UNDERSTANDING THE BIOLOGICAL IMPACT OF IONIZING RADIATION: MECHANISMS AND CLINICAL RELEVANCE

Dženita Hadžijunuzović-Alagić
Department of Clinical Veterinary Sciences, University of Sarajevo – Veterinary faculty, Sarajevo, Bosnia and Herzegovina, dzenita.alagic@vfs.unsa.ba
Nejra Hadžimusić
Department of Clinical Veterinary Sciences, University of Sarajevo – Veterinary faculty, Sarajevo, Bosnia and Herzegovina, nejra.hadzimusic@vfs.unsa.ba

Abstract: To explore the biological effects of ionizing radiation at molecular, cellular, and tissue levels, highlighting variations in severity based on radiation type, dose, and tissue radiosensitivity.
A detailed review of cellular and tissue responses to ionizing radiation, emphasizing the mechanisms of DNA damage, cell death pathways (mitotic death, apoptosis, necrosis, and autophagy), and classification of tissue effects into acute, subacute, and late stages.
Ionizing radiation induces DNA damage leading to diverse cellular responses depending on the cell type and dose. Acute effects predominantly affect rapidly renewing tissues and are often reversible with treatment, while subacute effects emerge during tissue remodeling. Late effects, particularly in slow-proliferating tissues like the central nervous system and kidneys, result in chronic and progressive damage with significant functional impairments. Factors such as radiation dose fractionation, cellular repair capabilities, and regenerative potential modulate the severity and timing of these effects.
Understanding the biological effects of ionizing radiation is critical for optimizing radiotherapy and managing risks in accidental or occupational exposures. The balance between therapeutic benefits and potential long-term damage hinges on a comprehensive grasp of these mechanisms.
Future research should prioritize uncovering molecular pathways involved in tissue regeneration and chronic damage, with the goal of enhancing therapeutic efficacy and minimizing long-term adverse effects.
Keywords: Ionizing radiation, DNA damage, tissue response, cell death pathways, radiotherapy

1. INTRODUCTION

Biological effects of ionizing radiation encompass all changes induced in organisms due to the absorption of energy and the radiochemical mechanisms occurring within the irradiated organism. The type and intensity of these changes depend on the radiation source and the sensitivity of the organism, tissue, or cell (Baeyens et al., 2023). As radiation passes through a living medium, it interacts with its constituents, resulting in changes in both. Ionizing radiation transfers its kinetic energy to the structures it traverses, causing excitation and ionization of atoms and molecules within living matter. This process demonstrates a direct correlation: higher energy deposition per unit mass of tissue per unit time leads to a greater number of ionizations and excitations, resulting in more severe lesions in living matter (Schettino et al., 2023).
Different types of radiation (α, β, γ, x-rays, protons, neutrons) produce varying degrees of ionization and excitation under identical conditions, leading to significant differences in the severity of radiobiological effects (Mohan and Chopra, 2022). This variation arises from differences in the Linear Energy Transfer (LET) of different radiation types, which is often expressed as the energy transferred per unit distance (keV/μm) (Russ et al., 2022). Energy deposition to the structures of living matter, and the resultant ionization and excitation, can disrupt molecular integrity, sometimes leading to complete functional failure. If critical molecules essential for normal cell function are affected, the resulting changes can lead to cell death (Bedoui et al., 2020).

2. EXPOSURE TO IONIZING RADIATION

Exposure to radiation can be categorized into the following types:

- General and localized exposure,
- Acute and chronic exposure,
- External and internal exposure.

General exposure involves the distribution of a specific dose of ionizing radiation across the entire body, whereas localized exposure affects only a specific part of the organism. A specialized therapeutic application of ionizing radiation is fractionated exposure, where the prescribed dose is delivered in parts over several days or weeks according to a precise therapeutic protocol (Koturbash et al, 2017). The organism is more sensitive to general

exposure; even if only a small skin area remains unexposed, the entire body exhibits increased resistance to radiation. Conversely, the same dose will cause more severe consequences under conditions of general rather than localized exposure.

Acute exposure refers to high-dose radiation delivered over a short period, leading to severe consequences. Chronic exposure occurs when an organism is subjected to low-dose radiation over an extended period, causing dysfunction of hematopoietic organs, skin changes (depilation, atrophy), and cataracts (Bray et al., 2016). External exposure occurs when the radiation source is outside the organism, while internal exposure occurs when the source is within the organism (Hashimoto et al., 2022). In clinical radiotherapy, external radiation is termed teletherapy, whereas radiation therapy with the source located inside the patient's body is referred to as brachytherapy (Khan et al., 2021), which will be further elaborated in subsequent chapters.

3. CELLULAR RESPONSE TO IONIZING RADIATION

Although all organic molecules are sensitive to ionizing radiation, the cell nucleus, particularly the unique DNA molecules within the cell, is the most critical target for radiation-induced damage. DNA damage represents the primary mechanism through which ionizing radiation harms and destroys cells (Ibáñez et al., 2024). Most DNA damage is repairable; however, lethal double-strand breaks persist as multiple permanent lesions in about 15-20 nucleotides, resulting in micronuclei formation, chromosomal aberrations, and cell death due to the loss of reproductive integrity of the cellular genome (Hosea et al., 2024).

Biological factors significantly influence the relationship between the physical energy deposited in the tissue, the extent of subsequent DNA damage, the number of destroyed cells, and the severity of tissue responses (McBride and Withers, 2004).

The biological mechanism of ionizing radiation effects on tissues can be divided into four phases. The first involves energy absorption and ion-pair formation, followed by free radical generation in the second phase. The third phase involves a cascade of chemical reactions, and the manifestation of pathological changes occurs in the fourth. The time interval between radiation dose application and the appearance of functional and morphological damage is termed the latent period. This period shortens with higher doses and in cells with higher mitotic activity (King et al., 2016).

4. SENSITIVITY OF MAMMALIAN CELLS TO IONIZING RADIATION

The sensitivity of mammalian cells to ionizing radiation varies significantly. For example, Marković and Spajić (2001) report a lethal dose range for humans of 103.2–154.8 mC/kg, compared to 206.4–258 mC/kg for rabbits. The lethal dose for humans is 10 Gy or higher, but adverse effects can occur at doses as low as 1 Gy, with anorexia manifesting at doses between 0.6 and 1.3 Gy. Biological effects occur within a range of 2.5 to 258 mC/kg. Single-celled plants, animals, and bacteria are the least sensitive, while mammals, including humans, are the most sensitive.

Cells with higher reproductive potential exhibit greater sensitivity to radiation. Based on this characteristic, French scientists Bourgonie and Trbondeaux formulated a law of tissue sensitivity: *"Tissue (cell) sensitivity to radiation is directly proportional to its reproductive activity and inversely proportional to its degree of differentiation (a differentiated cell no longer divides)"* (Haber et al., 1969).

Evaluating radiosensitivity of specific tissues relies on studying morphological and histopathological changes in cells after irradiation. Casarett (1968) proposed a classification of mammalian cell radiosensitivity based on histological observations of cell death, dividing parenchymal cells into four categories (Table 1). Supporting structures such as connective tissue and endothelial cells of small blood vessels exhibit intermediate radiosensitivity between Group II and Group III parenchymal cells.

Table 1. Categories of Mammalian Cell Radiosensitivity (Casarett, 1968)

Category	Cell Type	Characteristics	Example	Sensitivity
I	Vegetative intermitotic cells	Regular division; no differentiation	Erythroblasts, intestinal crypt cells, germinal epidermal cells	High
II	Differentiating intermitotic cells	Regular division; partial differentiation	Myelocytes, connective tissue cells	Moderate
III	Reversible postmitotic cells	Irregular division; variable differentiation	Hepatocytes	Low
IV	Fixed postmitotic cells	Do not divide; highly differentiated	Neurons, muscle cells	Lowest

Source: Casarett, 1968

Saračević (1999) proposed a slightly different classification, categorizing cells into three groups based on radiosensitivity: highly sensitive, moderately sensitive, and least sensitive cells (Table 2).

Table 2. Mammalian Cell Sensitivity to Ionizing Radiation (Saračević, 1999)

Highly Sensitive Cells	**Moderately Sensitive Cells**	**Least Sensitive Cells**
Lymphocytes, erythroblasts, myeloblasts, megakaryocytes, epithelial cells, basal testicular cells, intestinal crypt cells	Ovarian cells, skin cells, endocrine gland cells, pulmonary alveolar cells, biliary canaliculi	Vascular endothelial cells, connective tissue cells, renal tubule cells, bone tissue, neurons, muscle cells

Source: Saračević, 1999

Milošević et al. (2005) emphasize the need for a more comprehensive approach to evaluating radiosensitivity, suggesting the inclusion of biochemical testing alongside histopathological assessments. For instance, morphological changes in adrenal glands may require a dose of 15 Gy for detection, while biochemical analyses reveal significant functional disturbances at only 5 Gy. These authors also rank tissue radiosensitivity from highest to lowest: bone marrow, thymus, lymphatic tissue, gonads, gastrointestinal tract tissue, hair papillae, sweat glands, epidermis, lung tissue, thyroid gland, muscle tissue, connective tissue, bone tissue, and neural tissue.

Cell Death Modalities After Irradiation

Pioneers in radiobiology identified that lethally damaged cells exposed to clinically relevant doses of radiation often complete one or more mitotic cycles before ceasing division—referred to as "mitotic death" (Vitale et al., 2023). For example, after a 2 Gy dose, cells may attempt two to three mitotic cycles, after which they either perish or a portion survives to continue the reproductive cycle, potentially contributing to tumor regrowth. Unlike mitotic death, certain cell types, including many lymphocyte subtypes, oligodendrocytes, and serous cells of the salivary glands, thyroid, intestinal crypts, and hair follicles, undergo relatively rapid "interphase death," often within 2–6 hours post-irradiation. This occurs with relatively low doses, indicating that interphase death is characteristic of radiosensitive cells. Importantly, interphase death contributes nothing to the reproductive potential of the tissue. Although known for decades, interphase death—now recognized as rapid apoptosis—gained broader acceptance only recently (Vitale et al., 2023).

Apoptosis is characterized morphologically by nuclear condensation (karyopyknosis), cell shrinkage, membrane blebbing, and nuclear fragmentation (karyorrhexis), with the formation of apoptotic bodies that are phagocytized by neighboring cells. This process does not activate inflammatory mechanisms and concludes within hours, leaving no visible trace, often resulting in underestimation of apoptosis's role in overall cell loss (Ai et al., 2024; Vitale et al., 2023). Radiation-induced apoptosis in normal tissues frequently, but not always, depends on activating the tumor-suppressor gene p53. Apoptosis represents an active "self-destruct" mechanism involving metabolic processes and serves as a primary pathway for organ morphogenesis, often referred to as Programmed Cell Death Type I (McBride and Withers, 2004). Its rapid occurrence is restricted to specific cell types and developmental stages within tissues. Only cells with intrinsic pro-apoptotic molecular mechanisms undergo rapid apoptosis following radiation exposure. For example, lymphomas typically exhibit pro-apoptotic tendencies, while glioblastoma multiforme cells do not, regardless of radiation exposure (Giles et al., 2023).

Necrosis, unlike apoptosis, is primarily a pathological rather than a physiological phenomenon and does not require active cellular metabolism. It typically follows tissue damage or pathogen invasion and is characterized by membrane rupture, cell swelling, lysosomal enzyme release, and inflammatory responses due to cytokine release. Necrosis is often the default mechanism for cells lacking effective apoptotic machinery (Khalid and Azimpouran, 2020).

An alternative post-irradiation cell death pathway is autophagy, where cellular organelles are sequestered into vacuoles and digested. This form, termed Programmed Cell Death Type II (McBride and Withers, 2004), often occurs under nutrient deprivation and plays a crucial role in morphogenesis and tissue remodeling.

5. DYNAMICS OF CELLULAR RESPONSES IN HEALTHY TISSUES POST-IRRADIATION

The time from irradiation to the development of symptoms in healthy tissues is predominantly determined by the tissue's regenerative dynamics, including cell differentiation, death, and renewal. Terms such as acute, subacute, and late (chronic) are used to describe the timing of functional cellular disturbances after irradiation, reflecting the dynamic variation among tissue types. However, these terms inadequately capture the pathogenesis of cellular (tissue) responses and fail to account for specific tissue characteristics. Since tissues and organs consist of multiple cell types with distinct renewal dynamics, one tissue may exhibit both acute and late symptoms depending on the cell type critical for its function (McBride and Withers, 2004).

Severe acute damage caused by radiation can lead to nonspecific late sequelae such as fibrosis, atrophy, or ulceration—for instance, intestinal stenosis following mucosal ulceration or fibrosis, or necrosis of skin or oropharyngeal tissues after desquamation or acute ulceration (Withers et al., 1995).

Acute Responses

Acute responses to radiotherapy typically occur during the standard therapeutic window of 6–8 weeks and are observed in tissues with rapidly renewing cell populations, such as the mucosa of the gastrointestinal tract, bone marrow, skin, and oropharyngeal and esophageal mucosa. These tissues exhibit a hierarchical organization, with a small population of stem cells differentiating into mature, non-proliferative, fully differentiated functional cells. Radiation damages these stem and progenitor cells, but functional tissue integrity is maintained by differentiated cells until they are entirely lost through normal turnover processes.

The severity of acute damage depends on the depletion of stem and progenitor cells and the interval between radiation exposure and the emergence of new functional cells. Fractionated dosing can mitigate acute effects by allowing tissue regeneration through stem/progenitor cell differentiation during therapy. While the intensity of tissue damage increases with radiation dose, the transient nature of symptoms and the capacity for full recovery depend on maintaining a critical population of proliferative cells.

Subacute Responses

Certain tissues may exhibit subacute reactions several months post-irradiation due to disruptions in cell populations with slower renewal rates. These effects are generally reversible but may occasionally involve severe damage or mortality. Examples of transient effects include Lhermitte's syndrome following spinal cord irradiation, lethargy after brain irradiation, or subacute pneumonitis 2–3 months post-lung irradiation. Subacute effects typically arise during the tissue remodeling phase and before the onset of late effects associated with slowly progressing damage (Stone et al., 2003).

Late Responses

Late responses of healthy tissues to radiotherapy can be severe, with limited recovery potential. These effects are generally attributed to the gradual loss of proliferative target cells. For instance, oligodendrocytes in the central nervous system, Schwann cells in the peripheral nervous system, tubular epithelial cells in the kidneys, vascular endothelial cells, dermal fibroblasts, and osteoclasts or chondroblasts in bone and cartilage are examples of such cells. Some injuries, like radiation-induced arteriosclerosis or heart disease, may manifest decades after exposure, presenting growing concerns due to increased cancer survival rates (Koutroumpakis et al., 2022).

Late tissue damage exhibits variability in pathological findings. For example, late demyelination after brain irradiation may result from oligodendrocyte loss or neuron loss, as well as gliosis or microglial proliferation preceding or accompanying neurological damage (Rübe et al., 2023). Similarly, vascular lesions with edema, hemorrhage, or inflammatory infiltration can occur (Gorbunov and Kiang, 2021).

Unlike hierarchically organized acute-response tissues, slowly proliferating late-response tissues contain functional cells capable of proliferation as needed. However, their limited regenerative ability contributes to chronic damage that reduces the patient's quality of life. Furthermore, interactions among surviving cells, radiation dose, and injury evolution over time influence the nature and severity of tissue damage (Prasanna et al., 2023).

6. REGENERATION OF HEALTHY TISSUES AFTER IRRADIATION

The timing and progression of tissue regeneration following irradiation vary significantly depending on the tissue type. Acute-response tissues exhibit early regeneration due to their rapid cell turnover and loss. For example, in the jejunal mucosa, the onset of radiation-induced proliferation may occur within 24 hours, while in colonic and gastric mucosa, this period is slightly longer. Conversely, in renal tubules, histological evidence of cell destruction is absent for several months post-irradiation, and repopulation may take over a year. For instance, in mice, renal tubule regeneration may take more than 12 months (Withers et al., 1995).

The rate of repopulation is insufficiently quantified for both acute- and late-response tissues. In mice, estimated doubling times for clonogenic cells are approximately 8 hours for the jejunum, 12 hours for the colon and 22 hours for the skin (Withers, 1995). In humans, tissue renewal is slower and inferred from responses to fractionated dose regimens. Mucosal inflammation begins 14–21 days into a regimen of 2 Gy fractions administered five days per week, with regeneration starting around 10–12 days. High initial doses can shorten the latent period by 1–2 days.

Tissue regeneration increases mucosal tolerance to conventional fractionation regimens by at least 1 Gy/day on average, equating to the doubling of clonogenic cell numbers every two days and possibly occurring faster (Withers et al., 1995). Temporary suspension of daily irradiation (e.g., for 10–14 days during an accelerated fractionated regimen) can allow clonogenic cells to regenerate 2–3 times faster (Withers et al., 1995).

The historical significance of tissue repopulation in radiotherapy lies in optimizing treatment regimens to benefit patients. Extended treatment times improve outcomes by allowing acute-response tissues to regenerate, thus

reducing toxicity. However, accelerated schedules increase the severity of acute tissue responses and impose stricter dose limits (McBride and Withers, 2004).

7. TISSUE-SPECIFIC DYNAMICS IN RADIATION RESPONSES

Acute-Response Tissues

In acute-response tissues, regeneration typically begins early due to rapid cell turnover and loss. For example, the jejunal mucosa begins repopulation within a day of radiation exposure, whereas colonic and gastric mucosa take slightly longer. Tissue damage in such areas is characterized by the depletion of stem cells, and the functional integrity is maintained until fully differentiated cells are lost. Fractionated radiation therapy allows stem and progenitor cells to regenerate during the treatment, mitigating the severity of acute effects.

Despite the severity of acute damage increasing with radiation dose, recovery is possible if the proliferative cell base is not critically depleted. Clinical experience and dose fractionation have demonstrated that temporary interruptions in therapy, such as pauses in accelerated fractionation schedules, allow substantial recovery of clonogenic cells, thereby reducing acute toxicity and improving therapeutic outcomes (Kepka and Socha, 2021).

Subacute-Response Tissues

Subacute responses occur months after irradiation, particularly in tissues with slower cell renewal rates. These effects are generally reversible but can be severe, involving transient conditions like Lhermitte's syndrome (spinal cord irradiation), lethargy (brain irradiation), or pneumonitis (lung irradiation). Such effects arise during tissue remodeling, preceding more chronic late effects (McBride and Schaue, 2020).

Late-Response Tissues

Late-response tissues exhibit delayed and often irreversible damage. This is attributed to the gradual loss of critical proliferative cells, such as oligodendrocytes, Schwann cells, tubular epithelial cells, and endothelial cells. Late effects may include fibrosis, necrosis, or functional failure in tissues like the skin, liver, or kidneys. These responses are influenced by radiation dose, cell repair mechanisms, and interactions among damaged cells over time (McBride and Withers, 2004).

Furthermore, non-specific injuries like fibrosis or arteriosclerosis may develop years or even decades after exposure, particularly in long-term cancer survivors. The variability of pathological findings—such as demyelination or gliosis in brain tissue—highlights the complexity of late radiation-induced tissue responses (Lumniczky et al., 2017).

8. CONCLUSION

The biological effects of ionizing radiation are highly complex and multifaceted, involving interactions at molecular, cellular, and tissue levels. The severity of radiation-induced damage depends on factors such as radiation type, dose, tissue radiosensitivity, and exposure conditions. Acute responses arise in rapidly proliferating tissues and often demonstrate potential for recovery through effective regeneration mechanisms. Subacute effects, though typically transient, may indicate underlying disruptions in slower-renewing tissues. Late responses, characterized by progressive and often irreversible damage, pose significant challenges due to their chronic nature and long latency periods.

Understanding these dynamics is crucial for optimizing radiotherapy protocols, balancing therapeutic efficacy against potential side effects. Strategies such as dose fractionation and tailored treatment schedules have demonstrated efficacy in mitigating acute toxicity while preserving long-term tissue integrity. However, further research into cellular responses and tissue regeneration mechanisms is necessary to enhance the precision and safety of radiation applications in medicine. This knowledge is also vital for addressing the broader implications of radiation exposure in environmental and occupational contexts.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest related to this manuscript.

REFERENCES

Ai, Y., Meng, Y., Yan, B., Zhou, Q., & Wang, X. (2024). The biochemical pathways of apoptotic, necroptotic, pyroptotic, and ferroptotic cell death. Molecular Cell, 84(1), 170-179.

Baeyens, A., Abrantes, A. M., Ahire, V., Ainsbury, E. A., Baatout, S., Baselet, B., ... & Wozny, A. S. (2023). Basic Concepts of Radiation Biology. In Radiobiology Textbook (pp. 25-81). Cham: Springer International Publishing.

Bedoui, S., Herold, M. J., & Strasser, A. (2020). Emerging connectivity of programmed cell death pathways and its physiological implications. Nature reviews Molecular cell biology, 21(11), 678-695.

Bray, F. N., Simmons, B. J., Wolfson, A. H., & Nouri, K. (2016). Acute and chronic cutaneous reactions to ionizing radiation therapy. Dermatology and therapy, 6, 185-206.

Casarett, G. W. (1968). *Clinical radiation pathology*.

Giles, B., Nakhjavani, M., Wiesa, A., Knight, T., Shigdar, S., & Samarasinghe, R. M. (2023). Unravelling the glioblastoma tumour microenvironment: Can aptamer targeted delivery become successful in treating brain cancers?. Cancers, 15(17), 4376.

Gorbunov, N. V., & Kiang, J. G. (2021). Brain damage and patterns of neurovascular disorder after ionizing irradiation. Complications in radiotherapy and radiation combined injury. Radiation research, 196(1), 1-16.

Haber, A. H., & Rothstein, B. E. (1969). Radiosensitivity and rate of cell division:" Law of Bergonie and Tribondeau". *Science*, *163*(3873), 1338-1339.

Hashimoto, S., Komatsu, M., & Miura, S. (2022). Basic Knowledge to Understand Radioactive Contamination. In Forest Radioecology in Fukushima: Radiocesium Dynamics, Impact, and Future (pp. 11-20). Singapore: Springer Nature Singapore.

Hosea, R., Hillary, S., Naqvi, S., Wu, S., & Kasim, V. (2024). The two sides of chromosomal instability: drivers and brakes in cancer. Signal Transduction and Targeted Therapy, 9(1), 75.

Ibáñez, B., Melero, A., Montoro, A., San Onofre, N., & Soriano, J. M. (2024). Molecular Insights into Radiation Effects and Protective Mechanisms: A Focus on Cellular Damage and Radioprotectors. Current Issues in Molecular Biology, 46(11), 12718.

Kepka, L., & Socha, J. (2021). Dose and fractionation schedules in radiotherapy for non-small cell lung cancer. Translational lung cancer research, 10(4), 1969–1982.

Khalid, N., & Azimpouran, M. (2020). Necrosis.

Khan, F. M., Sperduto, P. W., & Gibbons, J. P. (2021). *Khan's Treatment Planning in Radiation Oncology:*. Lippincott Williams & Wilkins.

King, S. N., Dunlap, N. E., Tennant, P. A., & Pitts, T. (2016). Pathophysiology of radiation-induced dysphagia in head and neck cancer. Dysphagia, 31, 339-351.

Koturbash, I., Merrifield, M., & Kovalchuk, O. (2017). Fractionated exposure to low doses of ionizing radiation results in accumulation of DNA damage in mouse spleen tissue and activation of apoptosis in a p53/Atm-independent manner. International journal of radiation biology, 93(2), 148–155. https://doi.org/10.1080/09553002.2017.1231943

Koutroumpakis, E., Deswal, A., Yusuf, S. W., Abe, J. I., Nead, K. T., Potter, A. S., ... & Palaskas, N. L. (2022). Radiation-induced cardiovascular disease: mechanisms, prevention, and treatment. Current oncology reports, 24(5), 543-553.

Lumniczky, K., Szatmári, T., & Sáfrány, G. (2017). Ionizing Radiation-Induced Immune and Inflammatory Reactions in the Brain. Frontiers in immunology, 8, 517. https://doi.org/10.3389/fimmu.2017.00517

Majeed, H., & Gupta, V. (2022). Adverse Effects of Radiation Therapy StatPearls.

Marković, S., & Spaić, R. (2001). *Radijacija i zdravlje*. Društvo za biomedicinsko inženjerstvo i medicinsku fiziku SR Jugoslavije.

McBride, W. H., & Schaue, D. (2020). Radiation-induced tissue damage and response. *The Journal of pathology*, *250*(5), 647–655. https://doi.org/10.1002/path.5389

McBride, W. H., & Withers, H. R. (2004). Biologic basis of radiation therapy. *Principles and Practice of Radiation Oncology, Lippincott Williams and Wilkins, Philadelphia*, 96-136.

Milošević H., Saračević L., i Čaklovica F. (2005) *Radijacijska bolest domaćih životinja.* Veterinarski fakultet, Sarajevo.

Mohan, S., & Chopra, V. (2022). Biological effects of radiation. In Radiation dosimetry phosphors (pp. 485-508). Woodhead Publishing.

Prasanna, P. G., Aryankalayil, M., Citrin, D. E., & Coleman, C. N. (2023). Radiation-induced pulmonary fibrosis: roles of therapy-induced senescence and microRNAs. *International journal of radiation biology*, *99*(7), 1027-1036.

Rübe, C. E., Raid, S., Palm, J., & Rübe, C. (2023). Radiation-induced brain injury: age dependency of neurocognitive dysfunction following radiotherapy. Cancers, 15(11), 2999.

Russ, E., Davis, C. M., Slaven, J. E., Bradfield, D. T., Selwyn, R. G., & Day, R. M. (2022). Comparison of the Medical Uses and Cellular Effects of High and Low Linear Energy Transfer Radiation. Toxics, 10(10), 628. https://doi.org/10.3390/toxics10100628

Saračević, L. (1999) *Veterinarska radiobiologija sa radijacionom higijenom.* DES, Sarajevo.

Schettino, G., Baatout, S., Caramelo, F., Da Pieve, F., Fernandez-Palomo, C., Edin, N. F. J., ... & Villagrasa, C. (2023). Mechanistic, Modeling, and Dosimetric Radiation Biology. In Radiobiology Textbook (pp. 191-236). Cham: Springer International Publishing.

Stone, H. B., Coleman, C. N., Anscher, M. S., & McBride, W. H. (2003). Effects of radiation on normal tissue: consequences and mechanisms. *The lancet oncology*, *4*(9), 529-536.

Vitale, I., Pietrocola, F., Guilbaud, E., Aaronson, S. A., Abrams, J. M., Adam, D., ... & Pasparakis, M. (2023). Apoptotic cell death in disease—Current understanding of the NCCD 2023. Cell Death & Differentiation, 30(5), 1097-1154.

Withers, H. R., Peters, L. J., Taylor, J. M., Owen, J. B., Morrison, W. H., Schultheiss, T. E., ... & Hanks, G. E. (1995). Late normal tissue sequelae from radiation therapy for carcinoma of the tonsil: patterns of fractionation study of radiobiology. *International Journal of Radiation Oncology* Biology* Physics*, *33*(3), 563-568.