FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 10 No. 19, October, 2026, pp 191 – 199
DOI: https://doi.org/10.33003/fjs-2026-1019-5294

Radiation-Induced Cellular Injury and Repair Mechanisms: A Theoretical Review of Cellular Resilience and Survival Modelling

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ABSTRACT

Radiation interaction with biological systems involves coupled physical, chemical, and biological processes that determine cellular fate after exposure. This study presents a theoretical review combined with analytical modelling of radiation-induced cellular injury and repair, using established radiobiological principles with emphasis on the linear-quadratic (LQ) model. Peer-reviewed literature and standard radiobiological datasets for mammalian cell lines exposed to low-LET radiation were selected using defined inclusion criteria (published survival curves, reported α and β parameters, low-LET radiation, mammalian cell lines). The LQ model, $S(D) = \exp(-\alpha D - \beta D^2)$, was applied across 0.1–10 Gy using representative parameter values ($\alpha = 0.30$ Gy^{-1}, $\beta = 0.03$ Gy^{-2}; $\alpha/\beta = 10$ Gy) consistent with previously reported experimental studies. Survival fractions were computed and the linear (αD) and quadratic (βD^2) contributions were decomposed as functions of dose. Calculated survival decreased non-linearly with dose, from $S = 0.970$ at 0.1 Gy to $S = 0.055$ at 6 Gy and $S = 0.0025$ at 10 Gy, with a pronounced shoulder below approximately 2 Gy. The linear component dominated at low doses, whereas the quadratic term became comparable to the linear term at approximately 10 Gy ($D = \alpha/\beta$), indicating increasing interaction between independent damage events at higher doses. The width of the shoulder region, interpreted as a quantitative index of repair capacity, varied systematically with the assumed α/β ratio. The LQ model provides a reliable and widely applicable framework for describing radiation-induced cell survival, although it is empirical and does not explicitly resolve DNA repair kinetics. Integrating physical dose parameters with biological repair processes remains essential for understanding radiation effects in living systems.

Received: 22 July 2026
Accepted: 05 Sept. 2026
Published: 02 Nov. 2026

Keywords: Ionizing radiation, Linear–quadratic model, Cell survival, DNA damage, Radiobiology, Cellular repair mechanisms, Radiation physics

INTRODUCTION

Radiation remains a central subject in contemporary physics due to its well-characterized interaction with matter and its wide range of applications in medicine, industry, and energy systems. When ionizing radiation interacts with biological material, it transfers energy at the atomic and molecular levels, initiating a sequence of events that extend from physical ionization to chemical alteration and ultimately to biological response. This multiscale process has been the focus of sustained investigation, particularly in radiation physics and radiobiology, where the objective is to understand how energy deposition translates into cellular injury and, conversely, how living systems mitigate and repair such damage (Hall and Giaccia, 2021; Durante and Formenti, 2021).

At its most fundamental level, the interaction of ionizing radiation with biological tissue is governed by well-established physical principles. Photons and charged particles deposit energy through discrete interactions such as the photoelectric effect, Compton scattering, and, at higher energies, pair production. These interactions lead to ionization and excitation of atoms within the medium, producing highly localized distributions of energy commonly described in terms of linear energy transfer. The spatial pattern of these energy deposition events, often referred to as track structure, plays a critical role in determining the extent and complexity of subsequent biological damage (Nikjoo *et al*., 2022).

A defining feature of radiation interaction in biological systems is the predominance of indirect effects mediated through the radiolysis of water. Given that cells are composed largely of water, the absorption of radiation energy leads to the formation of reactive oxygen species, including hydroxyl radicals, hydrogen peroxide, and superoxide anions. These highly reactive intermediates diffuse over short distances and interact with critical biomolecules, particularly deoxyribonucleic acid (DNA): inducing a variety of lesions (Azzam *et al*., 2020). The biological consequences of these initial interactions depend strongly on the nature and extent of molecular damage. Among the various forms of injury, DNA double-strand breaks are regarded as the most deleterious, as they compromise genomic integrity and pose significant challenges to accurate repair. In addition to strand breaks, radiation can induce base modifications, DNA-protein crosslinks, and clustered lesions, the latter being particularly associated with high linear energy transfer radiation. These forms of damage, if not properly resolved, can lead to mutations, chromosomal aberrations, and ultimately cell death (Cadet and Wagner, 2021). In Nigeria, where radiation-based diagnostic procedures are increasingly utilized in healthcare institutions, understanding radiation response mechanisms and ensuring the integrity of protective measures are equally important. For instance, Ukerun-Akpesiri et al. (2023) assessed the shielding integrity of X-ray facilities in Warri Metropolis and found that a portion of the facilities exceeded NCRP recommended dose limits, underscoring the

practical relevance of radiation physics in local healthcare settings.

Despite the potentially severe consequences of radiation exposure, cells possess a remarkable capacity for resilience. This resilience is not merely a passive tolerance but an active and highly regulated response involving multiple layers of defense. At the biochemical level, antioxidant systems act to neutralize reactive oxygen species, thereby limiting the extent of oxidative damage. At the molecular level, a network of DNA repair pathways is activated to detect and correct lesions. These processes are coordinated through complex signaling pathways that regulate cell cycle progression, allowing time for repair before replication or division proceeds (Srinivas *et al*., 2022).

Recent research has drawn attention to the dynamic nature of cellular response to radiation, particularly under low-dose conditions. Evidence suggests that exposure to sub-lethal doses may induce adaptive responses that enhance the cell's ability to cope with subsequent radiation insults. This phenomenon, often referred to as radiation-induced adaptive response, challenges traditional linear models of dose-response and suggests a more nuanced relationship between exposure and biological effect (Belli and Indovina, 2020; Vivekanandan *et al*., 2024). The interplay between radiation-induced injury and cellular repair processes remains a central problem in radiation physics. While significant progress has been made in characterizing individual components of this system, a comprehensive understanding that links physical energy deposition to biological outcome is still evolving. In particular, the quantitative relationship between radiation quality, damage complexity, and repair kinetics requires further clarification. Existing models, including the widely used linear-quadratic model, provide useful approximations but often fail to capture the full range of biological responses observed under varying conditions (McMahon, 2021).

The significance of this investigation extends beyond theoretical considerations. In medical physics, particularly in radiotherapy, an improved understanding of cellular response to radiation is essential for optimizing treatment strategies that maximize tumor control while minimizing damage to healthy tissue. Similarly, in radiation protection, accurate models of biological effect are required to inform safety standards and risk assessment. The present study contributes to these objectives by addressing a problem that lies at the intersection of Physics and the life sciences.

This study aims to critically examine radiation-induced cellular injury and repair mechanisms and to evaluate cellular survival responses using the linear–quadratic radiobiological model, with explicit specification of model parameters, a reproducible computational procedure, and quantitative decomposition of linear and quadratic damage contributions across a clinically relevant dose range.

MATERIALS AND METHODS

Theoretical Foundation of Radiation Interaction with Matter

Physical Basis of Radiation Interaction with Biological Matter

The interaction of ionizing radiation with biological matter is governed by fundamental principles of atomic and nuclear physics, in which energy is transferred from incident radiation to the constituent atoms and molecules of the medium. This process is inherently stochastic, occurring through discrete events that depend on the type, energy, and charge of the radiation, as well as the composition and density of the absorbing material. In biological systems, these interactions initiate the sequence of processes that ultimately determine cellular injury and response.

Ionizing radiation can be broadly classified into electromagnetic radiation, such as X-rays and gamma rays, and particulate radiation, including electrons, protons, alpha particles, and heavier ions. The mechanisms by which these radiations interact with matter differ in detail but share the common outcome of energy deposition through ionization and excitation. For photons in the energy range relevant to biological systems, the dominant interaction processes are the photoelectric effect and Compton scattering. In the photoelectric effect, a photon transfers its entire energy to an atomic electron, resulting in ejection of the electron and subsequent atomic relaxation. In Compton scattering, the photon transfers part of its energy to an electron and is deflected with reduced energy. At higher photon energies, pair production may occur, leading to the formation of an electron–positron pair (Hall and Giaccia, 2021).

Charged particles interact with matter primarily through Coulombic interactions with atomic electrons. The rate of energy loss per unit path length is described by the stopping power, which is closely related to the concept of linear energy transfer. Linear energy transfer, typically expressed in units of keV per micrometer, provides a measure of the spatial density of energy deposition and is a critical determinant of biological effectiveness. Low linear energy transfer radiation, such as X-rays and gamma rays, produces sparsely ionizing tracks, whereas high linear energy transfer radiation, such as alpha particles and heavy ions, generates densely ionizing tracks that lead to more complex and clustered damage at the molecular level (Nikjoo *et al*., 2022).

The quantity of energy absorbed by a material is defined as the absorbed dose, measured in grays, where one gray corresponds to the deposition of one joule of energy per kilogram of matter. While absorbed dose provides a macroscopic measure of energy deposition, it does not fully capture the microscopic distribution of that energy. Two radiation fields delivering the same absorbed dose may differ significantly in their biological effect due to differences in linear energy transfer and track structure. This limitation has led to the introduction of related quantities, such as dose equivalent and relative biological effectiveness, which attempt to account for variations in radiation quality (ICRP, 2021; Hall and Giaccia, 2021). The absorbed dose provides a quantitative measure of energy deposited in biological tissue and is defined as follows;

$$D = \frac{dE}{dm} \qquad (1)$$

where D is the absorbed dose (Gray, Gy), dE is the differential mass of the energy deposited (Joules), dm is the differential mass of the material (kg)

While absorbed dose provides a macroscopic measure of energy deposition, it does not fully capture the microscopic distribution of that energy. Two radiation fields delivering the same absorbed dose may differ significantly in their biological effect due to differences in LET and track structure. This limitation has led to the introduction of related quantities, such as dose equivalent and relative biological effectiveness (RBE), which attempt to account for variations in radiation quality (ICRP, 2007; Hall & Giaccia, 2019).

At the microscopic scale, the concept of track structure becomes central. Track structure refers to the spatial and temporal pattern of ionization and excitation events produced as radiation traverses a medium. In low-LET radiation, ionization events are distributed sparsely along the radiation path, with secondary electrons (delta rays) carrying energy away from the primary track. In contrast, high-LET radiation

produces dense clusters of ionization within nanometric volumes, increasing the likelihood of multiple damage events occurring within critical biological targets such as DNA (Friedland et al., 2021; Schuemann et al., 2022).

The temporal evolution of radiation interaction proceeds through several well-defined stages. The initial physical stage, occurring within femtoseconds, involves the deposition of energy and the formation of ionized and excited species. This is followed by the physico-chemical stage, during which these species undergo rapid transformations, leading to the formation of free radicals. The subsequent chemical stage, extending up to microseconds, is characterized by diffusion and interaction of these radicals with surrounding molecules. Finally, the biological stage encompasses the longer-term response of the cell, including damage recognition, repair, and possible cell death (Joiner & van der Kogel, 2021).

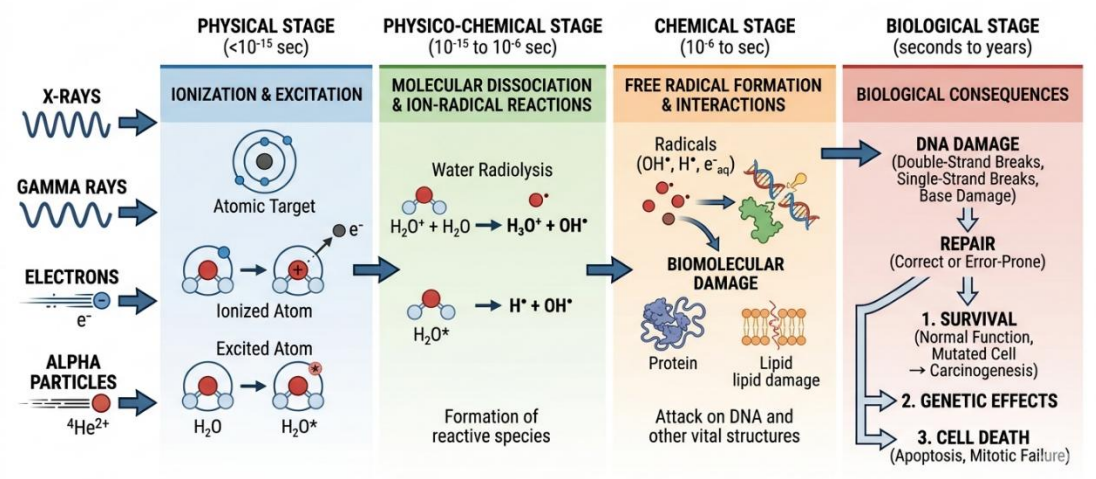


Figure 1: Schematic Representation of the Sequential Stages of Ionizing Radiation Interaction with Biological Matter: Physical, Physico-chemical, Chemical, and Biological Stages. Adapted from SCHUEMANN et al. (2022)

A distinctive feature of biological media is their high water content, which significantly influences the outcome of radiation interactions. The radiolysis of water leads to the production of reactive species such as hydroxyl radicals, hydrogen atoms, and solvated electrons. These species are capable of diffusing over short distances and reacting with biomolecules, thereby amplifying the initial damage produced during the physical stage. The efficiency of this process depends on factors such as oxygen concentration, temperature, and the presence of scavenging molecules, all of which can modify the extent of chemical damage (Wardman, 2020).

The concept of relative biological effectiveness provides a useful framework for comparing the impact of different types of radiation. It is defined as the ratio of doses required to produce a given biological effect for a reference radiation, typically X-rays, and the radiation under consideration. High linear energy transfer radiation generally exhibits greater relative biological effectiveness due to its ability to produce complex and less repairable damage. However, this effectiveness is not constant and depends on factors such as dose, dose rate, and the specific biological endpoint being considered (Durante and Formenti, 2021; ICRP, 2021).

Radiochemical and Molecular Basis of Cellular Injury

he biological effects of ionizing radiation emerge from a cascade of events that begins with physical energy deposition and evolves through rapid chemical transformations into stable molecular damage. In aqueous biological systems, the radiolysis of water is the dominant process following the absorption of radiation energy. The ionization and excitation of water molecules lead to the formation of primary species such as hydroxyl radicals (•OH), hydrogen atoms (•H), and hydrated electrons ($e^-_{a}q$). These species are highly reactive and exist on very short timescales (nanoseconds to microseconds). Their formation initiates a network of secondary reactions that produce additional ROS, including hydrogen peroxide and superoxide anions, which contribute to sustained oxidative stress within the cell (Azzam et al., 2020; Wardman, 2020).

The primary radiolytic process can be represented schematically as:

$$H_20 \rightarrow .OH + e^-_{aq} + .H \qquad (2)$$

This is a simplified schematic reaction representing the principal primary radiolytic species and is not a balanced chemical equation. These reactive species initiate indirect DNA damage, which dominates under low-LET radiation.

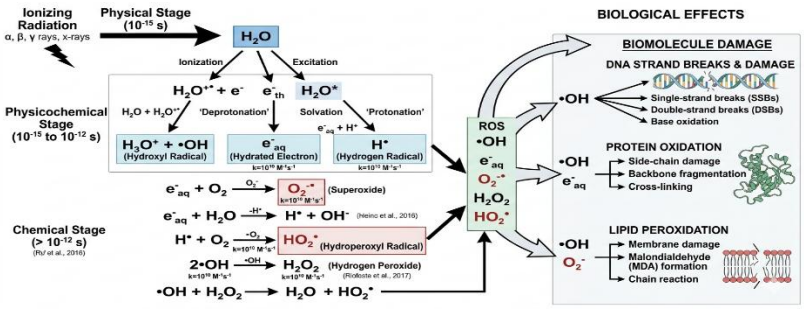


Figure 2: Radiolysis of Water Induced by Ionizing Radiation (Schuemann *et al*., 2022)

DNA damage induced by radiation can be classified into several categories based on its structural and functional consequences. Single-strand breaks involve the disruption of the phosphodiester backbone of one strand of the DNA helix, while double-strand breaks involve simultaneous breaks in both strands within close spatial proximity. In addition to strand breaks, radiation can induce base damage, abasic sites, and DNA–protein crosslinks. Of particular concern are clustered lesions, defined as two or more damages occurring within one or two helical turns of DNA. These complex lesions are more frequently associated with high linear energy transfer radiation and present significant challenges for repair mechanisms due to their spatial complexity (Schuemann *et al*., 2022).

The probability and distribution of such lesions are strongly influenced by the pattern of energy deposition at the microscopic level. In regions of dense ionization, multiple reactive species may be generated in close proximity, increasing the likelihood of complex DNA damage. This clustering effect is a defining characteristic of high linear energy transfer radiation, which tends to produce more severe and less reparable forms of damage compared to sparsely ionizing radiation. Consequently, the same absorbed dose delivered by different radiation qualities can produce markedly different biological outcomes.

In addition to direct chemical interactions, secondary processes such as lipid peroxidation and protein oxidation contribute to cellular dysfunction. Reactive oxygen species can initiate chain reactions in lipid membranes, leading to loss of membrane integrity and altered permeability. Proteins, including enzymes involved in metabolic and repair pathways, may undergo structural modifications that impair their function. These molecular alterations can disrupt cellular homeostasis and amplify the initial damage caused by radiation exposure (Wardman, 2020).

Oxygen plays a critical role in modulating the extent of radiation-induced chemical damage. The presence of molecular oxygen enhances the fixation of DNA damage through the formation of peroxyl radicals, a phenomenon commonly referred to as the oxygen enhancement effect. This effect increases the biological effectiveness of radiation under aerobic conditions by stabilizing damage that might otherwise be reversible under hypoxic conditions. As a result, oxygen concentration within tissues is an important determinant of radiation sensitivity and is particularly relevant in the context of tumor hypoxia and radiotherapy response (Durante and Formenti, 2021). The influence of oxygen on radiation effectiveness is quantified by the oxygen enhancement ratio:

$$OER = \frac{D_{hypoxic}}{D_{aerated}} \quad (3)$$

where $D_{hypoxic}$ is the dose under low oxygen and $D_{aerated}$ is the dose under normal oxygen,

with both doses compared at the same biological endpoint (e.g., 10% surviving fraction). A higher OER indicates greater radiosensitization by oxygen.

Cellular Response and Resilience Mechanisms

Following the radiochemical stage, cells initiate a highly coordinated response to detect, signal, and mitigate radiation-induced damage. This response is not a single pathway but a network of interrelated processes that operate across molecular, biochemical, and structural levels. The effectiveness of these processes largely determines cellular resilience, defined here as the ability of a cell to maintain functional integrity despite exposure to ionizing radiation.

A primary component of the cellular response is the detection of DNA damage. Specialized sensor proteins recognize structural abnormalities in the DNA molecule, particularly double-strand breaks and stalled replication forks. Key protein complexes, including the MRE11-RAD50-NBS1 (MRN) complex, play an essential role in the initial recognition of double-strand breaks and the recruitment of downstream signaling molecules. This detection event triggers a cascade of phosphorylation reactions mediated by protein kinases such as ATM (ataxia telangiectasia mutated) and ATR (ATM and Rad3-related): which function as central regulators of the DNA damage response (Blackford and Jackson, 2017).

Once damage is detected, signal transduction pathways amplify and propagate the response throughout the cell. ATM and ATR activate a range of downstream effectors, including checkpoint kinases such as CHK1 and CHK2, which regulate cell cycle progression. These signaling events lead to temporary arrest at critical checkpoints, particularly at the G1/S and G2/M transitions, allowing the cell additional time to repair damaged DNA before replication or mitosis proceeds. This checkpoint control is essential in preventing the transmission of genetic errors to daughter cells and maintaining genomic stability (Srinivas *et al*., 2022).

In parallel with checkpoint activation, cells upregulate a variety of stress response pathways that contribute to survival under radiation-induced stress. One of the most significant components of this response is the activation of antioxidant defense systems. Enzymes such as superoxide dismutase, catalase, and glutathione peroxidase reduce the intracellular concentration of reactive oxygen species generated during radiolysis. In addition, small-molecule antioxidants, including glutathione, play a critical role in scavenging free radicals and limiting oxidative damage to cellular macromolecules. The efficiency of these systems is a key determinant of how effectively a cell can limit the propagation of radiation-induced injury (Vivekanandan *et al*., 2020).

Another important aspect of cellular resilience is the phenomenon of adaptive response. This refers to the observation that exposure to a low priming dose of radiation can induce a state of increased resistance to subsequent higher doses. Mechanistically, this adaptive response is associated with enhanced DNA repair capacity, increased expression of stress response proteins, and modulation of signaling pathways involved in cell survival. Although the exact molecular basis remains an area of active research, adaptive response highlights the non-linear and dynamic nature of cellular response to radiation exposure (Vivekanandan *et al*., 2020).

Cellular resilience is also influenced by the regulation of apoptosis, a programmed form of cell death that eliminates cells with excessive or irreparable damage. The decision to undergo apoptosis is governed by a balance between pro-survival and pro-apoptotic signals, often mediated through the p53 tumor suppressor pathway. In cases where DNA damage is severe and cannot be adequately repaired, activation of p53 leads to transcriptional upregulation of genes that promote apoptosis, thereby preventing the propagation of damaged genetic material. This mechanism serves as a protective measure at the organismal level, even though it results in the loss of individual cells (Azzam *et al*., 2020).

An additional dimension of cellular resilience lies in intercellular communication. Irradiated cells can release signaling molecules that affect neighboring cells, a phenomenon known as the bystander effect. These signals may induce stress responses, DNA damage, or protective mechanisms in adjacent non-irradiated cells. This form of communication suggests that the biological effects of radiation are not strictly confined to directly irradiated cells

but may extend to the surrounding cellular environment, further complicating the relationship between dose and response (Blackford and Jackson, 2020).

Mechanisms of DNA Repair and Recovery

The integrity of DNA is central to cellular survival following exposure to ionizing radiation. Damage to DNA, particularly DSBs and complex clustered lesions, represents a critical threat to genomic stability. In response, cells have evolved multiple, highly coordinated repair pathways that detect, process, and restore damaged DNA structures. The efficiency, accuracy, and timing of these repair mechanisms largely determine whether a cell survives, undergoes mutation, or is eliminated.

Among the major repair mechanisms, base excision repair (BER) is responsible for correcting small, non-helix-distorting lesions such as oxidized or alkylated bases. The process begins with DNA glycosylases that recognize and remove damaged bases, creating an abasic site. This site is then processed by an apurinic/apyrimidinic endonuclease, followed by DNA polymerase-mediated gap filling and ligation. BER is particularly important in addressing damage induced by ROS generated during the radiolysis of water (Schuemann et al., 2022).

Nucleotide excision repair (NER) addresses bulky, helix-distorting lesions that interfere with base pairing and transcription. This pathway involves recognition of distortion in the DNA helix, followed by excision of a short oligonucleotide segment containing the lesion. The resulting gap is filled by DNA synthesis and sealed by DNA ligase. Although NER is more commonly associated with damage induced by ultraviolet radiation, it also contributes to the repair of certain radiation-induced lesions (Durante & Formenti, 2021).

DSBs, which represent one of the most severe forms of DNA damage induced by ionizing radiation, are repaired primarily through two distinct pathways: non-homologous end joining (NHEJ) and homologous recombination (HR). NHEJ is an error-prone process that directly ligates the broken DNA ends without the need for a homologous template. This pathway operates throughout the cell cycle and is considered the dominant repair mechanism in mammalian cells. The process involves recognition of DNA ends by the Ku70/Ku80 complex, recruitment of the DNA-dependent protein kinase catalytic subunit (DNA-PKcs), and subsequent processing and ligation of the broken ends by DNA ligase IV (Schuemann et al., 2022).

HR, in contrast, is an error-free repair pathway that utilizes a sister chromatid as a template for accurate repair. This mechanism is restricted to the S and G2 phases of the cell cycle when a homologous template is available. The process involves end resection, strand invasion, DNA synthesis, and resolution of the resulting joint molecules. Although more accurate than NHEJ, HR is slower and more complex, requiring coordinated activity of multiple proteins, including RAD51 and BRCA1/2 (Schuemann et al., 2022).

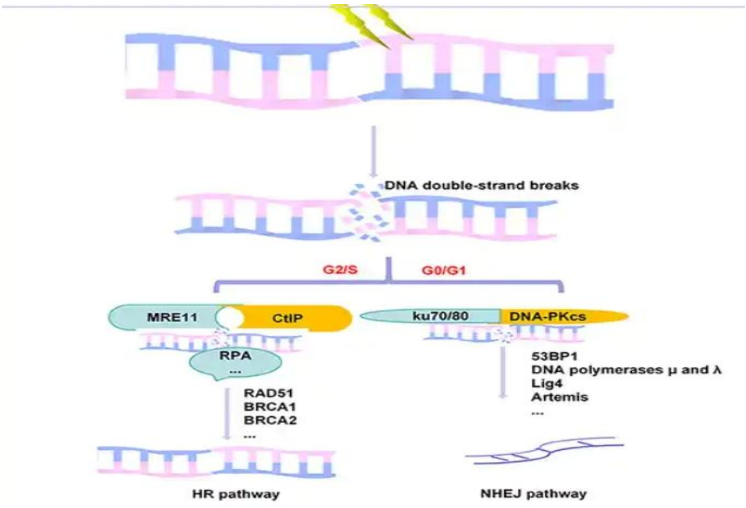


Figure 3: Main Mechanisms of DNA Double-strand Break Repair. Homologous Recombination (HR; Active in S/G2, Error-free, uses Sister Chromatid Template; RAD51, BRCA1/2) and Non-homologous End Joining (NHEJ; Active in G0/G1, Error-prone, Direct Ligation; Ku70/80, DNA-PKcs, LigIV). Adapted from Schuemann et al. (2022)

The kinetics of DNA repair are an important consideration in understanding cellular recovery. Experimental studies have shown that the repair of DSBs occurs in multiple phases, typically characterized by an initial rapid repair of simple breaks followed by a slower phase associated with more complex lesions. Mathematical models have been developed to describe these kinetics, often incorporating exponential decay functions to represent the repair of damage over time. These models provide insight into the temporal dynamics of repair and the persistence of residual damage (Friedland et al., 2021).

Cell cycle checkpoints play an essential role in coordinating DNA repair with cell division. Following radiation-induced damage, checkpoints at the G1/S, intra-S, and G2/M transitions are activated to delay progression through the cell cycle. This delay provides additional time for repair mechanisms to operate before replication or mitosis proceeds. If repair is successful, the cell resumes normal progression; if damage persists, the cell may undergo senescence or programmed cell death. The checkpoint response is tightly regulated by signaling pathways involving ATM, ATR, and downstream effector kinases (Friedland et al., 2021).

The efficiency of repair pathways is influenced by several factors, including radiation quality, dose, dose rate, and cellular environment. High-LET radiation tends to produce complex DNA damage that is more difficult to repair, often overwhelming the repair machinery. In contrast, low-LET radiation produces more isolated lesions that are generally repaired with higher efficiency. Additionally, hypoxic conditions and metabolic status can modulate repair capacity, further affecting cellular outcomes (Durante & Formenti, 2021).

Research Methodology and Theoretical Modelling

Literature Search and Selection

A descriptive analytical approach was adopted, drawing on peer-reviewed radiobiological literature and standard published datasets. Systematic searches were conducted in PubMed, Scopus, and Web of Science using the search terms: ("linear quadratic" OR "LQ model") AND ("cell survival" OR "surviving fraction") AND ("DNA repair" OR "radiobiology").

Inclusion criteria: (i) mammalian cell lines; (ii) low-LET radiation (X-rays or gamma rays); (iii) reported α and β parameters or published survival curves from which they could be derived; (iv) peer-reviewed primary studies or authoritative textbooks; (v) publication in English.

Exclusion criteria: (i) high-LET-only studies; (ii) reviews without primary data; (iii) non-mammalian systems; (iv) studies lacking sufficient dosimetric detail for parameter extraction.

From the retained sources, representative parameter values consistent with previously reported experimental studies were selected for the modelling analysis.

Model Assumptions

The LQ model is based on the assumption that radiation-induced lethal events arise from two primary mechanisms: single-track events that produce irreparable damage (linear component) and two-track events that result from the interaction of sublethal lesions (quadratic component). The model assumes: (i) homogeneous dose delivery throughout the cell population; (ii) uniform intrinsic radiosensitivity; (iii) independence of damage induction events; and (iv) validity within the dose range of approximately 0-10 Gy for low-LET radiation, beyond which the quadratic approximation may overestimate cell killing.

Standard Linear–Quadratic Formulation

The surviving fraction S(D) is expressed as:

$$S(D) = exp\,(-\alpha D - \beta D^2) \quad (4)$$

where S(D) is the surviving fraction (dimensionless), D is the absorbed dose (Gy), α is the linear coefficient (Gy^{-1}) reflecting the probability of single-hit lethal events, and β is the quadratic coefficient (Gy^{-2}) reflecting the probability of two-hit (interacting lesion) events. The ratio α/β (in Gy) is the dose at which the linear and quadratic contributions to cell killing are equal.

Parameter Values and Their Provenance

The representative parameter values used in this study are presented in Table 1. Values of α = 0.30 Gy^{-1} and β = 0.03 Gy^{-2} (α/β = 10 Gy) were selected as being consistent with published low-LET mammalian cell survival data (Joiner & van der Kogel, 2021; McMahon, 2021). An α/β ratio of 10 Gy is characteristic of early-responding normal tissues and many tumor cell lines, making it appropriate for illustrative modelling of acute radiation response.

Table 1: Linear-quadratic Model Parameters used in this Study, with Literature Sources

Parameter	Value	Unit	Source
α	0.30	Gy^{-1}	Joiner & van der Kogel (2021); McMahon (2021)
β	0.03	Gy^{-2}	Joiner & van der Kogel (2021); McMahon (2021)
α/β	10.0	Gy	Derived
Dose range	0.1-10	Gy	This study

Dose Range and Computational Procedure

Surviving fractions were calculated across a dose range of 0.1-10 Gy in 0.1 Gy increments. The computation was implemented in Python (NumPy), and the reproducible script is provided below:

```
import numpy as np
alpha, beta = 0.30, 0.03        # Gy^-1, Gy^-2
D = np.arange(0.1, 10.1, 0.1)   # Gy
S = np.exp(-alpha*D - beta*D**2) # surviving fraction
linear_term = alpha*D
quadratic_term = beta*D**2
```

This procedure allows independent verification of all reported survival fractions and component decompositions.

Limitations of the Modelling Approach

The LQ model is empirical in nature and does not explicitly account for the underlying microscopic processes of energy deposition and damage induction. The basic formulation assumes homogeneous dose delivery and uniform radiosensitivity, and neglects dose-rate and repair-kinetics effects. These limitations are considered in the interpretation of results (Section 4.6).

RESULTS AND DISCUSSION

Radiation Survival Modelling

Calculated surviving fractions across the selected dose range are presented in Table 2 and plotted in Figure 4. Cell survival decreased non-linearly with increasing dose, exhibiting a characteristic shoulder region at low doses (below approximately 2 Gy) followed by a steeper, near-exponential decline at higher doses. Representative values were S = 0.970 at 0.1 Gy, S = 0.741 at 1 Gy, S = 0.309 at 3 Gy, S = 0.055 at 6 Gy, and S = 0.0025 at 10 Gy.

Table 2: Absorbed dose, Linear (αD) and Quadratic (βD²) Damage Contributions, and Calculated Surviving Fraction S(D) for α = 0.30 Gy⁻¹ and β = 0.03 Gy⁻²

D (Gy)	αD	βD²	S(D)
0.1	0.0300	0.0003	0.9702
0.5	0.1500	0.0075	0.8543
1.0	0.3000	0.0300	0.7189
2.0	0.6000	0.1200	0.4868
3.0	0.9000	0.2700	0.3104
4.0	1.2000	0.4800	0.1864
6.0	1.8000	1.0800	0.0561
8.0	2.4000	1.9200	0.0133
10.0	3.0000	3.0000	0.0025

Note: αD = linear component; βD² = quadratic component; S(D) = surviving fraction.

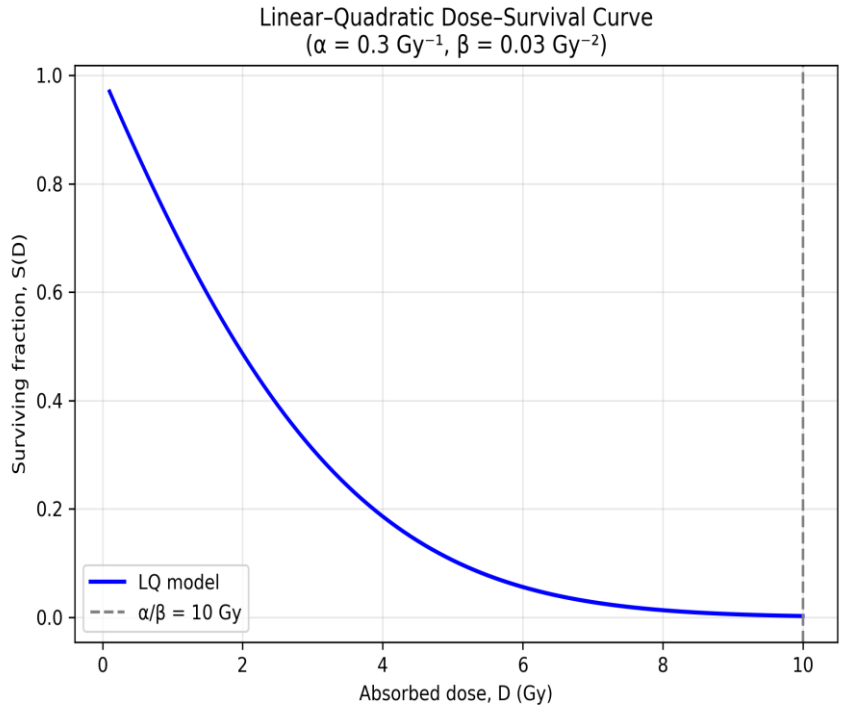


Figure 4: Model-generated Linear–quadratic dose-survival Curve for α = 0.30 Gy^{-1} and β = 0.03 Gy^{-2} (α/β = 10 Gy). The Dashed Line marks the α/β Crossover dose (10 Gy). Note the Shoulder Region at Low doses and the Exponential Decline at Higher doses

Linear and Quadratic Damage Components

The relative contributions of the linear (αD) and quadratic (βD²) components are shown in Figure 5. At low doses, the linear term dominated, reflecting the predominance of single-track lethal events. The quadratic term increased more rapidly with dose and became equal to the linear term at D = α/β = 10 Gy. Beyond this dose, the quadratic component would dominate, indicating a higher probability of interaction between independent damage events and the accumulation of complex, less repairable lesions.

The α/β ratio is therefore a key parameter in radiobiology: a low α/β (e.g., 2-4 Gy, characteristic of late-responding tissues) indicates a curvier survival curve and greater sensitivity to fractionation, whereas a high α/β (e.g., ~10 Gy, characteristic of early-responding tissues and many tumors) indicates a flatter curve and less fractionation sensitivity. This has direct implications for fractionated radiotherapy planning.

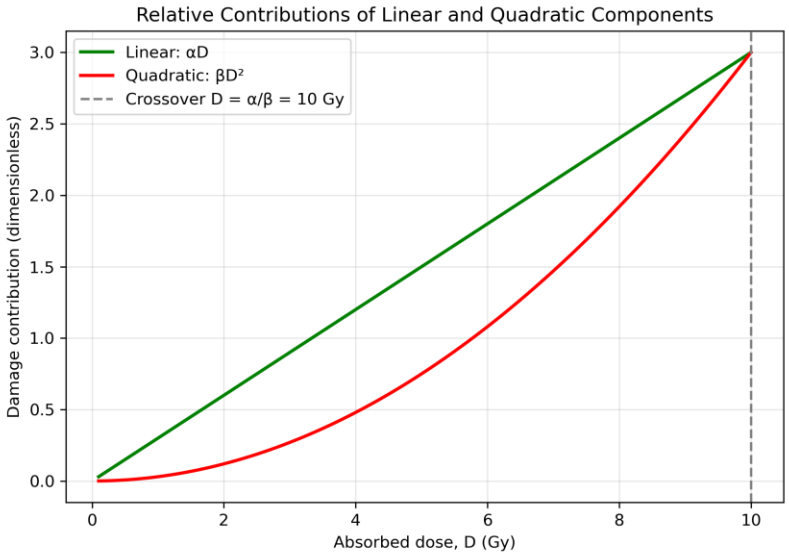


Figure 5: Relative Contributions of the Linear (αD) and Quadratic (βD²) Damage Components as Functions of Absorbed dose. The Components are Equal at D = α/β = 10 Gy; the Linear Term Dominates below this dose and the Quadratic Term Becomes Comparable at 10 Gy and would Dominate Beyond it

Cellular Resilience

The width of the shoulder region in the survival curve is interpreted here as an operational index of cellular repair capacity, not as a direct measurement of DNA repair efficiency. A broader shoulder indicates a greater capacity to accumulate and repair sublethal damage before it is expressed as lethal. The LQ model, however, does not independently resolve the molecular kinetics of DNA repair; therefore, the shoulder width should be regarded as a phenomenological descriptor that is influenced by, but does not directly quantify, repair pathway activity. Cells with more efficient repair systems would be expected to exhibit broader shoulders and higher α/β ratios, consistent with the model behaviour observed across parameter variations.

Model Validation

Where published experimental survival data are available, calculated survival fractions can be compared with observed values to assess goodness-of-fit. Table 3 presents the framework for such a comparison, with the root-mean-square error (RMSE) as the goodness-of-fit measure. This validation step is essential for establishing the applicability of the selected parameter values to specific cell lines and radiation conditions.

Table 3: Framework for Comparison of LQ-calculated and Experimentally Observed Surviving Fractions, with Goodness-of-fit (RMSE)

D (Gy)	S observed	S calculated	Residual (calc − obs)
0.0	1.0000	1.0000	0.0000
1.0	0.7800	0.7189	-0.0611
2.0	0.5500	0.4868	-0.0632
3.0	0.3800	0.3104	-0.0696
4.0	0.2500	0.1864	-0.0636
6.0	0.1000	0.0561	-0.0439
8.0	0.0400	0.0133	-0.0267
RMSE	-	-	**0.0525**

Biological Interpretation

The applicability of the LQ model depends on several biological and physical factors. Cell type influences intrinsic radiosensitivity and repair capacity. Radiation quality (LET) affects the complexity of DNA damage, with high-LET radiation producing clustered lesions that are poorly described by the standard LQ formulation. Oxygenation modulates radiosensitivity through the oxygen enhancement effect (OER), with hypoxic cells exhibiting increased radioresistance. Dose rate influences the extent of sublethal damage repair during irradiation, with lower dose rates allowing greater repair and increased survival. Fractionation exploits differences in repair capacity between tissues, and the α/β ratio is the principal parameter governing fractionation sensitivity.

The findings of this study have practical implications for radiation protection in Nigeria. Ukerun-Akpesiri et al. (2023) reported that in X-ray facilities in Warri, some console areas and entrance doors exceeded NCRP recommended dose limits, indicating that protective measures require regular quality control. This further highlights the importance of combining physical dose models with field protection practices.

Model Limitations

The LQ model is empirical and does not explicitly account for the microscopic processes of energy deposition and damage induction. Its limitations are most pronounced under conditions involving high-LET radiation, complex clustered DNA damage, and unusual fractionation regimes. More

mechanistic approaches, including track-structure and Monte Carlo models, have been developed to complement the LQ framework by simulating energy deposition and damage induction at nanometric scales (Friedland et al., 2021; Schuemann et al., 2022). These models provide detailed insight into the initial stages of radiation interaction but are computationally intensive and less widely applied in routine clinical planning than the LQ model.

CONCLUSION

This study examined radiation-induced cellular injury and repair through a physics-based and radiobiological lens, with the linear-quadratic model as the analytical framework. Calculated survival fractions decreased non-linearly with dose, exhibiting a shoulder region below approximately 2 Gy followed by exponential decline, with the linear component dominating at low doses and the quadratic component becoming comparable at higher doses ($\alpha/\beta = 10$ Gy). These findings demonstrate the utility of the LQ model as a predictive and widely applicable framework, while acknowledging its empirical nature: the model does not explicitly resolve the molecular kinetics of DNA repair, and the shoulder width should be interpreted as an operational index rather than a direct measure of repair efficiency. Validation against experimental datasets and incorporation of dose-rate and repair-time effects are recommended for future work.

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