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# *A CASE SERIES AND LITERATURE REVIEW: MANAGEMENT STRATEGIES FOR RADIATION-INDUCED ULCERS OF THE CHEST*

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ABSTRACT

**Introduction:** Radiotherapy as an adjunct to cancer treatment causes a high incidence of radiation-induced tissue injury, ranging from radiation dermatitis to severe osteoradionecrosis. Currently, no gold standard exists in the management of radiation injury. Various strategies ranging from modern wound treatment to surgical management have been studied.
**Case Illustration:** Three women presented with varying degrees of ulceration in the chest during or shortly following radiotherapy. Each case followed different approaches to management. One case solely received wound treatment, another received wound treatment and a sequestrectomy, and the third required surgical reconstruction of the chest wall and defect.
**Discussion:** Methods of wound treatment range from topical agents, barrier films and dressings, hydrogel and hydrocolloid dressings, miscellaneous treatments, and biodressings. Surgery is required in severe cases, particularly with osteoradionecrosis. This may include wound debridement, biopsy, chest wall stabilization, closure using various flaps, and potential breast reconstruction.
**Conclusion:** Radiation-induced ulcers of the chest pose a complex issue. Understanding effective treatment methods and key surgical principles is important for ensuring better outcomes. Further studies are needed to provide a complete guide to treatment.

**Highlights:**

1. Radiotherapy leads to a high occurrence of skin alterations and can advance to different levels of tissue damage, presenting challenges in treatment.
2. Management can be effective employing diverse wound treatment methods, although severe cases may necessitate surgical intervention.
3. Surgery takes into several key considerations to increase chances of success and tackle specific issues of chest wall instability and breast reconstruction.

## INTRODUCTION

Radiotherapy serves as an essential adjunct to surgical tumor resection in breast cancer treatment, aiming to eradicate microscopic disease and reduce cancer recurrence. However, a significant challenge associated with radiotherapy is the high incidence of radiation-induced tissue injury, ranging from acute radiation dermatitis to severe osteoradionecrosis and radiation-induced sarcoma. Approximately 95% of radiotherapy patients experience some degree of skin changes attributed to radiation injury. DNA damage caused by the radiation

primarily affects the proliferative phase of the cell cycle. This may explain how the earliest symptoms of radiation toxicity typically occur in cells with high turnover rates, such as skin and mucosa.[1,2]

Currently, no established gold standard exists for the management of radiation-induced tissue injuries. This is attributed to conflicting results from clinical trials and a scarcity of high-quality, large-sample studies.[2,3] Additionally, there is no universally applicable surgical approach and when indicated, requires careful consideration of factors such as the location, shape, and size of the affected tissue, as well as the choice of the most suitable flap for desired outcomes.

In this report, we present three cases of women who developed varying degrees of ulceration in the chest region during or shortly after undergoing radiotherapy for breast cancer. These cases highlight different approaches to management, ranging from wound treatment alone to surgical reconstruction of the chest wall and defect. By examining these cases and reviewing the available evidence, we aim to provide valuable insights into effective treatment strategies for radiation-induced ulcers of the chest.

## CASE ILLUSTRATION

### Case 1

The patient, a 48-year-old female foreigner with recurrent breast cancer, underwent radical mastectomy, split-thickness skin graft, chemotherapy, and radiotherapy. Following completion of radiotherapy while continuing capecitabine chemotherapy, she developed ulcers on her right thoracic region. The wound was initially treated with silver sulfadiazine hyaluronic acid cream, and as the wound bed improved, non-adherent hydrophilic foam dressings were applied. Subsequently, signs of epithelialization appeared, and after three months of treatment, the patient was able to independently continue wound care upon returning to her home country.


Figure 1. (A) Case 1 initial clinical presentation showing moist desquamation, (B) 3-month follow-up with nearly complete epithelialization.

### Case 2

In the second case, a 51-year-old female patient underwent a right mastectomy, chemotherapy, and radiotherapy, while also receiving anastrozole for hormonal therapy. Following the completion of radiotherapy, she presented with ulcerative radionecrosis of her right chest. The wound exhibited a large, ulcerated mass with necrotic tissue, slough, and pus. Initially, local debridement was performed, and hydrogel dressings were applied for further autolytic debridement. However, during routine follow-up appointments, the wound exhibited hypergranulation and serous discharge. By the third month, exposed bone became visible, prompting a sequestrectomy. Following the procedure, an antibiotic and hydrocortisone cream mixture was applied, along with tulle

dressings. After nearly six months of treatment, the wound eventually healed well, and the patient experienced no further complications.

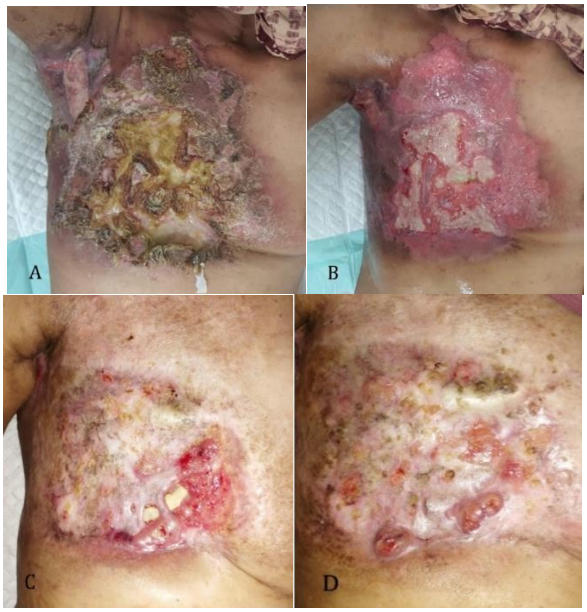


Figure 2. (A) Case 2 clinical presentation showing necrotic tissue, slough, and pus, (B) after local debridement, (C) granulation tissue and exposed bone at 3-month follow-up, (D) the wound nearly fully healed at five months.

## Case 3

The patient, a 34-year-old female with recurrent breast cancer and a history of left mastectomy, underwent chemotherapy and radiotherapy. Upon presentation, she exhibited ulcerative wounds on her left chest, containing necrotic tissue, slough, and pus. Initially, the wound was treated with dialkylcarbamoyl chloride (DACC)-coated dressings until the completion of radiotherapy. Subsequently, hydrogel dressings were employed. By the third month, the wound had significantly enlarged, measuring approximately 15x20cm, with exposed second to fourth left costae indicating osteoradionecrosis. Surgical intervention was deemed necessary, involving the removal of necrotic tissue and segments of the second to fourth costae. Reconstruction ensued, utilizing sternal wire, a 15x15cm surgical mesh, a latissimus dorsi (LD) flap, and split-thickness skin grafts. During follow-up, the graft achieved approximately 99% viability, resulting in a small defect and minimal seroma presence. Despite this, the wound exhibited no signs of improvement over three months and necessitated closure with a transpositional flap from the right chest, alongside the maintenance of a drain for two weeks. Following seven months of treatment, the wound healed successfully, and the patient experienced no further complications.

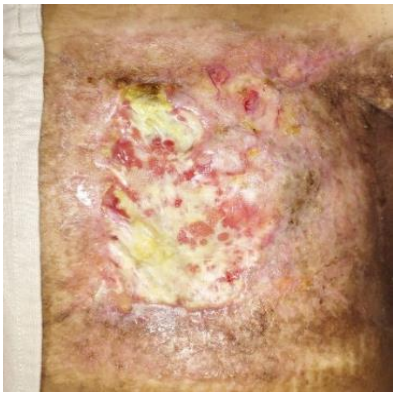

Figure 3. Case 3 displaying exposed bone on the chest after three months of treatment.

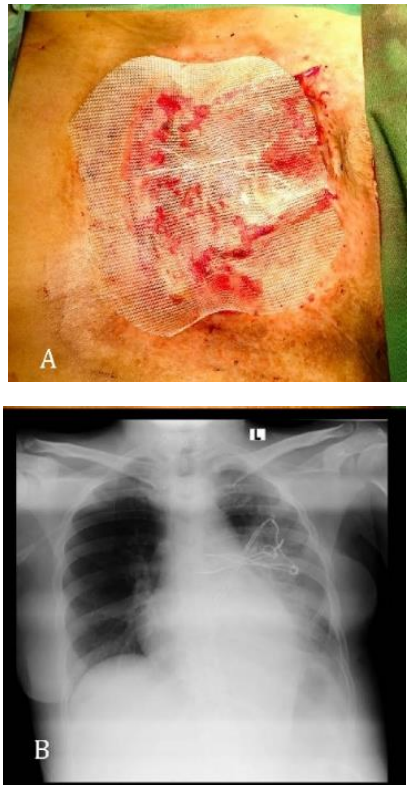


Figure 4. (A) Intraoperative view of the surgical mesh (B) Postoperative X-ray demonstrating sternal wires.


Figure 5. (A) Small defect post-treatment (B) Closure achieved with a transpositional flap

## DISCUSSION

Radiation dermatitis manifests in acute and chronic stages, with acute changes occurring within 90 days of treatment initiation. Severity is often graded using the Common Terminology Criteria for Adverse Events (CTCAE).[1,2] Grade 1 presents with pruritus, epilation, scaling, and depigmentation, while grades 2 and 3 exhibit moist desquamation, especially with cumulative radiation doses exceeding 40 Gy, increasing the risk of infection and pain. Untreated grade 4 changes can lead to progressive ulcerations and fibrosis.[3,4] Chronic changes, appearing months to years post-exposure, include telangiectasia, epidermal thinning, dermal atrophy, pigmentation changes, fibrosis, edema, keratosis, and necrosis.[1,5,6]

Table 1. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0

| Grade | Clinical Description |
|---|---|
| 1 | Faint erythema or dry desquamation |
| 2 | Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema |
| 3 | Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion |
| 4 | Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated |
| 5 | Death |

The most severe forms of localized radiation injury include osteoradionecrosis and radiation-induced sarcoma. Osteoradionecrosis is characterized by exposed irradiated bone failing to heal over three months without tumor evidence.[7] It typically presents with slowly worsening skin ulceration, sometimes accompanied by extensive soft tissue changes. While most commonly found in the mandible, osteoradionecrosis may also develop in other regions such as the chest wall. In cases of full-thickness necrosis of the chest wall, pathologic rib fractures may cause discomfort and instability of the chest wall. Tissue necrosis progresses due to compromised vasculature, inflammation, and infection, potentially exposing thoracic viscera and causing complications like empyema and septicemia if left untreated.[8,9]

Preventing radiation-related tissue damage is crucial, necessitating communication between surgeons and radiation oncologists to minimize complications. Additionally, Ethical considerations in clinical decision-making, as well as the role of patients in the treatment

process, including patients' rights to make decisions and understand information, and relevant bioethical principles, are essential. Prevention of radiation injury in breast cancer involves a series of strategies to reduce the risk of injury before, during, and after radiation therapy. Before Radiation Therapy, providing patients with information about potential side effects that may occur during and after radiation therapy, as well as steps that can be taken to reduce the risk of injury. Evaluate the skin before radiation therapy to identify areas vulnerable to radiation dermatitis. Good skin care before radiotherapy can help reduce the risk of injury. and ensuring the patient's overall health and identifying factors that may increase the risk of radiation injury, such as obesity, smoking history, and certain skin conditions. During Radiation Therapy, using advanced radiotherapy techniques, such as three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiation therapy (IMRT), or volumetric modulated arc therapy (VMAT), to control radiation dose and minimize exposure to surrounding healthy tissues. Utilizing appropriate skin care, such as non-adherent hydrophilic cream, to protect the skin from radiation effects and reduce the risk of radiation dermatitis. Conducting regular monitoring during radiation therapy to detect changes in the skin or other symptoms that may require further intervention. After Radiation Therapy, providing continued care to reduce symptoms of radiation dermatitis, such as using topical corticosteroid cream or hydrogel. Providing patients with information about skin care needed after radiation therapy, as well as signs and symptoms to watch for. and Conducting long-term monitoring to detect long-term complications of radiotherapy, such as osteoradionecrosis, and providing appropriate intervention if needed.

When planning radiotherapy, factors like timing, dosage, fractionation, and techniques such as three-dimensional conformal RT (3D-CRT), intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and brachytherapy are vital for dose control.[10,11] Utilizing topical agents and dressings as preventive measure may not only reduce the occurrence of skin and tissue-related complications, but also reduce the severity of injuries sustained. Consequently, this may represent a more efficient and cost-effective strategy in patient management. Several preventive treatments with the most promising evidence include the use of mometasone furoate and betamethasone topical corticosteroids, polyurethane and silicone-based polyurethane films, photobiomodulation (low-level laser) therapy, topical olive oil, and oral enzyme mixtures. Early application of these treatments has shown to reduce skin changes incidence and severity.[2,3] Unfortunately, the reported cases did not receive any preventive treatment prior to radiotherapy.

Management of radiation dermatitis and osteoradionecrosis remains a challenge for many physicians. Conflicting results among studies and the lack of high-quality evidence further complicate the issue. To the authors' knowledge, this is the first report focused on management strategies published in Indonesia. Furthermore, as injuries often progress and manifest as a spectrum, it can be challenging to decide between treatment approaches. A comprehensive report and discussion encompassing both surgical and non-surgical treatment options may offer valuable insights for clinicians. While conservative treatments and modern dressings may suffice for some cases, severe instances, such as illustrated in case 3, may require surgical intervention.

This report demonstrates the use of topical agents, namely silver sulfadiazine hyaluronic acid cream and an antibiotic and hydrocortisone cream mixture. Some creams and ointments may help reduce skin inflammation caused by radiation. They are often utilized for minor cases and low-resource settings. Several topical non-steroidal agents and corticosteroids have

been expected to decrease inflammation in radiation dermatitis and are often considered a simple treatment option in limited settings.[2] Silver-containing dressings have long been utilized as burn dressings and noted primarily for their effectiveness against gram-positive and gram-negative bacteria, as well as some fungal infections. However, silver dressings have yet to demonstrate improved healing rates for radiation-induced tissue injuries. Limited evidence, however, suggests they may alleviate pain and itching in patients.[3] Hyaluronic acid preparations have been studied for their effectiveness in preventing radiation dermatitis, show promise for treatment. However, other non-steroidal agents or corticosteroids have demonstrated minimal benefit.[2] Hydrocortisone was specifically used in case 3 after the patient developed hypergranulation tissue. Topical steroids have shown effectiveness in cases of aberrant wound healing resulting in hypergranulation tissue.[12,13]

During radiotherapy, barrier films and dressings are usually suggested for prevention. Recent studies have explored their role in managing skin conditions. In this report, non-adherent hydrophilic foam dressings were applied to mildly exudative wounds with moist desquamation. Absorbent foam dressing is preferred over creams and standard wound care. Silicone-based polyurethane film dressings can be an alternative for non-exudative wounds. They are waterproof and transparent, facilitating easy care and assessment without removal. Although mainly for prevention, they may also be effective in managing wounds.[2,3]

Hydrogel and hydrocolloid dressings are utilized for maintain skin moisture in severe radiation skin problems. Hydrogel was applied in cases 2 and 3 for autolytic debridement of necrotic tissue and slough. However, evidence shows conflicting results regarding healing rates compared to other methods of care (e.g., gentian violet dressings, water-based spray, dry dressing). A silicone-based topical gel forms a thin, flexible, semi-occlusive, waterproof dressing that allows gas permeability. Studies have confirmed its efficacy in the prophylaxis of radiation dermatitis and improving specific clinical outcomes (e.g., erythema, itch, pain, burning sensation, inflammation, and hydration) when used as treatment in patients who have developed radiation dermatitis.[14]

There are still many alternatives worth mentioning that have not been covered in these cases. Studies have explored the possible effects of various miscellaneous therapies. Henna-containing ointment, lianbai liquid, hydrotherapy, and an emulsion were found to be effective in managing symptoms, but further research is required to warrant their use.[2]

Biodressings, described as conventional fibers combined with bioactive molecules such as growth factors and stem cells, are primarily reserved for use in severe cases of radiation dermatitis. They represent highly advanced biomaterials that have been a key focus of recent development. Stem cells derived from placental membrane and lipoaspirates have shown effectiveness in treating chronic radiation-induced injuries, even in cases where other modalities have failed.[15,16] Additionally, a combination of stem cell-released molecules from various types of skin stem cells has demonstrated efficacy in acute radiation dermatitis, leading to significant symptom reduction and complete wound healing.[17] Very few studies have utilized platelet rich plasma, although it may provide accelerated wound healing.[18] Other notable dressings yielding significant results include foam dressings containing epidermal growth factor, gauze impregnated with granulocyte-macrophage colony-stimulating factor, and irradiated human amniotic membrane.[3,19] Novel approaches gaining attention include functional hydrogels with complex properties, photoresponsive hydrogels combined with light-based therapy, and hydrogels integrated with biopolymers.[3,20]

Patients with osteoradionecrosis should undergo surgical treatment with the primary

goals of eliminating infection, excising all damaged tissue, and providing stability to the chest wall during reconstruction. Surgical intervention should involve the removing infected tissue and skin affected by radiation to facilitate proper healing. It is important to reduce the bacterial load of soft tissue as much as possible before surgical resection, which can be achieved through mechanical, enzymatic, or maggot debridement therapy. Biopsy of tissue margins is necessary to identify possible cancer recurrence or Marjolin's ulcer. Although a frozen section is recommended, it cannot detect changes in bony margins and may miss infiltrating breast cancer that can only be identified by permanent pathology.[8,9]

Surgical treatment options may include no reconstruction, prosthetic reconstruction, or biological reconstruction. In Case 2, wound healing was achieved through a simple bedside sequestrectomy and continued wound care. Full-thickness resection of the chest wall may lead to loss of chest wall rigidity, causing paradoxical respiration and ineffective respiratory effort. Stabilization of the chest wall is particularly recommended in sternectomy, large anterior and anterolateral defects, and resection of >3-4 ribs. A rigid prosthetic chest wall reconstruction can provide mechanical support, often accomplished using mesh, sometimes combined with methyl methacrylate or rib plating devices. In our case, mesh and sternal wires provided adequate stabilization of the chest after the removal of the second to fourth costae. However, using a prosthetic device increases the risk of infection, especially in contaminated wounds. Biological meshes, such as bovine acellular matrix, may decrease the risk of infection but generally provide inferior mechanical support.[8,9] Contaminated wounds of the thoracic wall can also be reconstructed using a thick musculocutaneous flap alone.[21]

Reconstruction of the resected area must consider the size and location of the tissue defect. Axial-pattern flaps such as pectoralis major, latissimus dorsi (LD), and upper rectus abdominal musculocutaneous flaps may be utilized in chest wall reconstruction. While a latissimus dorsi musculocutaneous flap presents minimal donor site problems compared to the rectus abdominal musculocutaneous flap, these flaps carry the risk of failure when radiation affects the nutrient vessel of the flap or damages the muscle itself. Free flaps may prove useful when axial-pattern flaps are at risk of failure, a flap has been previously utilized, or the defect is too large to cover with the flap. However, it is essential to consider the quality of vessels in free flap surgery, as certain flaps can damage blood vessels and lead to issues at the donor site. Alternatively, perforator flaps receiving blood supply from isolated perforating vessels may provide adequate coverage when the ulcer is relatively small and the perforator vessel and flap are outside the radiation field.[9,21]

Breast reconstruction commonly utilizes the Latissimus Dorsi (LD) musculocutaneous flap, free or pedicled transverse rectus abdominis musculocutaneous (TRAM) flaps, deep inferior epigastric perforator (DIEP) flaps, and omental flaps. While an omental flap may be a versatile biological implant, the need for intraabdominal surgery poses increased risk. Implant-based breast reconstruction may be possible but carries the added risk of infection and may not be suitable with a mesh already in place.[8,9,22]

Although there was no postoperative infection, our patient developed minimal seroma. Seroma is a common complication in many surgical procedures but is notably frequent in breast surgeries. Management may include serial aspirations, sclerosing agents in the seroma cavity, surgical marsupialization or excision of the seroma capsule, and drainage.[23]

Varying degrees of radiation-induced tissue injury, ranging from radiation dermatitis to osteoradionecrosis, require different therapeutic approaches. Prevention is the ideal initial approach; however, the

incidence of radiation-induced ulcers remains a complex issue. Some of the most promising treatments include foam dressings, silicone barrier films, and film-forming topical gel. Novel therapies include biodressings with stem cells, epidermal growth factor, granulocyte-macrophage colony-stimulating factor, and functional hydrogels, have also shown potential. Despite these advancements, simpler and more affordable options can still be utilized. Surgical intervention becomes necessary in more severe cases, particularly those involving osteoradionecrosis. Although various surgical options exist, adhering to key principles in the resection and reconstruction of the chest wall will ensure a better outcome. However, conflicting results and minimal available evidence suggest further studies are necessary to provide a comprehensive treatment guideline.

Management actions for radiation dermatitis and osteoradionecrosis can significantly impact the quality of life of patients. Here are some ways in which these management actions can affect patients' quality of life. Management actions such as the use of topical creams or gels, proper wound care, and other medical interventions can help reduce painful and disruptive symptoms such as itching, pain, and inflammation on the affected skin. By reducing physical symptoms and discomfort associated with radiation dermatitis and osteoradionecrosis, these management actions can help improve patients' psychological well-being. Patients may feel more comfortable and have lower levels of stress. In cases of osteoradionecrosis where surgical intervention may be necessary, proper management actions can help accelerate the healing process and physical recovery of patients after surgical procedures. This can improve patients' ability to perform daily activities and enhance overall quality of life.In some cases, effective management actions can help improve the function of tissues affected by radiation, such as the skin and surrounding soft tissues. This can help patients better navigate daily life and reduce the negative impact of the condition. Additionally, management for radiation dermatitis and osteoradionecrosis can effectively enhance treatment success, reduce infection risk, and improve the affected tissue's condition by optimizing treatment response, minimizing infection risk, and providing necessary interventions to repair tissue damage. [24,25]

Cost and financial coverage are crucial considerations when determining the optimal strategy for individual patients. Limited publications address wound management of radiation ulcers in low-income environments. Moreover, several complex procedures may also not be feasible in settings of limited equipment. Similarly, cases 2 and 3 involved patients covered by Indonesia's Social Security Administrative Body (BPJS). While these cases may not represent the most advanced treatment options, this report demonstrates that simple wound treatment and standard reconstruction of the chest when applied appropriately, may still provide satisfactory results.

## CONCLUSION

Managing radiation-induced tissue injuries, such as radiation dermatitis and osteoradionecrosis remains challenging due to conflicting evidence and limited high-quality studies. Preventive measures, such as optimizing radiotherapy planning and early use of topical agents and dressings, are crucial. Tailoring treatments to individual patients based on the severity of tissue damage and available resources is essential. While complex surgical interventions may be necessary in some cases, simpler wound treatments and standard reconstruction techniques can still yield satisfactory outcomes, particularly in low-resource settings. Collaborative, multidisciplinary approaches among healthcare professionals are essential for optimizing patient care and outcomes.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## AUTHOR CONTRIBUTION

The author contributions are as follows: conceptualization: E.K. and S.P.; data collection and analysis: E.K. and S.P.; drafting of the article: E.K.; critical revision of the article: S.P. Syed Faqeer Hussain Bokhari; critical revision of the article and Proofread. All authors reviewed and agreed to the published version of the manuscript.

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