Reviews in Cardiovascular Medicine

Rev. Cardiovasc. Med. **2026**; 27(11): 54873
https://doi.org/10.31083/RCM54873

Review

Right Ventricular Toxicity After Thoracic Radiotherapy: From Pathophysiological Mechanisms to Multimodality Imaging and Personalized Surveillance

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Academic Editor: John Lynn Jefferies
Submitted: 14 June 2026 Revised: 6 August 2026 Accepted: 19 August 2026 Published: 12 November 2026

Abstract

Radiotherapy (RT) is a cornerstone of treatment for several thoracic malignancies, most notably breast and lung cancers, and has significantly improved long-term survival. However, rising survivorship has heightened recognition of radiation-induced heart disease as a major contributor to long-term cardiovascular morbidity. While most cardio-oncology research has historically focused on left ventricular dysfunction, the right ventricle (RV) has recently emerged as a potentially vulnerable yet underrecognized target of radiation-related injury. Owing to its anterior position within the thorax, the RV free wall is frequently exposed to substantial radiation doses during thoracic irradiation, particularly when internal mammary nodal irradiation is required. Radiation-induced RV toxicity results from a complex interplay of direct myocardial injury and indirect cardiopulmonary interactions. At the myocardial level, ionizing radiation promotes endothelial dysfunction, microvascular rarefaction, chronic inflammation, and progressive interstitial fibrosis, ultimately impairing RV contractile mechanics. Simultaneously, radiation-induced lung injury contributes to pulmonary vascular remodeling, increased pulmonary vascular resistance, and RV–pulmonary artery uncoupling, further accelerating RV dysfunction. Contemporary multimodality imaging has substantially improved detection of these alterations in their subclinical phase. Advanced echocardiographic techniques, particularly RV free-wall longitudinal strain, enable early identification of mechanical abnormalities before conventional indices become abnormal. Cardiac magnetic resonance provides a highly reproducible assessment of RV volumes and function and offers unique capabilities for myocardial deformation analysis, tissue characterization, and quantification of diffuse fibrosis through extracellular volume mapping. Cardiac computed tomography has emerged as a critical tool for cardiac substructure dosimetry, facilitating personalized RT planning and RV sparing strategies. In parallel, radiomics and artificial intelligence approaches are opening new opportunities for individualized risk prediction and long-term surveillance. This narrative review summarizes the current understanding of the pathophysiological mechanisms underlying radiation-induced RV injury, critically examines the role of multimodality imaging in its detection and monitoring, and proposes an integrated clinical framework to improve early diagnosis, risk stratification, and prevention of RV dysfunction in patients exposed to thoracic RT.

Keywords: breast cancer; cardio-oncology; cardiac magnetic resonance; radiotherapy; right ventricular dysfunction

1. Introduction

Radiotherapy (RT) is a cornerstone of modern cancer treatment and exerts its antitumor effects primarily through the induction of deoxyribonucleic acid (DNA) damage, ultimately leading to cancer cell death [1]. Ionizing radiation is most commonly delivered using high-energy photons, although electrons and particle-based modalities, such as proton therapy, may also be employed. Contemporary RT planning relies on the use of multiple conformal radiation beams delivered from different angles to maximize tumour coverage while minimizing irradiation of surrounding healthy tissues [1]. Furthermore, treatment is typically administered in multiple fractions over several days or weeks, allowing normal tissues to recover from sublethal radiation injury between sessions [1]. RT may be used as a definitive treatment or in combination with surgery, chemotherapy, immunotherapy, or targeted therapies as part of a multimodal cancer management strategy. Radiation prescriptions are generally expressed as a total dose, measured in Gray (Gy), delivered over a predetermined number of fractions according to tumour type, location, and therapeutic intent [1].

Over the past two decades, remarkable technological advances have transformed RT practice, enabling increasingly precise and personalized treatment delivery. The implementation of image-guided RT, intensity-modulated RT,

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and other advanced planning techniques has significantly improved target localization and dose conformity, thereby reducing unnecessary exposure of adjacent organs [1]. Despite these advances, incidental cardiac irradiation remains unavoidable in many patients receiving thoracic RT. The landmark study by Darby et al. [2] established that incidental cardiac irradiation increases the rate of ischemic heart disease proportionally to the mean heart dose, with no apparent threshold. Consequently, radiation-induced heart disease (RIHD) has emerged as a major concern in long-term cancer survivorship, encompassing coronary artery disease, valvular heart disease, pericardial disease, conduction abnormalities, and myocardial dysfunction [1,3,4].

In the vast landscape of cardio-oncology, breast cancer represents the most conspicuous clinical model for investigating treatment-related cardiotoxicity [5,6]. Historically, guidelines and surveillance protocols have primarily focused on left ventricular (LV) dysfunction, evaluating cardiotoxicity through serial changes in left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS) [1,2,5,6,7,8]. This paradigm has largely been driven by the well-established cardiotoxic effects of anthracyclines and anti-human epidermal growth factor receptor 2 (HER2) therapies. However, growing evidence suggests that cancer therapy-related cardiovascular toxicity is not exclusively a left-sided phenomenon. In recent years, the right ventricle (RV) has emerged as the true "forgotten ventricle" in cardio-oncology, attracting increasing attention because of its unique anatomy, physiology, and prognostic relevance [9].

Evidence from systemic cancer therapies has demonstrated that RV dysfunction may develop early during treatment and may even precede overt declines in conventional functional parameters. Rossetto et al. [10] prospectively demonstrated in 83 breast cancer patients treated with anthracyclines that 28% developed subclinical RV cardiotoxicity detectable by Speckle Tracking Echocardiography (STE) and three-dimensional transthoracic echocardiography (3D TTE), with RV and LV alterations occurring concomitantly, reinforcing the concept that cardiotoxicity represents a diffuse biventricular process. Similarly, Zhao et al. [11] showed in a cohort of 74 lymphoma patients that three-dimensional echocardiography (3DE)-derived RV longitudinal free-wall strain (RV-FWLS) declined before right ventricular ejection fraction (RVEF), and that a relative reduction >12.4% during chemotherapy predicted subsequent RV cardiotoxicity (area under the curve [AUC] 0.80), establishing 3D TTE as a powerful tool for the early identification of RV injury.

While the impact of systemic therapies on RV function is increasingly recognized, the specific contribution of thoracic RT to RV injury remains poorly defined. This knowledge gap is particularly important because the RV may be uniquely vulnerable to radiation exposure. Adjuvant RT remains a cornerstone of breast cancer management, significantly reducing loco-regional recurrence and improving overall survival [7]. However, its cardiovascular consequences continue to represent a major challenge. From an anatomical standpoint, the RV occupies the most anterior position within the mediastinum, placing the RV free wall in close proximity to radiation fields used for breast and mediastinal malignancies [12]. Consequently, the RV is frequently exposed to disproportionately higher radiation doses than other cardiac chambers. Recent high-resolution multiphase dosimetric analyses using Coronary Computed Tomography Angiography (CCTA) have further demonstrated that dynamic cardiorespiratory motion during post-mastectomy radiotherapy (PMRT) may exacerbate RV radiation exposure [12].

The pathophysiology of radiation-induced RV injury fundamentally differs from that of drug-induced cardiotoxicity. Rather than causing direct cardiomyocyte apoptosis, ionizing radiation primarily induces endothelial dysfunction, microvascular rarefaction, chronic inflammation, and extracellular matrix remodelling, ultimately leading to diffuse interstitial fibrosis [3,13]. Because the RV is a low-pressure, highly compliant chamber characterized by thin myocardial walls, it is particularly susceptible to structural remodelling and functional deterioration in response to these pathological processes [9,14,15]. Supporting this concept, Sławiński et al. [16] demonstrated in lung cancer patients that cancer treatment-related RV toxicity (CTRRVT) occurred in approximately 40% of irradiated patients, with significant reductions in RV GLS and tricuspid annular plane systolic excursion (TAPSE) occurring within the first three months after RT. Importantly, the mean RV radiation dose correlated directly with impairment of 3D-derived RVEF, suggesting a dose-dependent relationship between radiation exposure and RV dysfunction [16].

The growing recognition of RV involvement in RIHD has highlighted the need for sensitive imaging tools capable of detecting early myocardial injury before overt RV dysfunction develops. The American Heart Association Scientific Statement on Cardiovascular Imaging in Cardio-Oncology and the JACC Scientific Statement on Multimodality Imaging of Right Heart Function emphasize that RV functional parameters—including TAPSE, fractional area change (FAC), RV-FWLS, and RVEF assessed by cardiac magnetic resonance (CMR)—carry independent prognostic value and should be incorporated into comprehensive cardio-oncology surveillance strategies [8,17]. Although conventional TTE remains the first-line imaging modality, traditional indices such as TAPSE and FAC may lack sensitivity for the detection of subclinical dysfunction [1,7,9]. In contrast, two-dimensional STE enables early assessment of RV myocardial deformation through RV-FWLS analysis [16,18,19]. Furthermore, CMR, considered the reference standard for RV volumetric assessment [17], provides unique opportunities for tissue characterization through feature tracking (CMR-FT) and extracellular volume (ECV)

mapping, allowing the identification of diffuse myocardial fibrosis before the onset of overt dysfunction [20].

Given the increasing number of long-term cancer survivors and the growing awareness of RV involvement in RIHD, a comprehensive understanding of radiation-induced RV injury has become increasingly important. Therefore, this review aims to synthesize the distinct pathophysiological mechanisms underlying radiation-induced RV injury in patients undergoing RT; the diagnostic and prognostic value of advanced multimodality imaging techniques, including STE, CMR, and CCTA, and a practical clinical framework for the early detection, risk stratification, and targeted right-sided cardio-protection of patients exposed to thoracic RT.

2. Literature Search

A non-systematic, narrative literature search was performed in PubMed/MEDLINE, Embase, and Web of Science from database inception to June 2026. Search terms included combinations of "radiation-induced heart disease", "cardiotoxicity", "right ventricular toxicity", "right ventricular dysfunction", "thoracic radiotherapy", "breast cancer radiotherapy", "lung cancer radiotherapy", "cardio-oncology", "speckle-tracking echocardiography", "right ventricular strain", "cardiac magnetic resonance", "extracellular volume mapping", "cardiac substructure dosimetry", and "radiomics", combined using the Boolean operators AND/OR. Reference lists of retrieved articles, related systematic reviews and meta-analyses, and major society scientific statements and consensus documents were manually screened to identify additional relevant publications not captured by the primary search. Preclinical, observational, and imaging-based clinical studies published in English were considered eligible for inclusion; conference abstracts, case reports, and non-peer-reviewed sources were excluded, with priority given to publications from the past ten years. Given the narrative design of this review, no formal systematic screening, dual independent reviewer assessment, or PRISMA-based selection flow was applied; article selection, appraisal, and synthesis were performed by the authors based on relevance, methodological quality, and recency. This narrative review was prepared with reference to the Scale for the Assessment of Narrative Review Articles (SANRA) criteria, ensuring adequate justification of the topic's importance, an explicit statement of the review's aims, a transparent description of the literature search strategy, and appropriate scientific reasoning in the presentation and discussion of the retrieved evidence [21].

3. Pathophysiological Mechanisms of Radiation-Induced Right Ventricular Toxicity

The pathophysiology of RIHD is characterized by a complex and multifaceted cascade of events that fundamentally differs from the direct cardiomyocyte apoptosis typically observed in drug-induced cardiotoxicity [3]. Following radiation exposure, ionizing radiation triggers an immediate endothelial and inflammatory response that progressively evolves into chronic structural and functional remodelling of the heart [18,19]. Increasing translational and clinical evidence suggests that the RV is particularly vulnerable to these processes through two complementary mechanisms: direct myocardial injury affecting the RV myocardium itself and indirect hemodynamic stress resulting from radiation-induced pulmonary vascular and parenchymal damage [4,13] (Fig. 1). Importantly, the same intrinsic characteristics that render the RV susceptible to radiation injury may also explain why both anthracycline-induced and radiation-induced cardiotoxicity tend to impair RV contractile mechanics before overt reductions in global RVEF become apparent [10,11,14,16].

3.1 Direct Myocardial Injury: Microvascular Rarefaction and the Fibrotic Cascade

The direct effects of ionizing radiation on the RV myocardium begin at the endothelial level. Within hours of exposure, radiation-induced radiolysis of water generates large amounts of reactive oxygen species (ROS), resulting in DNA double-strand breaks, oxidative stress, and endothelial cell senescence or apoptosis [3,13]. This injury initiates a progressive process of microvascular rarefaction, characterized by a reduction in capillary density and chronic impairment of myocardial perfusion. As a consequence, a state of persistent local hypoxia develops within the RV myocardium, promoting further cellular damage and adverse remodelling [4].

The unique architecture of the RV may amplify the functional consequences of these changes. As highlighted by the JACC Scientific Statement on Multimodality Imaging of Right Heart Function, RV systolic performance is predominantly driven by the longitudinal shortening of the RV free wall, which is generated by a thin subendocardial longitudinal fiber layer [17]. Consequently, pathological processes affecting the subendocardial microcirculation are likely to impair longitudinal mechanics before alterations become detectable using global volumetric indices. This pathophysiological framework helps explain why parameters such as GLS and RV-FWLS frequently deteriorate earlier than RVEF in patients exposed to both chemotherapy and radiation [9,15].

Microvascular injury is followed by the activation of a sustained inflammatory and profibrotic response [4]. Damaged endothelial cells, infiltrating inflammatory cells, and resident cardiac macrophages promote the persistent release of cytokines and growth factors, including transforming growth factor-beta 1 (TGF-β1), TNF-α, and IL-6 [3,7]. These mediators stimulate myofibroblast activation and accelerate extracellular matrix deposition, ultimately leading to diffuse interstitial fibrosis [4].

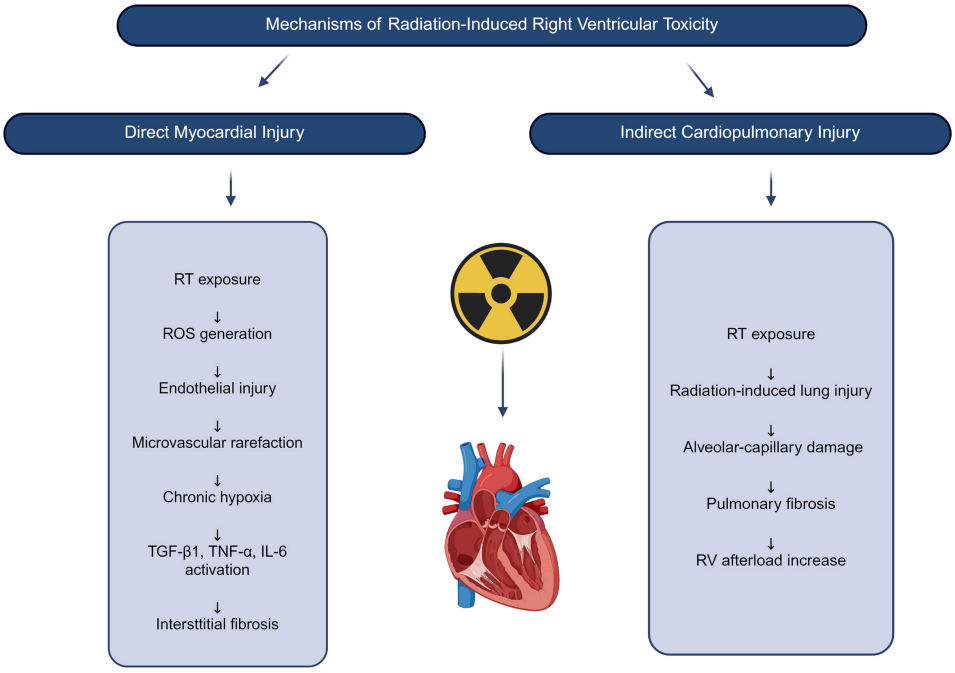


Fig. 1. Dual-hit pathophysiological model of radiation-induced RV toxicity. Created in BioRender. Piscione, M. (2026) https://BioRender.com/r40mjwu. Ionizing radiation induces RV dysfunction through two complementary and mutually reinforcing mechanisms. Abbreviations: IL-6, Interleukin-6; ROS, reactive oxygen species; RT, radiotherapy; RV, right ventricle; TGF-β1, Transforming Growth Factor Beta 1; TNF-α, Tumor Necrosis Factor-α.

The clinical relevance of this mechanism is supported by several imaging studies. Keramida and Farmakis [22] reported that RV-FWLS is the TTE parameter showing the most consistent and reproducible performance across oncological populations, with an absolute cut-off of −18.2% for dysfunction (distinct from the relative percentage-change threshold discussed in Section 6.1), and high diagnostic accuracy (AUC 0.87) using 3D STE imaging. Similarly, Rossetto et al. [10] demonstrated that STE and 3D TTE could detect subclinical RV injury through early reductions in GLS and 3D TTE EF. Collectively, these findings suggest that radiation-induced microvascular and fibrotic remodelling initially manifests as impairment of RV myocardial deformation before overt deterioration of global systolic function occurs.

3.2 Indirect Mechanical Insult: Radiation-Induced Cardiopulmonary Interaction

In addition to direct myocardial injury, the RV is exposed to a second pathophysiological pathway mediated by RT-induced damage to the lungs and pulmonary vasculature [4,13]. Because the lung parenchyma and pulmonary microcirculation are frequently included within thoracic radiation fields, particularly during internal mammary nodal irradiation (IMNI), incidental pulmonary irradiation is often unavoidable [7,12]. The resulting radiation-induced lung injury (RILI) contributes substantially to RV stress by altering the cardiopulmonary interaction.

Experimental and clinical studies have shown that RILI is characterized by progressive alveolar-capillary membrane thickening, endothelial dysfunction, microvascular occlusion, and pulmonary fibrosis [13]. Moraes et al. [13] demonstrated that these pathological changes extend beyond the lung itself, affecting cardiovascular performance. As pulmonary vascular remodelling progresses, pulmonary vascular resistance (PVR) and pulmonary artery pressure (PAP) increase, thereby imposing a chronic afterload burden on the RV [13].

The importance of this mechanism has been elegantly demonstrated by Wiedemann et al. [4], who showed in a preclinical model that thoracic irradiation induces a substantial and progressive increase in PVR and PAP, whereas cardiac-sparing radiation protocols facilitate long-term recovery of the cardiopulmonary circulation. Therefore, radiation exposure simultaneously affects both sides of the RV load equation: it directly impairs myocardial contractility through fibrosis while increasing afterload through pulmonary vascular disease [13].

As pulmonary vascular remodeling progresses, the resulting increase in PVR and PAP may ultimately lead to impairment of right ventricle–pulmonary artery (RV–PA) coupling, a key determinant of RV adaptation to afterload stress [13]. Under physiological conditions, the RV maintains efficient energy transfer to the pulmonary circulation through a balanced relationship between RV contractility and pulmonary arterial load. However, radiation-induced

pulmonary vascular disease may progressively disrupt this relationship, leading to RV–PA uncoupling, reduced mechanical efficiency, and eventual RV failure [13]. From a hemodynamic perspective, RT-associated pulmonary hypertension (PH) may involve both pre-capillary and post-capillary mechanisms. Direct pulmonary vascular injury and parenchymal fibrosis predominantly contribute to a pre-capillary phenotype through increased PVR, whereas concomitant left-sided radiation-induced heart disease, including myocardial fibrosis, valvular disease, and diastolic dysfunction, may promote post-capillary PH [13]. In advanced stages, the coexistence of both mechanisms may result in combined pre- and post-capillary PH, further increasing RV workload and accelerating adverse remodelling.

The convergence of these mechanisms creates a self-perpetuating cycle of RV dysfunction. A fibrotic and mechanically impaired RV is required to operate against progressively increasing PVR, thereby accelerating adverse remodelling and functional deterioration [13]. Clinical observations strongly support this concept. Sławiński et al. [16] reported that CTR-RVT occurred in approximately 40% of irradiated lung cancer patients despite a reportedly low mean RV radiation dose in the source cohort, consistent with the value reported in the original publication (mean RV dose 4.38 ± 3.18 Gy); the source study attributes this to the RV being generally less exposed than the LV during lung cancer radiotherapy in their specific cohort and demonstrated a direct correlation between mean RV dose and impairment of 3D-derived RVEF. These findings underscore the remarkable sensitivity of the RV to radiation exposure, even at modest dose levels [16].

Additional evidence comes from thoracic oncology populations. Chen et al. [23] evaluated 128 patients with inoperable stage III non-small cell lung cancer (NSCLC) undergoing concurrent chemo-radiotherapy (CCRT) and demonstrated significant declines in both RV-FWLS and RV-GLS at six months after treatment (–28.3 ± 4.6% vs. –25.5 ± 4.8%, $p < 0.001$). Importantly, mean RV radiation dose correlated directly with worsening RV GLS (r = 0.303, $p = 0.001$), while the percentage change in RV-FWLS emerged as an independent predictor of all-cause mortality (hazard ratio [HR] 1.296, 95% confidence interval [CI] 1.202–1.428, $p < 0.001$) [23]. Consistent with these observations, Banfill et al. [7] highlighted the critical importance of minimizing radiation exposure to anterior cardiac substructures and emphasized the need for dedicated RV dose constraints in future thoracic RT protocols.

Taken together, current evidence suggests that radiation-induced RV toxicity is the result of a dual-hit mechanism involving direct myocardial fibrosis and indirect cardiopulmonary coupling impairment (Table 1, Ref. [3,4,7,10,11,13,15,16,19]). This integrated model provides a plausible explanation for the early deterioration of RV strain parameters observed after thoracic RT and underscores the importance of sensitive imaging techniques capable of detecting subclinical RV dysfunction before irreversible remodelling develops.

4. Advanced Tissue Characterization and Geometric Assessment: The Role of Cardiac Magnetic Resonance

4.1 Early Detection of Subclinical Right Ventricular Dysfunction: The Emerging Role of CMR Feature Tracking

CMR has emerged as the reference standard for the comprehensive assessment of RV structure and function owing to its unparalleled accuracy and reproducibility. The superiority of CMR for serial assessment has been demonstrated by Grothues et al. [24], who reported markedly lower interstudy variability for ventricular volumes, myocardial mass, and EF compared with TTE, translating into substantially smaller sample sizes required for longitudinal follow-up studies. These characteristics are particularly valuable in cardio-oncology, where subtle treatment-related changes may carry important prognostic implications and where highly reproducible imaging biomarkers are required for long-term surveillance.

According to the JACC Scientific Statement on Right Heart Imaging, CMR-derived RVEF remains the most robust parameter for the assessment of global RV systolic function, with values below 45% generally considered indicative of clinically relevant RV dysfunction [17]. However, contemporary understanding of RV failure recognizes that abnormalities in myocardial mechanics frequently precede overt reductions in RVEF. Consequently, growing attention has shifted toward the identification of earlier imaging biomarkers capable of detecting subclinical RV dysfunction before the onset of overt volumetric impairment [17].

In this regard, CMR feature tracking (CMR-FT) has emerged as a promising technique for the quantification of RV myocardial deformation. By tracking myocardial motion throughout the cardiac cycle using conventional cine images, CMR-FT enables the assessment of longitudinal strain without the need for dedicated tagging sequences. Similar to STE, RV-FWLS may reveal subtle abnormalities in contractile performance despite preserved global systolic function, thereby identifying an early stage of RV maladaptation. Nevertheless, despite its considerable scientific potential, CMR-derived GLS remains largely confined to research settings. The absence of universally accepted acquisition and post-processing standards, together with limited software availability and longer analysis times, has restricted its widespread implementation in routine clinical practice. As a result, although CMR-FT provides important mechanistic insights into early radiation-induced myocardial injury, its current clinical role remains primarily investigational.

Table 1. Key molecular and physiological mechanisms of radiation-induced RV toxicity.

Phase	Direct pathway	Indirect (cardiopulmonary) pathway
Acute (hours–days)	ROS generation, DNA double-strand breaks, endothelial apoptosis [3,13]	Alveolar-capillary membrane damage, early microvascular occlusion [4,13]
Subacute (weeks–months)	Microvascular rarefaction, chronic hypoxia, macrophage/TGF-β1 activation [3,7]	Pulmonary microvascular fibrosis, rising PVR [4,13]
Chronic (months–years)	TGF-β1-driven myofibroblast activation, diffuse interstitial fibrosis, RV-FWLS impairment [10,11,16,19]	Progressive PAP elevation, RV afterload mismatch, maladaptive hypertrophy [4,7,15]

Abbreviations: DNA, deoxyribonucleic acid; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; RV-FWLS, right ventricular free-wall longitudinal strain.

4.2 Tissue Characterization and Detection of Subclinical Radiation-Induced Cardiac Remodeling

Beyond myocardial deformation, one of the greatest strengths of CMR lies in its ability to characterize myocardial tissue and identify structural abnormalities before conventional functional deterioration becomes apparent. Although evidence specifically focused on radiation-induced RV remodelling remains limited, available studies provide important insights into the long-term consequences of cardiac irradiation. In one of the earliest pilot CMR investigations in breast cancer survivors treated with cardiotoxic chemotherapy and 3D conformal RT, Bergom et al. [25] demonstrated significant associations between cardiac radiation exposure and adverse myocardial remodelling. Ventricular mean dose and dose-volume parameters such as V10 and V25 correlated with structural myocardial abnormalities, while expansion of ECV emerged as a marker of diffuse myocardial fibrosis and persistent tissue injury [25].

Similar observations have been reported in populations exposed to mediastinal irradiation. Using comprehensive CMR protocols, van der Velde et al. [26] evaluated lymphoma survivors and identified a high prevalence of previously unrecognized structural and functional abnormalities despite the absence of overt cardiovascular symptoms. These findings reinforce the concept that radiation-induced myocardial injury may remain clinically silent for prolonged periods while progressive remodelling continues at the tissue level. The ability of CMR to detect these abnormalities before the development of symptomatic heart disease represents one of its major advantages within contemporary survivorship programs.

Further evidence supporting the existence of a prolonged subclinical phase derives from studies investigating myocardial deformation. In a cross-sectional cohort of 109 breast cancer survivors, van den Bogaard et al. [27] demonstrated that conventional measures of systolic function, including LVEF, were not significantly associated with RT dose parameters. In contrast, LV-GLS showed a significant relationship with radiation exposure to the left main coronary artery, with coronary dose-volume histogram parameters emerging as stronger determinants of myocardial dysfunction than direct myocardial dose itself [27]. Although these observations primarily concern the LV, they support the broader concept that advanced imaging biomarkers may detect radiation-induced myocardial injury long before conventional measures of ventricular performance deteriorate.

4.3 Phase-Contrast CMR for Hemodynamic Assessment and Valvular Quantification

Beyond tissue characterization and deformation imaging, phase-contrast CMR provides unique hemodynamic information through direct quantification of intracardiac and great vessel blood flow. Phase-contrast sequences allow accurate measurement of forward and reverse flow volumes, stroke volume, shunt fractions, and regurgitant volumes with excellent reproducibility. This capability is particularly relevant in patients exposed to thoracic RT, who remain at increased risk of developing radiation-induced valvular heart disease. Unlike Doppler TTE, which relies on geometric assumptions and indirect velocity-based estimations, phase-contrast CMR enables direct volumetric quantification of valvular stenosis and regurgitation. Consequently, it represents an invaluable complementary technique for the assessment of tricuspid, pulmonary, mitral, and aortic valve disease, allowing accurate calculation of regurgitant fraction and severity. This aspect is particularly important for right-sided valvular lesions, where TTE quantification may be challenging and where accurate assessment of RV loading conditions is essential for understanding disease progression.

Taken together, these findings highlight the unique value of CMR for the evaluation of radiation-associated cardiac remodelling. By combining highly reproducible assessment of RV volumes and systolic function with advanced strain analysis, comprehensive tissue characterization, and quantitative flow assessment through phase-contrast imaging, CMR provides an integrated framework for identifying early myocardial injury, monitoring disease progression, and improving the detection of clinically silent cardiovascular abnormalities in cancer survivors exposed to thoracic RT (Fig. 2).

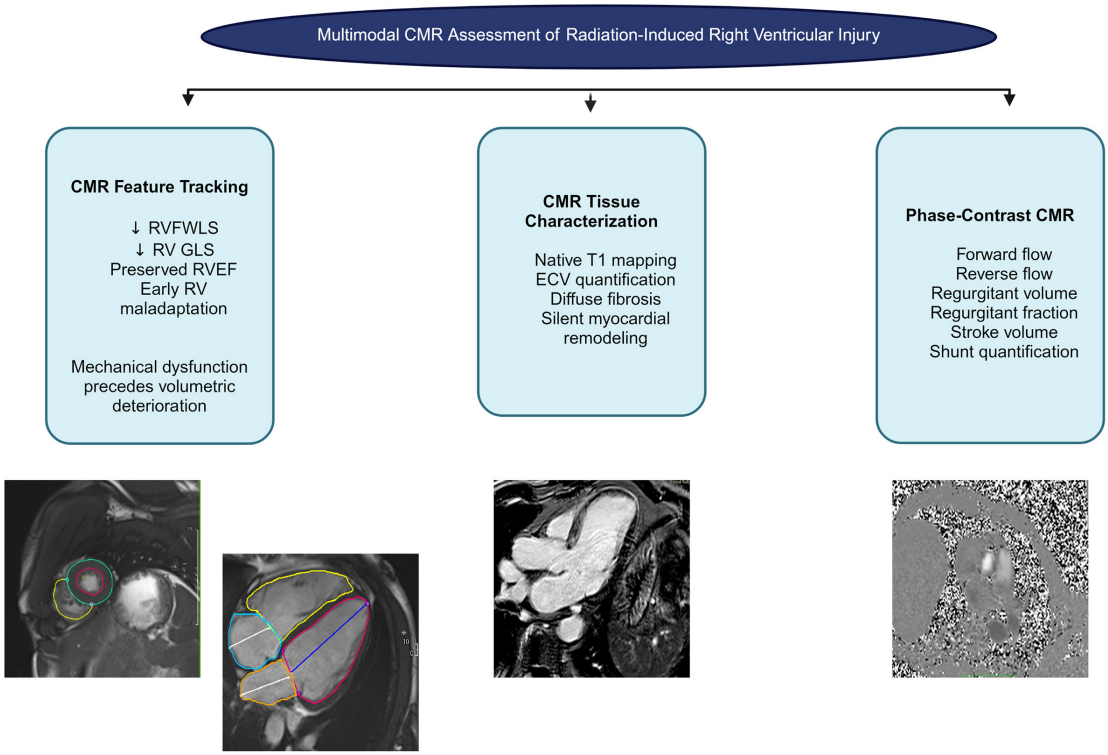


Fig. 2. Multimodal CMR assessment of radiation-induced right ventricular injury. Created in BioRender. Piscione, M. (2026) https://BioRender.com/4vcow6o. CMR provides a comprehensive framework for the evaluation of radiation-induced RV toxicity by integrating functional, structural, and hemodynamic information. Abbreviations: CMR, cardiac magnetic resonance; CMR-FT, cardiac magnetic resonance feature tracking; ECV, extracellular volume; RVEF, right ventricular ejection fraction; RV GLS, right ventricular global longitudinal strain.

5. Computed Tomography Dosimetric Planning and Radiomics: Preventing Right Ventricular Toxicity

While TTE and CMR remain the primary tools for the longitudinal assessment of radiation-induced cardiac injury, CCT plays a pivotal role in treatment planning and prevention. In this review, the term "CCT" is used as a general descriptor for CT-based cardiac imaging. When referring specifically to contrast-enhanced coronary CT angiography, the term "CCTA" is used. Beyond its established utility for the evaluation of coronary artery disease in cancer survivors [8], contemporary cardiac CT has become an indispensable component of thoracic radiotherapy planning, enabling detailed cardiac substructure contouring, precise dosimetric analysis, and the identification of patients at increased risk of developing radiation-induced right ventricular (RV) dysfunction [1,12]. Owing to its anterior anatomical position within the thorax, the RV free wall is particularly vulnerable to radiation exposure during breast and mediastinal irradiation, making accurate RV dosimetry a critical component of modern cardio-oncology strategies [12].

5.1 Multiphase Dosimetric Analysis and Cardiac Substructure Sparing

A major limitation of conventional radiotherapy planning is the assumption that cardiac structures remain static throughout treatment delivery. In reality, the heart undergoes continuous displacement due to both respiratory and cardiac motion, resulting in dynamic variations in radiation exposure that may not be captured by standard planning techniques [12]. This issue is particularly relevant for the RV, whose anterior location exposes it to substantial dose fluctuations during thoracic irradiation.

Recent advances in ECG-gated multiphase CCT have provided unprecedented insights into the dynamic interaction between cardiac motion and radiation delivery. Using multiphase CCTA datasets, Zhang et al. [12] demonstrated significant variations in minimum, maximum, and mean radiation doses delivered to the RV free wall throughout the cardiac cycle. Importantly, systolic anterior displacement of the RV resulted in transient increases in radiation exposure that occasionally exceeded the planned dose distribution, highlighting the limitations of static dosimetric models. These findings are particularly relevant in patients undergoing left-sided breast irradiation requiring internal mammary nodal irradiation (IMNI), where the proximity

between the target volume and the anterior cardiac structures substantially increases the risk of cardiac exposure [7,12].

The clinical importance of accurate RV dosimetry is supported by emerging outcome data. In a prospective cohort of lung cancer patients, Sławiński et al. [16] demonstrated a direct relationship between mean RV radiation dose and subsequent impairment of 3D-derived RVEF, suggesting that even relatively modest radiation exposure may contribute to measurable RV dysfunction. Similarly, Atkins et al. [28] reported that radiation dose delivered to specific cardiac substructures was associated with an increased risk of both tachyarrhythmias and bradyarrhythmias following thoracic radiotherapy. Together, these findings support the concept that cardiac substructure-based dosimetry may provide greater prognostic information than conventional whole-heart dose metrics.

Strategies aimed at minimizing RV exposure have therefore become increasingly important. In a comprehensive review of 159 comparative planning studies, Costin et al. [29] demonstrated that proton therapy consistently achieved the greatest reduction in cardiac substructure dose across different treatment settings. Among photon-based techniques, volumetric modulated arc therapy (VMAT) combined with deep inspiration breath hold (DIBH) provided the most effective reduction in radiation exposure to anterior cardiac structures, including the RV free wall [29]. These observations reinforce the growing consensus that modern radiotherapy planning should incorporate dedicated contouring of individual cardiac substructures rather than relying exclusively on whole-heart dose parameters [7,12,29].

5.2 Radiomics and Artificial Intelligence for Personalized Risk Prediction

Beyond treatment planning, CCT is increasingly being explored as a source of quantitative imaging biomarkers capable of identifying subclinical cardiovascular injury before the development of overt disease. Advances in radiomics and artificial intelligence have demonstrated that routine CT datasets contain a large amount of clinically relevant information that is not appreciable by visual inspection alone [30].

Several studies have shown that machine learning algorithms can extract complex imaging features associated with radiation-induced cardiovascular remodeling. Choi et al. [30] combined deep convolutional neural networks (CNNs) with dose-volume histogram (DVH) parameters derived from three-dimensional CT datasets and achieved high accuracy in predicting post-radiotherapy acute coronary events. Similarly, No et al. [31] demonstrated that quantitative imaging biomarkers integrated with radiation dose metrics improved prediction of subsequent cardiac events following radiotherapy for non-small cell lung cancer.

Although current radiomics investigations have primarily focused on coronary and global cardiovascular outcomes rather than RV-specific endpoints, these studies provide a proof-of-concept for the future development of personalized predictive models of radiation-induced RV injury. By integrating pre-treatment dosimetric data, cardiac substructure exposure, and post-treatment imaging features, artificial intelligence may ultimately enable individualized risk stratification and facilitate the implementation of targeted surveillance strategies.

This concept is consistent with the recommendations of the American Heart Association (AHA) Scientific Statement, which advocates the use of available CCT imaging not only for the assessment of established cardiovascular disease but also for the identification of subclinical cardiovascular risk and the implementation of preventive strategies tailored to the patient's overall oncological prognosis [8]. In the future, the integration of multiphase dosimetric planning, cardiac substructure analysis, and radiomics-based risk prediction may provide a comprehensive framework for preventing radiation-induced RV toxicity and optimizing long-term cardiovascular outcomes in cancer survivors.

6. Clinical Implications and Future Directions: Toward a Multimodality Right-Sided Framework

The clinical translation of advanced imaging and dosimetric modeling into daily practice represents a fundamental shift in cardio-oncology [1,7]. For decades, RV assessment in breast cancer survivors has been omitted from standard surveillance, creating a blind spot in the long-term management of therapy-related cardiotoxicity [9,14]. The ESC 2022 Guidelines on Cardio-Oncology [32], the Fischer-Bacca et al. [9] systematic review, and the AHA and JACC Scientific Statements [8,17] together establish a clear mandate: the RV must be managed with a structured pipeline from pre-treatment planning to late-stage survivorship.

6.1 High-Precision Surveillance Protocols

The progressive nature of radiation-induced right ventricular injury underscores the need to shift from the traditional paradigm of diagnosing established right heart failure toward a proactive strategy focused on early identification of subclinical dysfunction. Based on the currently available evidence, we propose an integrated multimodality surveillance pathway that combines advanced imaging, dosimetric information, and longitudinal functional assessment to facilitate earlier detection of RV injury and optimize long-term cardiovascular outcomes.

The first step should occur before treatment initiation and focus on risk stratification and dosimetric optimization. In patients undergoing thoracic RT, particularly when IMNI is planned, multiphase ECG-gated CCT

or advanced three-dimensional CT planning may provide valuable information regarding cardiac substructure exposure throughout the cardiorespiratory cycle [12]. Dedicated contouring of RV substructures should be incorporated whenever feasible, allowing evaluation of dynamic dose variations affecting the RV free wall during treatment delivery [12]. Modern radiation techniques, including volumetric modulated arc therapy (VMAT) combined with deep inspiration breath hold (DIBH), should be optimized to minimize radiation exposure to anterior cardiac structures and reduce RV dose-volume parameters whenever oncologically appropriate [7,12]. At the same time, a comprehensive baseline TTE examination should be performed to establish patient-specific reference values for RV-FWLS, RV GLS, and 3D-derived RVEF, thereby providing a robust foundation for subsequent longitudinal comparisons [11,17,19]. The ASE/EACVI Expert Consensus Statement by Plana et al. [33] established the framework for contemporary cardio-oncology echocardiographic surveillance, recommending serial assessment of LVEF, GLS, and cardiac biomarkers while also emphasizing the importance of quantitative RV evaluation through TAPSE, RV S′, and FAC as part of routine examinations. These recommendations provide a strong rationale for incorporating systematic RV assessment into surveillance programs for patients receiving thoracic RT.

Once treatment has commenced, surveillance should focus on the early identification of mechanical abnormalities before overt ventricular dysfunction develops. Emerging evidence suggests that RV impairment may become detectable during treatment or shortly thereafter. Sławiński et al. [16] demonstrated early reductions in RV function following thoracic irradiation, while Rossetto et al. [10] and Zhao et al. [11] reported similar findings in patients exposed to cardiotoxic systemic therapies, supporting the concept that myocardial deformation abnormalities frequently precede reductions in global systolic function. In this setting, serial 2D STE represents the most practical tool for detecting early RV injury. A decrease in RV-FWLS of more than 15% relative to baseline, by analogy with LV-GLS [33], may be suggestive of subclinical CR-CT. A relative decline in RV-FWLS exceeding 15% from baseline may be considered highly suggestive of subclinical CTR-CT, even in the presence of preserved TAPSE, FAC, and conventional systolic parameters [33]. This relative percentage-change criterion is distinct from, and should not be used interchangeably with, the absolute RV-GLS cut-off (below –18.2%) described in Section 3; the relative-change threshold is preferred when a reliable pre-treatment baseline is available, whereas the absolute cut-off may be applied when baseline values are unavailable. Consistent with this approach, the AHA Scientific Statement recommends that RV functional parameters be routinely acquired alongside LVEF and GLS during cardio-oncology follow-up assessments [8].

Long-term surveillance should focus on identifying persistent or progressive structural abnormalities that may not be fully captured by echocardiography alone. Between 9 and 12 months after RT, corresponding to the period during which radiation-related alterations in RV volumes and systolic performance may become more evident [9,20], CMR should be strongly considered in patients with suboptimal echocardiographic windows, documented reductions in RV strain, or intermediate-to-high cardiovascular risk profiles. Comprehensive CMR evaluation should include CMR feature tracking for assessment of RV global strain and right atrial mechanics, together with tissue characterization techniques such as native T1 mapping, T2 mapping, and ECV quantification to identify diffuse myocardial fibrosis and ongoing tissue remodelling [20,25,34]. In selected patients with persistent diagnostic uncertainty, complementary functional testing may provide incremental information. Myocardial perfusion imaging with SPECT has demonstrated the ability to detect subclinical perfusion abnormalities following thoracic RT before the development of clinically overt ischemic heart disease [35], while exercise stress TTE has shown prognostic value beyond resting measurements in irradiated breast cancer survivors [36].

Taken together, this integrated surveillance strategy combines advanced dosimetric planning, serial TTE assessment, and targeted use of CMR and functional imaging to facilitate earlier identification of radiation-induced RV injury (Table 2, Ref. [7,8,10,12,16,18,19,22,26,27,28,30,31,35,36,37,38,39]). Such an approach may allow clinicians to recognize myocardial damage during its subclinical stages, before irreversible remodelling and clinically overt right heart dysfunction develop.

6.2 Therapeutic Interventions and Research Horizons

The confirmation of early, subclinical right-sided mechanical failure provides a crucial window for targeted neurohormonal cardioprotection. Preclinical evidence from Boerma et al. [40] demonstrates that both statins and ACE inhibitors reduce myocardial injury in animal models of radiation-induced heart disease, acting via anti-inflammatory, anti-oxidant, and anti-fibrotic mechanisms; pentoxifylline combined with α-tocopherol reduced cardiac fibrosis and improved cardiac function when administered post-irradiation. The ESC 2022 Guidelines [32] advocate the initiation of ACEIs and beta-blockers in response to LV-GLS deterioration, but this recommendation derives predominantly from chemotherapy-related cardiotoxicity, and no dedicated trial has tested neurohormonal cardioprotection in radiation-induced cardiac injury or with RV-specific endpoints. Prospective trials are therefore needed to evaluate whether early initiation of these agents can mitigate the accelerated fibrotic remodeling and maladaptive hypertrophy of the afterload-sensitive RV. Zhao et al. [11] identified early, subclinical RV cardiotoxicity predictive of

Table 2. Comparative overview of multimodality imaging techniques for RV assessment in RIHD.

Modality	Key parameters	Clinical role	Limitations	Key references
2D-STE Echo	RV-FWLS, TAPSE, FAC, RV-GLS	First-line screening; serial surveillance; subclinical CTRCD detection	Acoustic window limitations; operator dependency	[7,10,16,18,19,36]
CMR-FT	RVEF, RV-GLS/GRS/GCS, RA reservoir strain	Gold standard RV volumes; tissue characterization; biatrial mechanics	Cost, availability, claustrophobia	[8,26,27]
CMR Parametric Mapping	T1/T2, ECV fraction, LGE	Non-invasive fibrosis quantification; pre-LGE interception	Technical complexity; hematocrit requirement	[8,22,26,37,35]
ECG-gated Cardiac CT	Substructure volumes, D_max, V5, cardiac cycle motion	Real-time dose tracking; RV sparing optimization; IMNI planning	Radiation exposure; contrast use	[7,12,16,28]
3D-CT + Radiomics/ DL-CNN	Radiomic features, DVH, AI-predicted ACE risk	Post-RT risk stratification; personalized follow-up scheduling	Validation heterogeneity; interpretability	[8,30,31,38,39]

Abbreviations: ACE, adverse cardiac events; AI, artificial intelligence; CCTA, coronary computed tomography angiography; CTRCD, cancer therapy-related cardiac dysfunction; DL-CNN, deep learning convolutional neural network; DVH, dose–volume histogram; D_max, maximum absorbed dose; FAC, fractional area change; GCS, global circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; IMNI, internal mammary nodal irradiation; LGE, late gadolinium enhancement; RA, right atrial; STE, speckle-tracking echocardiography; T1, longitudinal relaxation time; T2, transverse relaxation time; TAPSE, tricuspid annular plane systolic excursion; V5, cardiac volume receiving ≥5 Gy; 3D, three-dimensional; 2D-STE, two-dimensional speckle-tracking echocardiography.

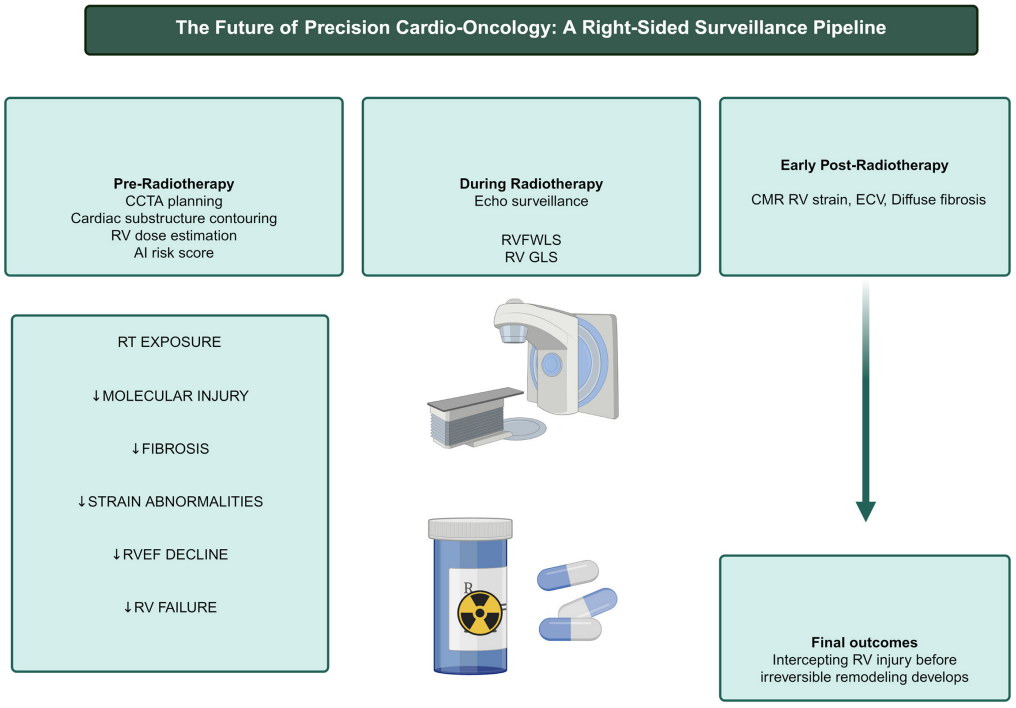


Fig. 3. The future of precision cardio-oncology: a right-sided surveillance pipeline. Created in BioRender. Piscione, M. (2026) https://BioRender.com/j9me6ye. Proposed multimodality framework for the prevention, early detection, and longitudinal monitoring of radiation-induced RV toxicity in patients undergoing thoracic RT.

subsequent RVEF decline in an anthracycline-treated lymphoma cohort in which cardioprotective medications were explicitly excluded and follow-up ended at completion of chemotherapy; this study does not support, and should not be cited for, a claim about stabilization following cardioprotective therapy. Rossetto et al. [10] separately reported that, among breast cancer patients who developed CTRCD and were subsequently started on cardioprotective

therapy (ACE-I/ARB and/or beta-blockers) per standard clinical practice, TTE-EF, RV-GLS, and RV-FWLS values were not significantly different between 6 and 12 months of follow-up (i.e., appeared to stabilize); however, as this was an observational, non-randomized cohort rather than a controlled intervention trial, this finding should be interpreted as hypothesis-generating rather than as established evidence of a therapeutic effect.

The integration of Deep Learning CNNs into standard post-RT 3D-CT datasets, as demonstrated by Choi et al. [30] and No et al. [31], offers an unexploited prognostic opportunity by automating the extraction of subclinical radiomic features. The JACC Scientific Statement on Right Heart Function [17] highlights that novel AI-based 3D TTE software can provide rapid and accurate quantitation of RV volumes and function, with deep learning algorithms showing high accuracy (97.6%) for detecting invasively confirmed PA-related RV dilatation. The novel beating cardiac phantom technology developed by Aubert et al. [37] provides the necessary experimental framework to validate sub-millimetric cardiac sparing protocols [4,37]. The evolving landscape of combined radiotherapy and targeted/immunotherapy in breast cancer—reviewed by Liu et al. [41]—introduces additional layers of cardiotoxic complexity that require integrated cardio-oncology surveillance frameworks addressing the full spectrum of RV-damaging treatments (Fig. 3).

6.3 Evidence Quality and Limitations

The evidence synthesized above should be interpreted with appropriate caution. Several of the key studies underpinning the proposed surveillance pathway are limited by small sample sizes (well under 100 patients in most cohorts, e.g., Rossetto et al. [10], n = 83; Zhao et al. [11], n = 74), single-center design, and the frequent absence of untreated or non-irradiated control arms. Furthermore, in breast cancer cohorts, concurrent anthracycline-based chemotherapy represents a substantial confounder that limits the ability to attribute observed right ventricular changes specifically to radiotherapy rather than to systemic cardiotoxic therapy or to the combined effect of both exposures. Findings derived from lung cancer/non-small cell lung cancer cohorts, which are treated with different dose-volume regimens and fractionation schedules than breast radiotherapy, should not be directly extrapolated to breast cancer patients without explicit acknowledgment of these differences. Accordingly, the multimodality surveillance framework proposed in this review should be regarded as a pragmatic, evidence-informed proposal rather than a validated clinical algorithm, and prospective, adequately powered, multicenter studies with appropriate control groups are needed before firm recommendations can be issued.

7. Conclusions

RV dysfunction in cancer patients receiving modern thoracic RT is a multi-layered pathology driven by direct fibrotic tissue injury and indirect pulmonary afterload mismatch [4,9,13]. The parallel vulnerability of the RV to chemotherapy-induced cardiotoxicity [10,11] and radiation-induced damage [14,16] confirms that the right ventricle requires systematic, longitudinal surveillance in all cardio-oncology patients. Conventional imaging methods fail to capture the subclinical onset of this remodeling, leading to an avoidable diagnostic delay [7,14,19]. By leveraging the combined sensitivity of multi-phase CT planning [12], 2D-STE strain analysis [16,18,19,36], 3D volumetric analysis [11,17], and multi-parametric CMR tissue characterization [20,25,37], contemporary clinicians can intercede within a subclinical diagnostic window. The epidemiological evidence from Darby et al. [2], the international guidance from ESC 2022 Guidelines [32] and the AHA and JACC Scientific Statements [8,17], and the growing clinical dataset from prospective RV-focused studies [10,16,19] together mandate a transition toward this high-precision cardio-oncology framework, essential to shield cancer survivors from the long-term burden of right-sided heart failure.

Author Contributions

DG, LA, AM, GM, MC, ML and MP designed the research study. SS, DG and MP performed the research. ML, LA, and AM provided help and advice on image search. DG, GM and MC wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflicts of Interest

Andrea Micillo is a staff member at Casa di Cura Villa delle Querce. The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT-5.5 in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content

as needed and take full responsibility for the content of the publication.

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