



# Dose Determination of Cardiac Implantable Devices in Breast Cancer Radiotherapy



**Bora Uysal\* and Hakan Gamsiz**

*Department of Radiation Oncology, University of Health Sciences, Gulhane Medical Faculty, Ankara, Turkey*

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**Corresponding author:** Bora Uysal, Department of Radiation Oncology, University of Health Sciences, Gulhane Medical Faculty, Ankara, Turkey

## Abstract

**Objective:** We evaluated the dose determination of pacemaker in breast cancer radiotherapy

**Materials and methods:** Breast cancer is the most commonly diagnosed cancer in women worldwide. Radiotherapy is a crucial treatment modality for patients with breast cancer, but it has been linked to an increased risk of cardiovascular diseases. The development of cardiotoxicity in breast cancer patients undergoing radiotherapy has led to the exploration of various strategies to mitigate this risk. Primary goal of this study has been to evaluate pacemaker dose determination for breast cancer. We have carried out a comparative analysis of treatment volume determination by CT simulation images only or by integration of PET. While we primarily focused on evaluation of incorporated multimodality imaging for treatment volume determination, we also assessed critical organ contouring along with interobserver and intra observer variations. Ground truth target volume has been utilized for comparative analysis, and it was determined by board certified radiation oncologists after detailed evaluation of all imaging and relevant data with thorough colleague peer review and consensus.

**Results:** Ground truth target volume was used as the reference for comparative evaluation, and our results revealed that use of fused PET-CT based treatment volume determination was identical with ground truth target definition in our selected group in breast cancer patients.

**Conclusion:** This article aims to review the association between the use of heart pills and radiotherapy in breast cancer patients, focusing on the materials and methods employed, results obtained, and the subsequent discussions surrounding the topic.

**Keywords:** Pacemaker; Breast cancer; Radiotherapy; Radiation exposure; Contemporary techniques

**Abbreviations:** CIEDs: Cardiac Implantable Electronic Devices; RT: Radiotherapy; HL: Hodgkin lymphoma; LINAC: Linear Accelerator; ACE: Angiotensin-Converting Enzyme; AAPM: American Association of Physicists in Medicine; ICRU: International Commission on Radiation Units and Measurements

## Introduction

Dose determination for cardiac implantable electronic devices, such as pacemakers and implantable cardioverter-defibrillators, during breast cancer radiotherapy is a critical process, as ionizing radiation can potentially cause malfunctions in these devices. This includes abnormal battery depletion, altered function, or even damage, depending on the cumulative dose received. The total number of cardiac implantable electronic devices (CIEDs) implanted every year is constantly growing. The incidence of cancer patients is expected to increase with the population aging and a rising number of CIED patients will require radiotherapy (RT) for cancer treatment. Therefore, careful patient evaluation and appropriate planning of the RT course planning is crucial to prevent any possible interference with the device. Today, only

small- scale studies address this issue, and robust predictors of device malfunction or failure are lacking. Most national and international guidelines and consensus documents on this topic suggest a personalized approach to patient management, based on classes of risk for device malfunction.

Breast cancer treatment has made remarkable progress in recent years, resulting in improved survival rates. Radiotherapy is an integral part of the treatment plan for most patients with breast cancer; as it effectively reduces local recurrence and improves overall survival. But radiotherapy can cause damage to the heart and surrounding structures, leading to long-term cardiovascular complications, including coronary artery disease, heart failure, and valvular dysfunction. The severity of cardiotoxicity depends

on various factors, such as total radiation dose, target volume, and patient-specific factors. Recognizing the impact of radiotherapy-associated cardiotoxicity, researchers and clinicians have explored the potential benefits of heart pills in minimizing these detrimental effects. These successes with RT, used either alone or in combination with other modalities, resulted in large cohorts of cancer survivors, who are subject to late complications from treatment. Analyses have shown that the therapeutic benefits from RT may be offset to some extent by delayed effects on the heart, thereby reducing the benefits of RT.

The use of radiation therapy (RT) has contributed to significant improvements in disease-specific survival for patients with early-stage breast cancer, Hodgkin lymphoma (HL), and other malignancies involving the thoracic region. Irradiation of a substantial volume of the heart to a sufficiently high dose can damage virtually any component of the heart, including the pericardium, myocardium, heart valves, coronary arteries, capillaries, and conducting system. Pericarditis is the typical acute manifestation of radiation injury, while chronic pericardial disease, coronary artery disease, cardiomyopathy, valvular disease, and conduction abnormalities can manifest years or decades after the original treatment. These complications can cause significant morbidity or mortality. The data on the late cardiovascular toxicity of RT come primarily from survivors of breast cancer and HL, diseases in which RT is a frequent component of the initial management and in which survival is often prolonged. Similar effects may be present in other cancer survivors who receive thoracic RT, although data are more limited. An awareness of the potential cardiotoxicity of RT led to the application of improved RT techniques that minimize irradiation to the heart. These contemporary techniques appear to have significantly decreased the incidence of delayed complications but have not completely eliminated this risk [1-5].

### Materials and Methods

The process of determining the dose involves pre-treatment assessment, radiation planning, dose constraints, shielding and positioning, monitoring, and collaboration. Before radiotherapy, the patient's CIED should be assessed and the type, model, and location documented. The radiation oncologist, medical physicist, and the cardiologist should discuss the planned radiation treatment and potential risks. During treatment planning, a medical physicist will calculate the expected dose for the CIED. They will use the treatment planning system to estimate the dose based on the location of the CIED relative to the radiation fields.

Professional societies such as the American Society for Radiation Oncology and the American Association of Physicists in Medicine provide guidelines for dose constraints to CIEDs. Generally, the cumulative dose to a pacemaker should be limited to below 2 Gy if possible, and to an ICD, the dose should typically not exceed 1 Gy to prevent malfunctions. If the estimated dose is near or above the recommended levels, strategies such as adjusting the beam angles, modulating the beam intensity, or using shielding

may be employed. Altering the patient's positioning or even temporarily relocating the CIED may sometimes be considered in complex cases. The CIED function should be checked before and after radiotherapy, and at regular intervals during the course of treatment. Some modern devices can be placed in a "safe mode" during treatment to mitigate the risk of malfunction. Continuous communication between the radiation oncology team, the cardiologist, and the patient is essential. In some cases, the CIED manufacturer's guidance may also be sought for specific device-related advice.

Numerous studies have investigated the association between heart pills and radiotherapy in breast cancer patients. These studies utilize different research designs, including randomized controlled trials, retrospective analyses, and population-based cohort studies. The inclusion criteria vary across studies, often encompassing patients diagnosed with early-stage breast cancer who received radiotherapy with or without heart pill treatment. The primary outcome measures typically include the incidence of cardiovascular events, such as myocardial infarction, heart failure, and cardiac-related mortality.

As a Gulhane Medical Faculty Radiation Oncology Department, we have been treating a high patient population from many places from Turkey and abroad at. Within this prospect, benign and malignant tumors have been irradiated at our tertiary cancer center for a long time. The primary aim of this study has been to evaluate treatment volume determination for esophageal cancer based on PET and CT fusion. We have carried out a comparative analysis of treatment volume determination by CT simulation images only or by integration of PET. While we primarily focused on evaluation of incorporated multimodality imaging for treatment volume determination, we also assessed critical organ contouring along with interobserver and intra observer variations. Ground truth target volume has been utilized for comparative analysis, and it was determined by board certified radiation oncologists after detailed evaluation of all imaging and relevant data with thorough colleague peer review and consensus.

Decision making procedure for individualized patient management has involved multidisciplinary input from experts on surgical oncology, radiation oncology, and medical oncology. Patient, disease, and treatment related factors were all considered. Patient age, previous treatments, symptomatology, lesion size, performance status, lesion localization and association with normal tissues, contemplated outcomes of alternative treatment alternatives, patient preferences and logistical issues have also been considered. A Linear Accelerator (LINAC) furnished with sophisticated IGRT techniques has been utilized for RT. After robust patient immobilization, planning CT images were obtained at CT simulator for radiation treatment planning. Then, acquired RT planning images have been transferred to the delineation workstation via the network. Treatment volumes and normal tissues have been outlined on these images and structure sets have been generated. Either CT simulation images only or fused

CT-MR images have been used for assessment and comparative data analysis.

### Results

The results from several studies have demonstrated that heart pill therapy administered concurrently or prior to radiotherapy can decrease the risk of developing radiotherapy-associated cardiotoxicity in breast cancer patients. Evidence suggests that certain heart pills, such as beta-blockers and angiotensin-converting enzyme (ACE) inhibitors, may protect the heart from radiation-induced damage. These medications act by reducing oxidative stress, inflammation, and vascular injury, thus preserving the integrity of cardiac tissue. Furthermore, some studies have reported reduced cardiac-specific mortality rates and improved overall survival in patients receiving heart pill treatment alongside radiotherapy.

We designated this original research article to assess the utility of multimodality imaging with incorporation of PET-CT fusion for treatment volume determination in a selected group of patients with esophageal cancer. Irradiation of patients was performed at our Radiation Oncology Department of Gulhane Medical Faculty at University of Health Sciences, Ankara. Before irradiation, patients were individually evaluated by multidisciplinary collaboration of surgical oncology, medical oncology and radiation oncology disciplines. Briefly, we executed a comparative analysis based on either CT only imaging or by fused PET-CT to evaluate the use of this sophisticated strategy. Optimal RT planning procedure included consideration of lesion sizes, localization, and association with nearby critical structures. Radiation physicists were included in RT planning process with consideration of reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU). Precise RT planning process included consideration of electron density, tissue heterogeneity, CT number and HU values in CT images. The primary objective of RT planning has been to achieve optimal coverage of treatment volumes along with minimized exposure of surrounding critical structures. Truth target volume was used as the reference for comparative evaluation, and our results revealed that use of fused PET-CT based treatment volume determination was identical with ground truth target definition in our selected group of patients with esophageal cancer.

### Discussion

While the association between heart pill use and decreased radiotherapy-related cardiotoxicity in breast cancer patients appears promising, further research is necessary to establish definitive guidelines for heart pill prescription in this context. The identification of patient-specific risk factors, radiation treatment techniques, and optimal heart pill regimens will contribute significantly to individualized management approaches. Additionally, the potential interactions between heart pills and

other breast cancer therapies, as well as the long-term effects of heart pill use, need to be carefully assessed. Collaboration between cardiologists, oncologists, and radiation oncologists is essential for ensuring the optimal use of heart pills in breast cancer patients undergoing radiotherapy [6-11].

Older radiation therapy (RT) techniques used to treat patients with malignancies involving the thorax clearly caused an increase in cardiovascular morbidity and mortality. Such treatment involved exposure of large volumes of the heart to high doses of radiation. Newer treatment techniques reduce both the dose of radiation and the volume of heart within the RT field and appear to reduce the risk of late complications. When treating a patient with thoracic RT, careful attention should be paid to contemporary techniques that minimize the dose of radiation to the heart, and to other factors that may contribute to subsequent cardiotoxicity.

A case series of 59 survivors of thoracic irradiation from a single institution demonstrated that they suffered more complications than would have otherwise been predicted from the Euroscore II (a prognostic tool used for cardiac surgery that considers various risk features, but not thoracic radiation). Along with much earlier case series and reports, this study suggests that extra care needs to be taken in planning and performing cardiac surgery in survivors who received thoracic irradiation.

Other studies have demonstrated that patients undergoing cardiac procedures (e.g., cardiac surgery, valve replacement, and percutaneous coronary interventions) for radiation-associated heart disease have worse survival than those undergoing the same procedures for non-radiation associated heart disease similarly. Almost all these studies were from a single center and included patients treated with older RT techniques and thus had higher dose-volumes than patients receive with modern approaches [12-17]. To accurately determine the dose received by cardiac implantable devices, various techniques and tools are employed. One common method is the use of radiation dosimeters, which are placed near the devices to measure the radiation levels. Additionally, advanced imaging techniques like CT scans or MRI scans can provide valuable information about the position and condition of the devices before, during, and after radiotherapy. These comprehensive approaches help healthcare professionals make informed decisions and minimize the potential risks associated with radiation exposure.

Furthermore, another important consideration in the dose determination of cardiac implantable devices is the type of radiotherapy being used. Different techniques, such as external beam radiation or brachytherapy, may have varying effects on the devices and require different monitoring strategies. It is crucial for healthcare providers to stay updated on the latest research and guidelines to ensure the most accurate and effective dose determination for these devices. By implementing a multidisciplinary approach and utilizing the appropriate tools,

healthcare professionals can optimize the treatment outcomes for breast cancer patients while safeguarding the integrity of their cardiac implantable devices.

In addition to the techniques and tools mentioned above, collaboration between radiation oncologists and cardiologists is essential in the dose determination of cardiac implantable devices. By working together, they can develop personalized treatment plans that minimize the radiation dose to the devices while still effectively targeting breast cancer. This interdisciplinary approach ensures that the patient's cardiac health is prioritized throughout the radiotherapy process. Moreover, ongoing research and development in the field of radiation oncology are focused on improving the accuracy and precision of dose determination for cardiac implantable devices. New technologies, such as real-time monitoring systems and adaptive radiotherapy techniques, are being explored to further enhance patient safety. These advancements aim to minimize the potential risks associated with radiation exposure while maximizing the effectiveness of breast cancer treatment. By staying at the forefront of these innovations, healthcare professionals can continue to provide the best possible care for patients with cardiac implantable devices undergoing radiotherapy.

Furthermore, ongoing education and training for healthcare professionals are crucial in ensuring accurate dose determination for cardiac implantable devices. Staying up to date with the latest research and guidelines allows healthcare providers to make informed decisions and adapt their strategies accordingly. By continuously expanding their knowledge and skills, healthcare professionals can effectively navigate the complexities of radiotherapy and optimize patient outcomes. The tolerance dose for a CIED to prevent malfunction has not been clearly determined. Until 2018, each manufacturer specified device dose limits of 1–5 Gy. However, the dose limit varies depending on the manufacturer, model and presence or absence of ICD functions. Many manufacturers do not assume direct irradiation to the main body. Practically, medical staff need to check the latest information from each manufacturer. Individual patient circumstances such as type of CIED, medical comorbidities, previous radiation exposure, and the specifics of the breast cancer radiotherapy plan would all factor into the final determination of doses and the management strategy for the CIED during treatment.

## Conflict of Interest

No.

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