Radiotherapy and the Heart: Damage, Protection, or Treatment?

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> Radiotherapy is a cornerstone of cancer treatment, utilised in over half of all oncological patients. Despite technological advancements, ionising radiation invariably causes damage to surrounding healthy tissues, leading to acute and chronic complications in multiple organs, including the heart.1 This presents a significant clinical challenge, impairing patient quality of life and limiting therapeutic doses. Recent research presented at ESC Cardio Oncology 2026 explores novel strategies for mitigating radiation-induced cardiac injury, including the use of hydrogels for tissue protection and regeneration.

KEY TAKEAWAYS

- The Pivot: Hydrogels are emerging as a novel biomaterial class for preventing and treating radiation-induced tissue damage, including cardiac injury.
- The Data: Hydrogels can act as ROS-scavenging matrices, barrier-forming injectable shields, and bioactive delivery vehicles, addressing distinct phases of inflammation and fibrosis.1
- The Action: Clinicians should be aware of ongoing research into protective strategies for radiation-induced cardiotoxicity, particularly in patients receiving adjuvant radiotherapy combined with targeted or immunotherapy.

Radiotherapy is a primary modality in cancer treatment, employed in more than 50% of all oncological patients.1 While effective against malignancies, ionising radiation can cause damage to adjacent healthy tissues, resulting in acute and chronic complications.1 The heart is among the organs susceptible to such injury, alongside the skin, mucosa, lungs, bones, and gastrointestinal tract.1 These radiation-induced injuries significantly diminish patients' quality of life and can restrict the maximum therapeutic radiation doses that can be administered.1 Managing these complications represents a major unmet clinical challenge.1

The clinical manifestations of radiation-induced heart disease (RIHD) are diverse and can include pericarditis, myocarditis, coronary artery disease, valvular heart disease, and conduction abnormalities. These complications often develop years or even decades after initial radiation exposure, posing a long-term burden on survivors. The incidence and severity of RIHD depend on several factors, including the total radiation dose, fractionation schedule, irradiated heart volume, and individual patient susceptibilities. For instance, patients treated for left-sided breast cancer or mediastinal lymphomas are at higher risk due to the proximity of the heart to the radiation field. The increasing survival rates for many cancers mean that a growing number of patients will live long enough to experience these late cardiac toxicities, underscoring the critical need for effective cardioprotective strategies.

Novel Strategies for Cardioprotection

Hydrogels have emerged as promising biomaterials for addressing radiation-induced damage.1 Their utility stems from their high water content, tunable mechanical properties, and ability to mimic the extracellular matrix.1 Recent innovations in hydrogel technology include stimuli-responsive, injectable, and bioactive systems.1 These advanced hydrogels are capable of delivering therapeutic agents such as antioxidants, growth factors, or living cells.1 A novel classification framework for hydrogels has been proposed, based on their mechanism of action within the pathophysiology of radiation injury.1 This framework evaluates how specific designs, including reactive oxygen species (ROS)-scavenging matrices, barrier-forming injectable shields, and bioactive delivery vehicles, can target distinct phases of inflammation and fibrosis.1 This approach aims to protect healthy tissues, suppress chronic inflammation, and promote effective tissue regeneration.1

The proposed hydrogel classification framework delineates three primary mechanisms of action. First, ROS-scavenging hydrogels are designed to mitigate the initial oxidative stress induced by radiation, which is a key trigger for cellular damage and inflammation. These hydrogels often incorporate antioxidant compounds or enzymes. Second, barrier-forming injectable shields physically protect healthy tissues by creating a temporary, biocompatible barrier between the radiation source and vulnerable organs like the heart. This physical separation can reduce the absorbed dose to critical structures. Third, bioactive delivery vehicles are engineered to release therapeutic agents in a controlled and sustained manner. These agents may include anti-inflammatory drugs, growth factors to promote tissue repair, or stem cells for regeneration. The precise targeting of these distinct phases of radiation injury - initial damage, chronic inflammation, and impaired regeneration - represents a sophisticated approach to cardioprotection.

The impact of adjuvant radiotherapy, particularly when combined with targeted or immunotherapy, on the heart in breast cancer patients is a specific area of concern.3 The European Association of Cardiovascular Imaging (EACVI), the European Association of Percutaneous Cardiovascular Interventions (EAPCI), the Heart Failure Association (HFA), and the Association for Acute CardioVascular Care (ACVC) of the ESC have issued a clinical consensus statement regarding women's heart centres.2 While the abstract provided for this consensus statement reiterates the general challenges of radiotherapy-induced damage and the potential of hydrogels, it underscores the broader recognition within cardiology of the need for specialised care and research into cardiac complications arising from cancer treatments.2

The ongoing development of hydrogel-based strategies for both prevention and therapy highlights the potential of these mechanistically aligned systems.1 By targeting the specific phases of radiation injury, these systems may offer a pathway to protect healthy tissues, mitigate chronic inflammation, and facilitate tissue repair.1 Further research is required to translate these preclinical insights into clinical applications, particularly in the context of specific organ systems like the heart and in patient populations receiving complex multimodal cancer therapies. The limitations of current preclinical models often include their inability to fully replicate the long-term, multifactorial nature of RIHD in humans. Future studies must focus on larger animal models and ultimately human trials to validate the safety and efficacy of these novel hydrogel systems, ensuring their integration into clinical practice for improved patient outcomes.

> **CLINICAL IMPLICATIONS**
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> The persistent challenge of radiation-induced cardiac damage, despite decades of technological refinement in radiotherapy, highlights a critical gap in patient care. While the focus has rightly been on tumour eradication,

the collateral damage to the heart remains a significant determinant of long-term morbidity and mortality. The exploration of hydrogels, as detailed in PawBowski et al., offers a genuinely interesting avenue for intervention, moving beyond mere dose reduction to active tissue protection and regeneration. Clinicians should view these developments not as a distant possibility, but as a call to integrate cardio-oncology principles more deeply into treatment planning, particularly for patients undergoing adjuvant radiotherapy for breast cancer, where the cardiac burden can be substantial.

The consensus statement from multiple ESC associations, though its abstract broadly covers the same ground as the hydrogel review, implicitly reinforces the growing recognition of sex-specific cardiovascular risks and the need for dedicated women's heart centres. This is not merely an administrative suggestion; it reflects an understanding that cardiovascular disease presentation, risk factors, and treatment responses can differ between sexes. For patients, this means a potential future where cardiac protection during cancer treatment is not an afterthought, but an integral, personalised component of their care plan, potentially leveraging innovative biomaterials to safeguard their long-term cardiovascular health.

From an industry perspective, the development of functional hydrogels represents a significant opportunity for innovation in medical devices and drug delivery. The shift from passive materials to active, stimuli-responsive systems capable of delivering specific therapeutic agents like antioxidants or growth factors is a sophisticated leap. Companies investing in this space, particularly those focusing on injectable or barrier-forming applications, could carve out a niche in supportive cancer care, potentially reducing the incidence of severe radiation-induced toxicities and improving patient outcomes. The evidence, while still largely mechanistic and preclinical for hydrogels, points towards a future where such interventions are as routine as advanced imaging in cardio-oncology.

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