1.47-2.55)	0.36
Patients (n) with MHD > 3 Gy	20 (18.8%)	7 (10%)	0.22
Maximum-heart dose (Gy) Median (25th–75th percentile)	40.51 (32.84-44.37)	41.31 (36.72-44.09)	0.45
Mean LAD dose(Gy): Median (25th–75th percentile)	10.3 (5.59-18.51)	11.47 (7.02-21.99)	0.09
Maximum-LAD dose (Gy) Median (25th–75th percentile)	34.71 (20.44-41.9)	37.33 (26.15-42.36)	0.12

For boost irradiation, patients with boost had no correlation to increasing heart dose and LAD dose (**as shown in Fig 4.5).** This can be related to the dose in boost irradiation which focused on the tumor region, away from the heart. Therefore, the dose with boost irradiation will increase the cancer cell death with a small effect on the OAR. But this is differing from patient to patient, according to the tumor location and boost region size, beside the type of treatment beam (electron or photon beam) which in photon beam the OAR affected more from scattered radiation.

The heart dose that received affected by the size of planning target volume (PTV), breast or chest wall region linearly **(Fig. 4.7)**. According to previous studies and based on three-dimensional treatment planning and clinical target volumes (CTV), the volume of breast can be measured and classified of ≥ 1600 cm^3, 975–1600 cm^3 , and ≤ 500–975 cm^3 have been defined as large, medium, and small breasts, respectively (Michalski et al. 2013, Ratosa et al.2018). As in this study the range of MHD was affected by breast/chest wall size **(Table 4.4). (Fig. 4.8)** demonstrated that no relationship of ages group in MHD (Group for patients ages < 40yrs, Group for patients ages ≥40 yrs), even though, no relations of MHD according to group ages, but the ages group affected in responding to radiation according to group age, the younger ages more sensitive to radiation, because the most composition of breast more of mammary gland tissue.

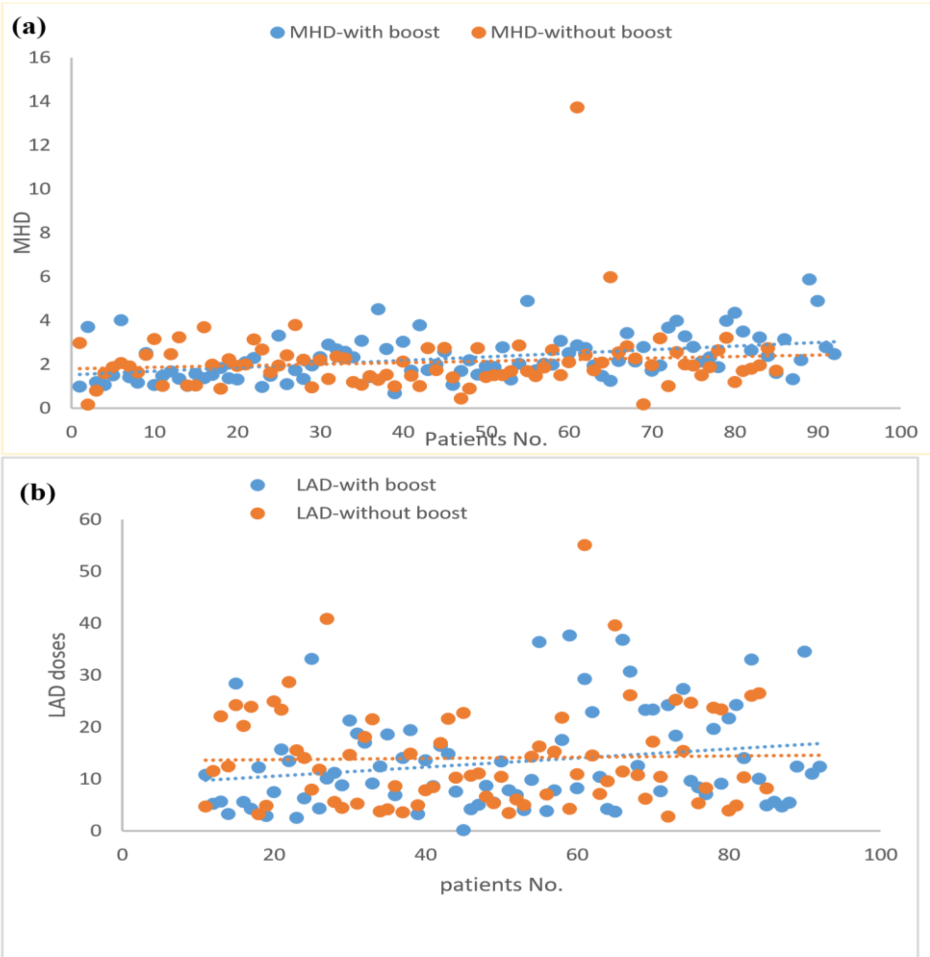


Fig 4.6 Correlation of dose for patients when using the boost in treatment plan, and when not used. (a) For Heart doses and (b) For LAD doses.

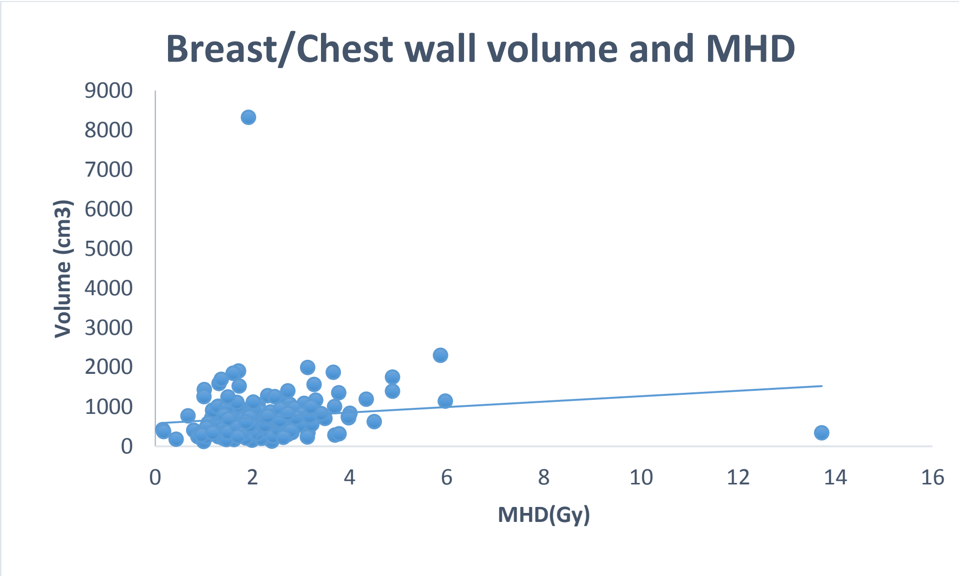


Fig 4.7 Correlation between the breast/chest wall volume and the MHD

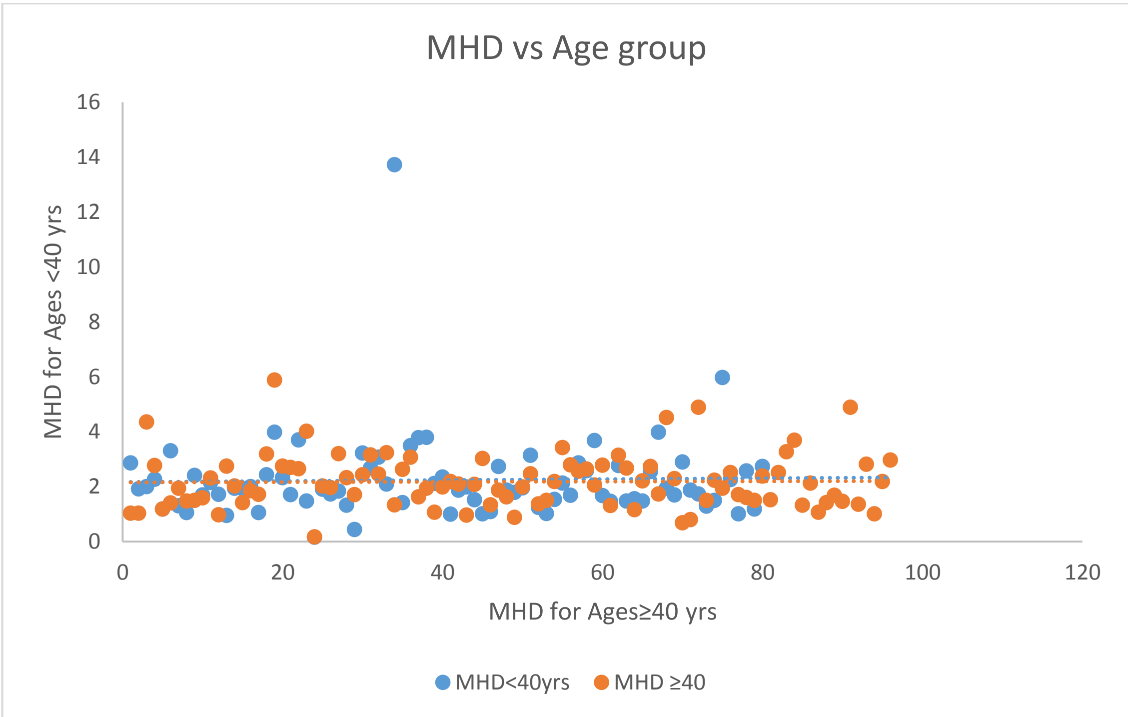


Fig 4.8 Relationships between MHD and Patients ages groups

Table 4.4 The classified volume of PTV and MHD of each group.

Breast size	N. (%)	Range of MHD
Large ≥ 1.600 cm^3	8 (10.52%)	1.36-5.873
Medium 975-1600 cm^3	28 (36.84%)	1.002-5.97
Small 500-975 cm^3	140 (79.5%)	0.157-13.721

4.2 Patient-to-patient variability in mean dose

There was a variability from patient to patient in MHD, but much less compared to LAD, which ranged from 0.157 to 13.721 Gy for left-sided irradiation. The patient-to-patient variability was greatest for LAD coronary artery dose. The mean LAD dose for 176 leftsided patients varied from 0.116 to 55.07 Gy (Mean 13.94). These results may be related to the location of each point, whether the anatomical location is near or farther from the irradiated field **(Fig. 4.5).** Also, the receiving dose differs from point to point on the length of LAD according to their location to the breast. Thus, emphasizes the need to measure and segment the length of the LAD to determine the most sensitive point on it. This type of data was challenging to collect for this paper (This clearly notable in **Fig 4.**6 when compared the boost using in LAD and Heart doses).

4.3 Dosimetric comparison between techniques

The technique used in this study is fixed to 3D conformal technique – free breathing. In which the obtained results of doses are acceptable compared to previous studies. When comparing them with the uses of the same technique (FB technique).

The dosimetric evaluation showed the mean heart dose from this study was 2.2 Gy and the LAD mean dose was 13.94 Gy. A low variation in MHD and LAD dose between this study and the FB technique study (Wang et al .2012), as variations in this study were in range when compared to the ranges from Wang et al. 2012, while dose differences increase when used DIPH technique. The differences of doses were clearly shown when comparing these results to the more recent study (Dell'Oro et al. 2019) for both FB and DIPH technique; especially for LAD doses, where the relative reduction (RR) from this study compared to DIBH plan from Wang et al.2012 is approximately half, and for Dell'Oro et al. 2019 the RR is about 74%, 82% for FB and DIPH respectively, while the RR for FB Wang et al.2012 was the only factor increased in LAD dose from this study. Recent studies show that most investigated patients benefited from the DIBH technique, but not all. Only a small difference in cardiac doses between FB and DIBH was observed (Mikaela et al. 2019,).The results from previous studies (as shown in Table 4.4) varied across both techniques of FB and DIPH, and the reduction of doses clearly demonstrated in Mikaela et al for both techniques. However, outcomes of these doses need further justification due to the small sample size. Still, the doses obtained in this study were high, specifically for LAD doses and need to be reconsidered based on the doses and techniques used. The variation in ranges compared to this study may be correlated to the small sample size of both previous studies. (**Table 4.5)**

Many recent studies approved that the DIBH technique used in left breast RT decreases the dose to heart and LAD compared to using free breathing technique. In DIBH technique, the heart is located away from the tangential field and shows a significant dose reduction.

Although, the use of DIBH technique can reduced the dose to heart, a number of challenges are associated with it. One of the challenges is that it’s unsuitable for all patients, either because it requires the ability to fully extended the lung, or patient’s tolerance in breath hold techniques to distant the heart from breast. Additionally, it may not be used for patients with unfavorable cardiac anatomy, which is a condition where the heart conjoins with chest wall. As a result, it’s important to balance the benefit of using the DIBH technique to avoided the unacceptable increase in the workload leading to time inefficiency.

Table 4.5 Dosimetric comparison between free-breathing of this study and free-breathing technique, deep inspiration breath-hold technique plans for other studies.

Variable	FB plans of this study	FB plans from Wang et al .2012 study	DIBH plan from Wang et al 2012 study	FB Dell'Oro et al. 2019	DIPH Dell'Oro et al. 2019
Heart dose(Gy) **Mean** **Range**	**2.184** **0.157-13.721**	**3.174** **1.53–7.385**	**1.317** **0.742–2.245**	**1.7** **0-3.8**	**1.0** **0-3.7**
LAD dose (Gy) **Mean** **Range**	**32.15** **0.287-65.61**	**41.555** **30.8-49.2**	**15.075** **3.5-41.5**	**8.2** **1-15.1**	**5.7** **4.5-12.5**
Relative reduction (%) from LAD dose	**-**	**~ 21%**	**~50%**	**~74%**	**~82%**

Abbreviations: FB = free breathing; DIBH = deep inspiration breath hold; LAD = left anterior descending artery 3D-CRT: three-dimensional conformal radiotherapy; Gy: gray; V: volume; D: dose

4.4 Strengths and limitations of the study

With respect to the strengths of this study, it is the first study done in Palestine discussing dose assessment of left breast irradiation. It includes data of boost doses, which most of studies in literature review for this paper lacked, showed data of LAD dose and mean heart dose, as well as including a wide range of female patient ages who have a long latent period that may show more effects post treatment period, allowing for a follow up in 10 years for more observations. The study also includes patients of both post-mastectomy and breast cancer surgery (lumpectomy), to provide more accurate results and a broader understanding of the findings.

As for the study limitations; at the beginning of the research, a long wait time passed before hospital approval is obtained to begin the research. Once started, existing LAD exams were not contoured and intravenous contrast was not used for CT planning. With the help of an oncologist at the hospital, contouring of the LAD was done manually for each patient, which might have reduced the accuracy of LAD contouring. Additionally, some data used to calculate risk according to normal tissue complication probability (NTCP) were not extracted due to movement restrictions caused by the recent spread of COVID-19.

Chapter Five:
Conclusions and Recommendations

5.1 Conclusions

Radiotherapy remains an integral part of breast cancer treatment which gives more local control benefit as well as improved survival. Therefore, confirms the need for careful RT planning and minimizing the irradiated volume of heart, especially for patients with a history of cardiac disease.

Radiation is a double-edged sword. It can cause harmful health effects, including incident cancer on one hand, or complications and side effects through the normal organs and tissues, and control cancer progression and spreading on the other. RT is still the preferred treatment modality for many types of human cancers, and it has emerged as an important treatment modality for breast cancer.

With all development in breast conservation therapy, there is a need to increase the focus towards a better dose adjustment planning parameters and similar OAR sparing benefits, but also to spare the patients from the disadvantage of low scattering dose, in order to obtained the optimum reduction of radiation dosage to the heart and left anterior descending coronary artery.

This study findings stimulate attention to the importance of screening of left breast irradiated patients, cardiac risk factor modification, and lifestyle modification.

The selection of the optimal radiation-delivery technique remains a critical component to individualize the breast cancer treatment, which requires adequate dose coverage as well as

The organs at risk sparing for each patient's unique anatomy. 3DCRT technique used in Augusta Victoria Hospital helps in improving the local control, but the normal tissue toxicities remain a big deal. For example, when treating left-sided breast cancer with 3DCRT, there is an unavoidable irradiation to OAR that include a portions of the underlying lung, the other breast and heart, and the coronary artery of heart, in which the injury of radiation is the most serious radiation induced complication of the heart.

The selection of optimal radiation technique could be a challenge, which requires adequate dose coverage and OARs sparing for each patient's unique anatomy. Therefore, the selection of optimal technique depends on many factors as patient's anatomy, patient's tolerance to breath hold in DIPH, and the history of cardiac risk, which explains the different and explicit appropriate techniques used for each patient.

The results of the current study shown that the whole heart mean dose and left anterior descending artery for left breast tumors were 2.2 Gy and 13.94 Gy, respectively. In which, 4.5% of all patients received MHD≥ 4Gy, and all of them have a V25% below than 10 cm expect one, and 11 % of patients received LAD maximum dose ≥45 Gy. The MHD and LAD dose of the results were not far from the similar free breathing published studied and protocols, however, doses were high when compared to studies that used Deep Inspiration Breath Hold Technique (DIPTH). Also, there was a high variation of dose range of MHD and LAD in this study.

Moreover, the cardiac radiation doses were equivalent to the QUANTIC guidelines in most patients in MHD doses, but LAD doses were mostly higher. Thus maybe related to the uncertainty of contouring process of the LAD, and related to the anatomical nature of LAD near in position to the breast, of each patient, and the technique used.

Because there is no standard protocol or a significant dose constrains to heart to follow, the option to maintain the lowest volume of heart or organ at risk, and dose received as low as possible, in addition to using advanced techniques as DIPH for qualified patients, to decrease the dose to normal tissues. Even though the latent effects will not be eliminated for patients treated with radiotherapy, the previous measures will help in decreasing it.

5.2 Recommendations

- Oncologist should consider patient's previous cardiac complications, family history of cardiac disease, smoking patients … etc, when preparing the treatment plan.
- Recommending AVH to use the DIBH for some patients, especially, the patients with cardiac problem history.
- Follow up of this study after 10-15 years for evaluation of cardiac mortality and radiation effects on these patients.
- Future studies and research about radiation dose assessment for patient treated with RT, should be conducted in Palestine to protect patients who suffer from late RT effects.
- Further studies and research focused on segmentation of heart regions should be done to assess the more sensitive segment of heart, to be considered in treatment planning.

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Appendix 1: Patients data

Variable	Mean	Range	Stand.Dev
Age	42	22-52	14.84
Heart Volume	457.6	240-786.8	68.24
Breast/chest wall Volume	734.4	120-8319	280.86
LAD Volume	2.42	0.8-5.3	0.49
Boost Volume	65.57	8.7-540.7	20.58
V 10%	3.2	0-30.52	20.45
V 25%	1.15	0-21.37	15.03
V 30%	0.77	0-18.90	13.36
Total Dose	49.61	40-66	7.52
MHD	2.2	0.157-13.72	8.66
Min Heart dose	0.20	0-1.002	0.61
Max Heart dose	38.62	0.47-64.23	19.22
LAD Mean dose	13.94	0.12-55.07	34.53
LAD Min dose	3.82	0-29.012	6.50
LAD Max dose	32.15	0.29-65.61	33.61
Boost Mean dose	56.66	40.25-70.13	21.19
Boost Min dose	38.74	8.9-62.49	11.84
Boost Max dose	60.02	42.02-74.36	22.62
Breast/chest wall mean dose	37.44	1.94-61.72	42.27
Breast/chest wall min dose	22.39	0.067-57.69	3.25
Breast/chest wall max dose	55.49	24.1-74.36	13.31

Approval Letter from AVH

The Lutheran World Federation
Augusta Victoria Hospital
Est. 1950 - Jerusalem

الإتحاد اللوثري العالمي
مستشفى الأوغستا فكتوريا / المُطّلع
تأسس ١٩٥٠ - القدس

2020/07/09

حضرة د. حسين المصري المحترم،

يسرني إبلاغكم ان لجنة الأخلاق الطبية في مستشفى المطلع قد اجتمعت يوم ٢٧ شباط الماضي ، وكان مقترحكم البحثي بخصوص "تقييم جرعة القلب للمصابين بسرطان الثدي والذين يتلقون العلاج بالإشعاع" للطالبه بيان سليمان على جدول أعمالها وتم الموافقة عليه طالما انه عبارة عن استبانة مفصلة .

مع التحية والاحترام،

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ملخص الدراسة

إعداد: بيان صالح علي سليمان
المشرف: د. حسين المصري

تقييم الجرعة الإشعاعية للقلب والشريان التاجي النازل الأيسر للمرضى خلال العلاج الشعاعي للثدي الايسر في فلسطين

هدف الدراسة: لتقييم الجرعة الإشعاعية التي تصل القلب خلال العلاج الاشعاعي لعلاج سرطان الثدي الايسر، حيث يتم العلاج الإشعاعي بواسطة تقنية تخطيط العلاج الإشعاعي الثلاثي الأبعاد المستندة إلى تخطيط التصوير المقطعي المحوسب.

الطرق والمواد: تم جمع البيانات بأثر رجعي استنادًا إلى صور أشعة مقطعية مؤرشفة، لـ 176 مريضة بسرطان الثدي الايسر، خضعن لإزالة كاملة او جزئية للثدي (70 مريضة خضعت لعلاج اشعاعي لجدار الصدر و 106 مريضة خضعت لعلاج اشعاعي للثدي). ، حيث تم تحليل الجرعة الاشعاعية التي تصل للقلب وللشريان التاجي الصاعد الأيسر استناداً للبيانات التي تم جمعها. بحيث تم علاج المريضات في مستشفى المطلع ما بين 2017-2019، .و تم الحصول على الرسوم البيانية لحجم الجرعة للقلب كله وللشريان التاجي الصاعد الأيسر.

كما تم حساب اجرعات، الحد الأدنى، الحد الأقصى، والمتوسط لهذه الجرعات التي تصل القلب والشريان التاجي. وتم تحليل الجرعات التي تصل القلب والشريان التاجي بناءاً على نسب الحجم (25%و 30% و 10%) من كمية الاشعة التي تصل الى حجم معين، ومقارنتها في بروتوكولات "التحليل الكمي المؤثر على الخلايا الطبيعية" ودراسات سابقة لتقييم مستوى الجرعة الاشعاعية التي تصل القلب والشريان التاجي الايسر.

نتائج الدراسة: أظهرت النتائج بأن متوسط الجرعة الاشعاعية التي تصل القلب 2.2 جرعة اشعاعية، و 13.94 جرعة اشعاعية للشريان التاجي الأيسر، بحيث 4.5 % من المريضات كان متوسط الجرعة الشعاعية للقلب اكبر من 4 جرعة اشعاعية، وكل المريضات كانت لديهن 25% من حجم القلب لم يتعرض لأكثر من 10 جرعة اشعاعية ما عدا واحدة. و 11% منهن تعرض الشريان التاجي لأكثر من 45 جرعة اشعاعية. على الرغم من أن هناك فروق في الجرعة الشعاعية للقلب والشريان التاجي بالإضافة لفروقات كبيرة ما بين اعلى وادنى جرعة شعاعية لمتوسط الجرعة الاشعاعية للقلب والشريان التاجي الايسر، عند مقارنة الجرعة الاشعاعية بدراسات حديثة تستخدم

نفس التقنية للعلاج او باستخدام أنواع احدث من العلاج الاشعاعي، مثل استخدام "تقنية الشهيق العميق".

هذه النتائج تبقى من ضمن الحد المعروف نسبياَ لبعض من الدراسات المنشورة في بروتوكولات "التحليل الكمي المؤثر على الخلايا الطبيعية" التي استخدمت نفس هذا البروتوكول (التنفس الحر).

ملخص الدراسة: النتائج بينت بأن استخدام العلاج الاشعاعي الثلاثي الأبعاد

لعلاج سرطان الثدي الايسر، بأن الجرعة الشعاعية للقلب كانت لأغلب المريضات من ضمن الحدود المعروفة، لكن أغلب الجرع الشعاعية الواصلة للشريان التاجي الأيسر كانت عالية.

ولعدم وجود بروتوكول مرجعي للجرعات التي تصل القلب في العلاج الشعاعي، يبقى الخيار الأنسب لتقليل الجرعة الشعاعية هو تقليل حجم القلب خلال اعداد الخطة العلاجية من ضمن المعقول للتقليل من كمية الاشعة بدون التأثير على جودة العلاج من خلال ضم اقل مساحة من القلب للمنطقة التي سيتم العلاج الاشعاعي لها، كإستخدام تقنيات أحدث للعلاج الشعاعي مثل تقنية الشهيق العميق لبعض المرضى، الذي يلعب دور كبير في ابعاد القلب عن منطقة الثدي وبالتالي التقليل من حجم القلب الداخل في العلاج. من اجل التخفيف من الاعراض المرضية المصاحبة للعلاج الشعاعي وخاصة المشاكل المرضية للقلب التي من الممكن ان تحدث بعد العلاج الاشعاعي.