Radiation and living tissue: mechanisms, damage, and clinical impact

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Abstract. This mini-review summarizes the principal mechanisms through which ionizing radiation affects living tissue, from the earliest physical and molecular events to cellular responses, tissue injury, and clinically relevant organ effects. Ionizing radiation induces damage both directly, by depositing energy in critical biomolecules such as DNA, and indirectly, through water radiolysis and the generation of reactive oxygen and nitrogen species that alter nucleic acids, proteins, and lipids. Depending on dose, dose rate, radiation quality, and tissue radiosensitivity, exposed cells may undergo successful repair, mutation, senescence, apoptosis, necrosis, or other forms of regulated death. At the tissue level, rapidly proliferating organs are especially vulnerable to acute injury, while late effects include fibrosis, vascular dysfunction, chronic inflammation, and secondary malignancies. The review also outlines current concepts of dose-response relationships, including the linear no-threshold model, and discusses emerging strategies to mitigate normal-tissue toxicity and improve radiological protection and therapeutic outcomes.

Keywords: ionizing radiation, reactive oxygen species, DNA damage, cell death, normal-tissue toxicity, acute radiation syndrome, breast cancer, radioprotection.

Introduction. Ionizing radiation interacts with living tissue across multiple biological levels, from the initial deposition of energy in atoms and molecules to complex alterations in cells, tissues, organs, and the whole organism. These interactions are clinically important because radiation has a dual role: it is indispensable in medical imaging and cancer therapy, yet it can also induce acute injury, chronic tissue dysfunction, and an increased long-term risk of malignancy. At the molecular level, radiation may act directly on DNA or indirectly through the radiolysis of water, generating reactive oxygen and nitrogen species that damage nucleic acids, proteins, and lipids while also activating signaling pathways involved in the DNA damage response.

The biological consequences of exposure depend on several factors, including absorbed dose, dose rate, radiation quality, and the intrinsic radiosensitivity of the exposed tissue. Cells may successfully repair radiation-induced lesions, but unsuccessful or incomplete repair can lead to mutation, senescence, apoptosis, other forms of regulated cell death, or persistent dysfunction that contributes to fibrosis, inflammation, and carcinogenesis. Rapidly proliferating tissues such as bone marrow, intestinal epithelium, skin, and germ cells are particularly sensitive to radiation, whereas slowly proliferating tissues often manifest late effects such as vascular damage and fibrosis after radiotherapy.

Current radiobiology also places strong emphasis on low-dose effects, normal-tissue protection, and the optimization of therapeutic benefit. Epidemiological and mechanistic evidence continues to support the use of the linear no-threshold model in radiological protection, although debate remains regarding the magnitude of risk at very low doses. At the same time, advances in precision radiotherapy, including proton therapy and other high-LET approaches, together with the development of radioprotective and mitigative strategies, have improved the capacity to limit damage to normal tissues while preserving antitumor efficacy. For these reasons, an integrated overview of radiation-induced effects in living tissue is essential for understanding both the hazards and the therapeutic value of ionizing radiation.

The Purpose of the Work. This mini-review aims to summarize the main effects of ionizing radiation on living tissues, from the earliest physical and molecular events to cellular responses and clinically relevant tissue and organ injury. The paper specifically seeks to outline the principal mechanisms of radiation-induced damage, describe major patterns of acute and late normal-tissue response, and discuss the relevance of dose-response concepts and radiological protection models for medical and biological practice. A further objective is to connect basic radiobiological mechanisms with their implications for radiotherapy toxicity, radiation emergencies, and cancer risk, including the particular vulnerability of breast tissue described in the reviewed literature.

Physical and Molecular Interactions. Ionizing radiation deposits energy in tissue either directly in DNA or indirectly via water radiolysis, generating reactive oxygen and nitrogen species (ROS/RNS) that attack DNA, lipids, and proteins (Saini & Gurung, 2024; Reisz et al., 2014; Boice, 2017; Salem et al., 2024). DNA lesions include single- and double-strand breaks, base modifications, cross-links, and DNA-protein adducts (Saini & Gurung, 2024; Boice, 2017; Okonkwo et al., 2022). Early mutational events relevant for carcinogenesis show approximately linear increases down to at least 10 mGy for low-LET radiation (Wei et al., 2026).

ROS act both as damaging agents and signaling molecules, modulating the DNA damage response (DDR) and influencing radiosensitivity and therapeutic response (Saini & Gurung, 2024; Boice, 2017; Wang et al., 2018). Persistent oxidative stress after irradiation contributes to chronic tissue injury and fibrosis (Laurier et al., 2023; McBride & Schaue, 2020).

Cellular Responses: Repair, Death, and Signaling. Cells sense DNA damage, activate DDR, arrest the cell cycle, and engage multiple repair pathways (Saini & Gurung, 2024; Ibáñez et al., 2024; Boice, 2017; Wang et al., 2018). Highly proliferative cells (e.g., S-phase) tend to be more radioresistant due to elevated repair capacity, whereas M-phase cells are particularly radiosensitive (Laurier et al., 2023). Outcomes range from accurate repair to mutation, senescence, apoptosis, necrosis, or regulated forms of cell death such as autophagy-related death (Saini & Gurung, 2024; Ibáñez et al., 2024; Islam, 2017; Cadet & Wagner, 2013; Wang & Tepper, 2021).

Irradiated cells also send "bystander" signals that alter neighboring non-irradiated cells, increasing oxidative stress, DNA lesions, and sometimes cell death (Laurier et al., 2023; Salem et al., 2024). Damage-associated molecular patterns (DAMPs) engage pattern recognition receptors, linking radiation injury to innate immune activation and inflammation (Saini & Gurung, 2024; Islam, 2017; Hu et al., 2025; Helm & Rudel, 2020).

Tissue and Organ Effects. Normal tissue responses depend on structure, stem-cell organization, and turnover time (Islam, 2017; Laurier et al., 2023; Hu et al., 2025). Rapidly dividing tissues (bone marrow, gut, skin, germ cells) are most sensitive, forming the basis of acute radiation syndrome involving hematopoietic, gastrointestinal, neurovascular, and cutaneous syndromes at high whole-body doses (Islam, 2017; Hubenak et al., 2014; Hu et al., 2025).

In radiotherapy, toxicity risk rises with increasing dose and irradiated volume; organ-specific constraints therefore guide treatment planning (Islam, 2017; Laurier et al., 2023; Srinivas et al., 2018; Hu et al., 2025). Late effects include fibrosis, vascular damage, chronic inflammation, and secondary cancers (Islam, 2017; Laurier et al., 2023; Srinivas et al., 2018; McBride & Schaue, 2020; Helm & Rudel, 2020). Breast tissue is particularly vulnerable: ionizing radiation increases breast cancer risk in an approximately linear fashion, through combined direct DNA damage, ROS, inflammation, and interactions with hormone-driven proliferation (Hu et al., 2025; McBride & Schaue, 2020; Helm & Rudel, 2020; Wei et al., 2026) (Table 1, Figure 1).

Table 1

Representative dose-effect relationships and organ sensitivities:
illustrative quantitative relations of dose and organ response

Concept / organ	*Key features or dose range*	*References*
Early mutational events	Linear down to ≥10 mGy (low-LET)	Wei et al., 2026
Epidemiologic excess cancer risk	Detectable at ≤100 mGy in some cohorts	McBride & Schaue, 2020; Wei et al., 2026
Highly proliferative tissues (marrow, gut, skin)	Greatest ARS sensitivity; damage at high acute whole-body doses	Islam, 2017; Hubenak et al., 2014; Hu et al., 2025
Breast cancer risk	Increased after low-moderate doses; broadly linear dose-response	Hu et al., 2025; McBride & Schaue, 2020; Helm & Rudel, 2020; Wei et al., 2026
Normal-tissue toxicity in radiotherapy	Risk increases with dose and volume; organ-specific limits	Islam, 2017; Laurier et al., 2023; Srinivas et al., 2018; Lu et al., 2022
Proton vs photon therapy	Similar toxicity spectrum but generally lower incidence with protons	Srinivas et al., 2018; Hu et al., 2025; Lu et al., 2022; Scott, 2024.

Note: ARS - Acute Radiation Syndrome.

Dose-response, Protection Paradigms, and Modulation. Radiation protection for stochastic effects (mainly cancer) is built on the linear no-threshold (LNT) model, which assumes risk is proportional to dose with no safe threshold (McBride & Schaue, 2020; Wei et al., 2026). Recent reviews conclude that most low-dose radiobiology and epidemiology remain broadly compatible with LNT, though some data suggest possible non-linearities and that any threshold, if present, would be at most a few tens of mGy (McBride & Schaue, 2020; Wei et al., 2026). Other authors argue that methodological uncertainties at very low doses undermine LNT and call for revised protection systems (Hubenak et al., 2014; Talapko et al., 2024).

At the tissue level, biological effect also depends on linear energy transfer (LET) and spatial energy distribution: low-LET photons distribute dose more homogeneously, whereas high-LET particles (e.g., protons, heavier ions) produce dense tracks and Bragg peaks, increasing relative biological effectiveness in the target while potentially sparing surrounding tissue (Hubenak et al., 2014; Hu et al., 2025; Lu et al., 2022; Scott, 2024).

Radioprotective approaches include radical scavengers, antioxidants, agents that enhance DNA repair, and pathway-targeted drugs (e.g., renin-angiotensin system inhibitors, TGF-β inhibitors, anti-VEGF agents, immunomodulators) now in clinical trials for mitigating fibrosis, inflammation, and organ dysfunction after exposure (Reisz et al., 2014; Laurier et al., 2023; Lu et al., 2022).

Conclusions. Ionizing radiation produces biological effects that begin with energy deposition and chemical radical formation and extend to DNA damage, altered cell signaling, tissue dysfunction, and cancer risk. The reviewed literature shows that radiation responses depend on dose, radiation quality, and tissue characteristics, explaining both its therapeutic usefulness and its capacity to injure normal organs. Understanding these mechanisms is essential for optimizing radiotherapy, improving radioprotection, and developing interventions that limit acute and late toxicity while preserving clinical benefit.

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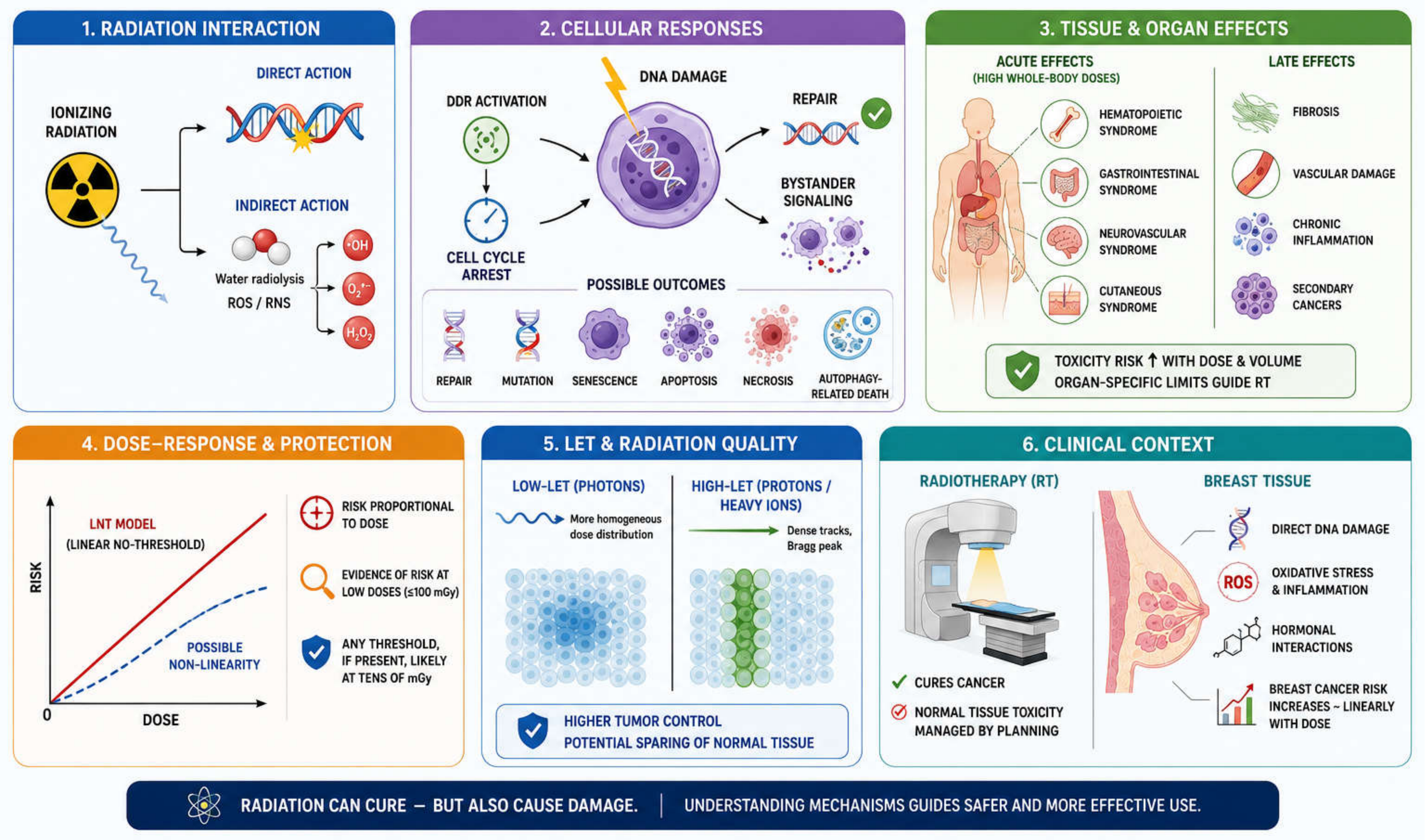

Figure 1. Radiation and living tissue: mechanisms, damage and clinical impact.

Conflicts of Interest. The authors declare that there is no conflict of interest.

Data Availability. Not applicable.

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