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Review Article

Radiation Therapy in Cancer: Current Approaches, Challenges, And Future Directions

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ABSTRACT

Modern oncology still relies heavily on radiation therapy (RT), which is an essential part of multimodal cancer treatment plans that also include immunotherapy, chemotherapy, surgery, and targeted medicines. Through the use of high-energy ionizing radiation, RT prevents tumor growth while attempting to protect nearby normal tissues by causing deadly DNA damage in cancerous cells through both direct ionization and indirect free radical production. Rapid technical advancements over the past few decades, including proton and heavy ion therapy, intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), and stereotactic procedures, have significantly improved the safety, accuracy, and conformance of treatment administration. Beyond these technical innovations, deeper insights into tumor biology, radiogenomics, and the tumor microenvironment have enabled more personalized approaches and synergistic combinations with immunotherapy, chemotherapy, and radiosensitizers. RT is now applied across a broad spectrum of cancers, including breast, lung, prostate, head and neck, gynecologic, and central nervous system tumors, where it plays a critical role in local control, organ preservation, and improved survival. Despite these advances, challenges persist, such as treatment-related acute and late toxicities, tumor hypoxia, and radioresistance, which limit efficacy in certain patient populations. Looking forward, integration of adaptive RT, artificial intelligence, nanotechnology, and molecular biomarkers promises to transform radiation oncology into a more precise, personalized, and effective discipline. This review provides a comprehensive overview of the principles, modalities, clinical applications, challenges, and emerging directions of radiation therapy in the management of cancer.

INTRODUCTION

Cancer continues to be a leading cause of morbidity and mortality worldwide, accounting for millions of new cases and deaths annually.

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According to the World Health Organization (WHO) and GLOBOCAN reports, the global cancer burden is projected to rise significantly in the coming decades, highlighting the urgent need for effective and accessible treatment modalities. Among the various therapeutic strategies, radiation therapy (RT) plays a pivotal role in cancer management, with nearly 50–60% of all cancer patients requiring RT at some stage of their treatment course, either as a curative or palliative measure.[1] The fundamental principle of RT lies in the use of ionizing radiation to induce DNA damage in cancer cells, thereby inhibiting their ability to proliferate and survive. Over the years, RT has evolved remarkably, moving from conventional two-dimensional (2D) radiotherapy

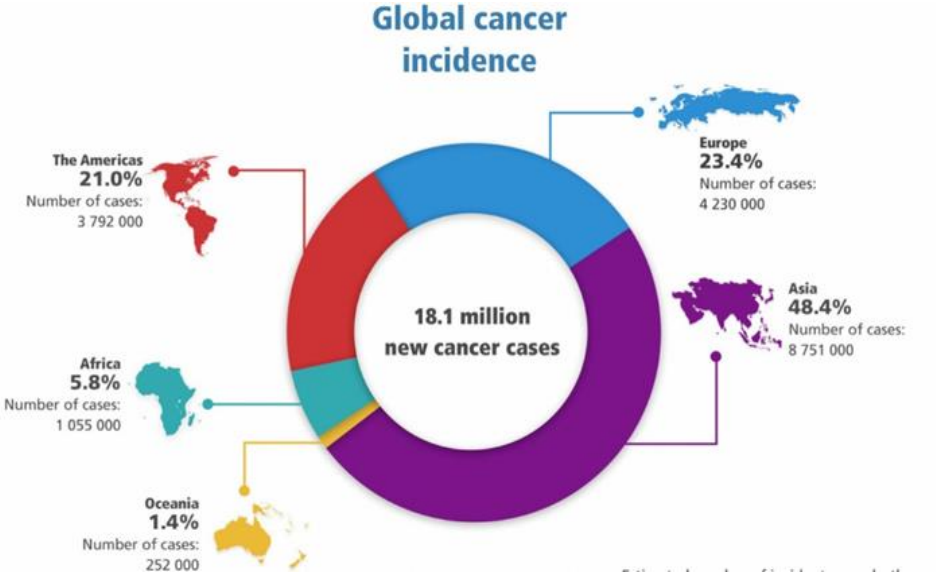

Fig 01 Global cancer incidence

techniques to more advanced modalities such as three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), stereotactic radiosurgery (SRS), stereotactic body radiotherapy (SBRT), and proton or heavy ion therapy. These innovations have greatly improved the precision of tumor targeting while sparing surrounding healthy tissues, thereby enhancing treatment efficacy and minimizing toxicities.[2] In addition to technological advancements, progress in radiobiology, imaging, and treatment planning systems has transformed RT into a highly sophisticated and individualized treatment modality. Integration with systemic therapies such as chemotherapy, immunotherapy, and targeted agents has further broadened its clinical applications, allowing for multimodal treatment approaches that improve survival outcomes and quality of life in cancer patients.[3] Despite these advances, RT still faces challenges, including radiation resistance, toxicity to normal tissues, high costs of advanced technologies, and limited accessibility in low- and middle-income countries (LMICs). Addressing these limitations requires continuous research and innovation in areas such as personalized RT, adaptive radiotherapy, artificial intelligence-driven treatment planning, and biological markers for radiosensitivity.[4] This review aims to provide a comprehensive overview of the fundamental principles, technological modalities, therapeutic applications, challenges, and future perspectives of radiation therapy in oncology, with an emphasis on its evolving role in modern cancer care.[5]

2. PRINCIPLES OF RADIATION THERAPY

2.1 Mechanism of action — direct and indirect damage

Ionizing radiation (photons, electrons, protons, heavy ions, and emissions from radiopharmaceuticals) damages cells by two complementary mechanisms:

Direct action: radiation deposits energy directly into DNA and other critical macromolecules, causing base damage, single-strand breaks (SSBs), double-strand breaks (DSBs) and clustered lesions. DSBs are the most lethal single event for clonogenic survival. [6]

Indirect action (ROS-mediated): the majority of low-LET radiation effects arise from radiolysis of water → reactive oxygen species (ROS: ·OH, H_2O_2, $O_2^{\cdot -}$) that chemically modify DNA (bases, sugars) and produce DSBs when lesions are closely spaced. ROS generation, antioxidant defenses, and redox status strongly influence outcome.[7]

Clinical note: different modalities differ in how damage is produced — e.g., high-LET particles (carbon ions) create dense ionization tracks leading to complex/clustered DNA damage that is less repairable than photon-induced damage; Auger emitters/radiopharmaceuticals can produce highly localized direct damage.[8]

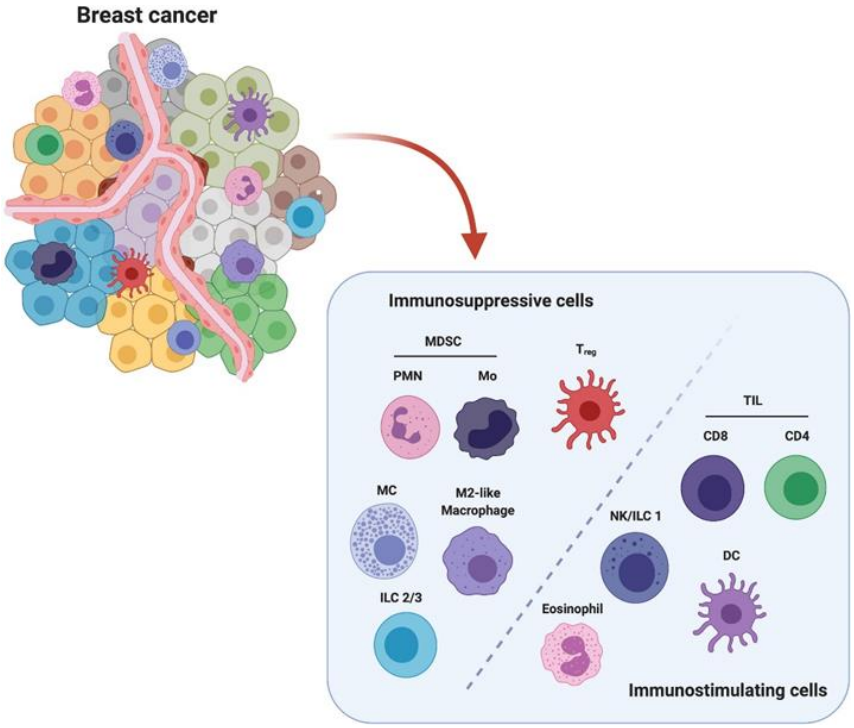

Fig. 02 Cancer Cell Distribution Infection

2.2 DNA damage response (DDR) and repair pathways: clinical importance

Cells sense DNA damage and mount the DNA damage response (DDR). Key pathways that repair IR-induced lesions:

Non-homologous end joining (NHEJ): fast, active throughout the cell cycle, error-prone — main DSB repair route after IR in mammalian cells.[9]

Homologous recombination (HR): accurate, restricted mainly to S/G2 when a sister chromatid is available.

Base excision repair (BER), nucleotide excision repair (NER), mismatch repair (MMR): handle base damage and SSBs.

DDR signaling (ATM/ATR/CHK1/CHK2/p53): coordinates cell-cycle arrest and repair or apoptosis if damage is irreparable.

Therapeutic implications: differences in DDR are exploited clinically — e.g., PARP inhibitors (block BER/SSB repair) sensitize tumors with HR defects; radiosensitizers aim to inhibit DSB repair. Conversely, normal-tissue radioprotectors (e.g., amifostine) attempt to mitigate ROS and DNA damage.[10]

2.3 Cellular outcomes after irradiation — types of death and non-lethal endpoints

Ionizing radiation produces a **spectrum** of cellular outcomes rather than a single "mode of death":

Clonogenic death / mitotic catastrophe: cells accumulate unrepaired chromosomal damage and fail during mitosis — a major determinant of long-term loss of reproductive capacity.

Apoptosis: programmed cell death (intrinsic/extrinsic) — prominent in lymphoid malignancies and some radiosensitive tumors; often p53-dependent.[11]

Senescence: permanent proliferative arrest with metabolic activity and SASP (senescence-associated secretory phenotype); contributes to late effects and modulates microenvironment.

Necrosis/necroptosis / ferroptosis / autophagy: context-dependent non-apoptotic death pathways increasingly recognized after IR.

Clinical note: which outcome predominates depends on dose, dose rate, cell type, p53/DDR status, and microenvironment — and this determines both tumor control and patterns of toxicity.12

2.4 Radiobiology fundamentals: the "R's", fractionation, and the LQ model

The Four R's (classical) — and extensions

Repair: sublethal damage repair in normal and tumor cells between fractions; underpins why fractionation reduces late normal-tissue toxicity.

Redistribution (reassortment): cells move through the cell cycle between fractions; since radiosensitivity varies by phase (most sensitive in G2/M, least in late S), redistribution can increase cell kill across fractions.

Repopulation: surviving tumor (and normal) cells proliferate during the course of treatment; accelerated repopulation in some tumors can reduce the effectiveness of prolonged schedules.

Reoxygenation: hypoxic (radioresistant) tumor regions may become reoxygenated between fractions, increasing radiosensitivity in subsequent fractions.[13]

Modern extensions add Radiosensitivity and Reactivation of anti-tumor immunity (some authors call these the "6 R's"). These concepts inform hypofractionation, adaptive RT, and combinations with systemic agents.

Fractionation & the Linear-Quadratic (LQ) model

The LQ model expresses the surviving fraction $S = \exp(-\alpha D - \beta D^2)$. The α/β ratio reflects tissue sensitivity to fraction size: early-responding/tumor tissues often have higher α/β; late-responding

normal tissues lower α/β → large fraction sizes produce relatively more late toxicity. Clinical fractionation (conventional vs hypofractionation vs SBRT) is chosen using α/β concepts and biologically effective dose (BED) calculations [14]

Limitations: LQ is robust for conventional and many hypofractionated regimens but has recognized limits at very high single doses (SRS/SBRT) and for very high dose-rates; alternative or corrected models are an area of active research.

2.5 Radiosensitivity tumor vs normal tissue: determinants and clinical consequences

Radiosensitivity is **multifactorial**:

Intrinsic factors: DNA repair capacity (NHEJ/HR), cell-cycle distribution (G2/M more sensitive; S-phase more resistant), p53 status, proliferative fraction.

Microenvironmental factors: oxygenation (hypoxia → reduced ROS fixation of damage), interstitial pressure, stromal support, and immune infiltrate.

Cell subpopulations: cancer stem cells (CSCs) often display enhanced DDR, antioxidant defenses, and quiescence — contributing to radioresistance and relapse. Targeting CSCs is an emerging strategy to boost RT efficacy.[15]

Clinical consequences: because normal tissues and tumors often have different α/β values and repair kinetics, fractionation and dose-constraints are designed to maximize the therapeutic ratio. Understanding tumor radiosensitivity guides decisions about dose escalation, hypofractionation, combination radiosensitizers, and use of particle therapy (higher LET) for radioresistant/hypoxic tumors.

2.6 Oxygen effect & hypoxia a major clinical challenge

Oxygen Enhancement Ratio (OER): oxygen "fixes" radiation damage; the dose required under hypoxia to achieve the same effect as normoxia is higher (OER ~2.5–3 for low-LET photons). OER depends on LET (OER decreases with increasing LET).

Hypoxia in tumors: Chronic and acute hypoxia are common in solid tumors and is strongly associated with radioresistance and poor outcome. Strategies to address hypoxia include hypoxia-activated prodrugs, oxygen mimetics (e.g., nitroimidazoles such as nimorazole in head & neck cancer), dose painting with functional imaging, and high-LET particle therapy.

2.7 Translational & therapeutic implications — modulating principles to improve outcomes

TABLE I. **Radiosensitizers:** agents that inhibit DNA repair (PARP inhibitors), cell-cycle modulators, hypoxia modifiers, and some targeted agents can increase tumor kill when combined with RT. Clinical trials increasingly test rational combinations based on tumor genomics (radiogenomics).

TABLE II. **Radioprotectors: pharmacologic agents (e.g., amifostine) and technical approaches** (IMRT/IGRT, proton therapy) reduce normal-tissue dose and toxicity.

TABLE III. **Biomarkers & personalization:** radiogenomics, radiomics, and functional imaging (PET, MRI) can potentially predict radiosensitivity/toxicity and guide adaptive RT.

TABLE IV. **Dose-rate & novel modalities:** ultra-high dose-rate (FLASH) RT and particle therapies alter biological responses (less normal-tissue

toxicity, different OER/RBE behavior) and are under active investigation. [16]

3. MODALITIES OF RADIATION THERAPY

- **3.1 External Beam Radiation Therapy (EBRT)**

The most widely used modality, EBRT, delivers radiation from a machine (linear accelerator, LINAC) outside the patient's body. Continuous technological refinements have drastically improved accuracy, sparing normal tissues while intensifying tumor dose.

- **Conventional 2D RT**
  - Based on X-rays and simple anatomical landmarks for field placement.
  - Limited precision, higher toxicity to normal tissues.
  - Historically important but now largely replaced by conformal methods.
- **3D Conformal Radiation Therapy (3D-CRT)**
  - Uses CT-based imaging to create 3D tumor volumes.
  - Multiple radiation beams shaped to the tumor geometry.
  - Improves dose distribution compared to 2D.
  - Still widely used for prostate, breast, lung, and CNS tumors.
- **Intensity-Modulated Radiation Therapy (IMRT)**
  - Delivers radiation with variable beam intensity using multileaf collimators (MLCs).
  - Allows "dose painting" — higher dose to tumor, lower dose to nearby organs (e.g., salivary glands in head & neck cancer).
  - Reduces xerostomia, rectal toxicity, and other late effects.
- **Image-Guided Radiation Therapy (IGRT)**
  - Integrates imaging (CT, MRI, ultrasound, cone-beam CT) before/during treatment.
  - Corrects for tumor movement and setup variations.
  - Essential for hypofractionation, SBRT, and adaptive RT.
- **Stereotactic Radiosurgery (SRS) & Stereotactic Body Radiotherapy (SBRT)**
  - SRS: single/few high-dose fractions to small brain lesions (metastases, AVMs).
  - SBRT: ablative doses to extracranial sites (lung, liver, pancreas, spine).
  - Highly precise, requires immobilization and IGRT.
  - Offers curative potential in inoperable early-stage cancers.[17]

3.2 Particle Therapy

Unlike photons, particle therapy uses charged particles with unique dose-distribution characteristics (Bragg peak), delivering maximum energy at a defined depth, sparing normal tissue beyond the tumor.

❖ **Proton Beam Therapy (PBT)**

- Protons deposit a little dose on entry, release most energy at Bragg peak, then stop.
- Ideal for pediatric tumors (minimizing long-term toxicity), skull base tumors, ocular melanoma, and head & neck cancers.
- High cost and limited availability.[18]

❖ **Heavy Ion Therapy (e.g., Carbon Ion RT)**

- Carbon ions have higher linear energy transfer (LET), producing complex DNA damage less repairable by cells.
- Particularly effective for radioresistant tumors (sarcomas, hypoxic tumors, chordomas).
- Superior biological effectiveness, but even higher infrastructure costs than protons.

3.3 Brachytherapy

Brachytherapy delivers sealed radioactive sources directly into or near the tumor, offering a very high local dose with rapid fall-off to spare normal tissues.

- **Intracavitary Brachytherapy**

Sources are placed in natural body cavities (e.g., the uterine cervix, vagina). Standard of care in cervical and endometrial cancers.

- **Interstitial Brachytherapy**

Radioactive seeds or catheters implanted within tissues (e.g., prostate, soft tissue sarcomas). Enables conformal dose from within the tumor itself.

▪ **Surface Mold / Plaque Brachytherapy**

Custom applicators are placed on the skin or sclera. Useful for skin cancers and ocular melanoma. Advantages: high dose to the tumour, short treatment time. Limitations: invasive procedure, requires expertise, limited to accessible sites.[19]

3.4 Emerging Modalities

FLASH Radiotherapy

Delivers ultra-high dose rates (≥40 Gy/s) in fractions of a second. Preclinical studies show equal tumor control but reduced normal tissue toxicity (the "FLASH effect"). Clinical trials ongoing; mechanisms under study (hypoxia modulation, ROS dynamics).

- **Radiopharmaceutical Therapy (Targeted Radionuclide Therapy)**

Uses systemically administered radiolabeled molecules that selectively target tumours.

Examples:

Lutetium-177 DOTATATE (neuroendocrine tumours).

Radium-223 dichloride (bone metastases from prostate cancer).

Iodine-131 (thyroid cancer).

Expanding rapidly with theranostics (combined diagnostic + therapeutic radioisotopes).

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Expanding rapidly with theranostics (combined diagnostic + therapeutic radioisotopes).[21]

4. CLINICAL APPLICATIONS

Radiation therapy (RT) is a versatile tool applied across a wide range of malignancies, either as a curative approach, an adjuvant treatment, or for palliation. The choice of modality depends on tumor type, stage, anatomical site, and patient-specific considerations.

❖ **Breast Cancer**

Standard of Care: After breast-conserving surgery (lumpectomy), whole-breast irradiation significantly reduces local recurrence and improves survival.

Hypo fractionation: Shorter treatment schedules (e.g., 40 Gy in 15 fractions) are widely adopted with comparable efficacy and safety [12]

Partial Breast Irradiation (PBI): Targeted irradiation of the tumour bed using 3D-CRT, IMRT, or brachytherapy for low-risk patients.

Emerging Approaches: Proton therapy and intraoperative radiotherapy are being explored to minimize cardiac and pulmonary toxicity.

➢ **Lung Cancer**

Early-Stage NSCLC: Stereotactic Body Radiotherapy (SBRT) provides local control rates comparable to surgery in medically inoperable patients.

Locally Advanced Disease: Concurrent chemo radiation is the standard, often followed by consolidation immunotherapy.

Proton Therapy: Reduces radiation exposure to critical thoracic structures (heart, oesophagus, spinal cord).

➢ **Head and Neck Cancers**

IMRT (Intensity-Modulated Radiation Therapy): Enables organ preservation by sparing salivary glands, mandible, and spinal cord while escalating dose to tumours.

Adaptive RT: Accounts for tumour shrinkage and weight loss during treatment.

Concurrent Chemo radiation: Standard for locally advanced disease.

SRS: Used in recurrent or small skull-base tumors.[8]

- **Prostate Cancer**

Brachytherapy: Low-dose rate (LDR) seed implantation or high-dose rate (HDR) catheters are effective for localized disease.

External Beam + Brachytherapy Boost: Improves biochemical control in high-risk cases.

Proton Therapy: Offers diametric advantages with reduced rectal and bladder toxicity.

[1] Brain Tumours

Stereotactic Radiosurgery (SRS): Single-session, high-dose treatment for brain metastases, arteriovenous malformations, and small benign tumours (meningiomas, acoustic neuromas).

Glioblastoma Multiform (GBM): Standard of care involves maximal safe resection followed by concurrent chemoradiation (Stupp protocol).

Proton Therapy: Beneficial for paediatric CNS tumours to minimize neurocognitive decline.

Cervical Cancer: Intracavitary brachytherapy remains a cornerstone, combined with external beam RT and chemotherapy.

Endometrial Cancer: Vaginal cuff brachytherapy post-hysterectomy in selected patients.

Ovarian Cancer: Palliative RT for localized recurrence or symptom relief.

Other Notable Applications

Pediatric Cancers: Proton therapy is increasingly favoured to reduce late toxicities (growth impairment, secondary malignancies).

Palliative RT: Short hypofractionated schedules (e.g., 8 Gy × 1) effectively relieve pain from bone metastases, spinal cord compression, or brain metastases.

Hematologic Malignancies: Total Body Irradiation (TBI) used as conditioning before stem cell transplantation.[22]

5. LIMITATIONS AND SIDE EFFECTS

Despite its central role in modern oncology, radiation therapy (RT) is associated with biological, technical, and clinical limitations that can affect treatment outcomes and patient quality of life. These drawbacks stem from both the intrinsic properties of tumors and the unavoidable effects of ionizing radiation on surrounding healthy tissues.[23]

5.1 Acute Effects

Acute toxicities typically manifest during or shortly after RT due to radiation-induced inflammation and damage to rapidly dividing normal cells.

1) Skin Reactions: Erythema, desquamation, hyperpigmentation ("radiation dermatitis").

2) Mucositis: Painful ulceration and inflammation of oral or gastrointestinal mucosa, especially in head & neck and pelvic irradiation.[17]

3) Nausea & Vomiting: Common with abdominal or cranial irradiation due to stimulation of the chemoreceptor trigger zone.

4) Fatigue: One of the most frequent but poorly understood side effects, likely multifactorial (metabolic, inflammatory, psychological).

5) Bone Marrow Suppression: When large bone marrow reservoirs (pelvis, sternum, vertebrae) are irradiated.[24]

5.2 Late Effects

Chronic toxicities may appear months to years after treatment, often irreversible and progressive.

1) Fibrosis: Replacement of normal tissue with scar-like fibrotic tissue, leading to stiffness and functional impairment (e.g., pulmonary fibrosis).

2) Radiation Necrosis: Localized tissue death, particularly in the brain or liver, due to vascular damage and impaired healing.

3) Lymphedema: Swelling due to lymphatic obstruction, especially after breast or pelvic RT.

4) Neurocognitive Decline: Observed in patients receiving cranial irradiation, particularly in children.

5) Secondary Malignancies: Ionizing radiation can induce DNA mutations, predisposing patients to sarcomas, leukaemias, or carcinomas years after exposure [25]

5.3 Biological and Clinical Challenges

1) Tumor Hypoxia: Hypoxic tumor cells are up to 2–3 times more resistant to radiation than well-oxygenated cells. This remains a major barrier to achieving complete tumour control.

2) Radioresistance: Certain cancers (e.g., melanoma, glioblastoma, sarcomas) exhibit intrinsic resistance due to enhanced DNA repair pathways and tumor microenvironment factors.

3) Dose-Limiting Toxicity: Normal tissue tolerance restricts escalation of tumor dose, particularly in radiosensitive organs (e.g., spinal cord, lungs, kidneys, and bowel).

4) Heterogeneity in Response: Variations in tumour biology, genetic mutations, and immune status affect individual outcomes.

5) Technical Constraints: Limited access to advanced modalities (proton/carbon ion therapy, MR-Linacs) due to high cost and infrastructure requirements.[26]

5.4 Strategies to Overcome Limitations

1) Radio protectors: Agents like amifostine to protect normal tissues.

2) Hypoxia Modifiers: Hyperbaric oxygen therapy, hypoxic cell radiosensitizers, and bioreductive drugs.

3) Combined Modality Therapy: Integration with chemotherapy, immunotherapy, and targeted agents to enhance radiosensitivity.[12]

4) Adaptive RT & Image Guidance: Adjusting plans during treatment to minimize toxicity.

5) Genomic & Biomarker-Guided RT: Personalized dose prescriptions based on tumor radiosensitivity signatures (radiogenomics).

6. RECENT ADVANCES AND FUTURE DIRECTIONS

The landscape of radiation oncology is rapidly evolving, driven by breakthroughs in imaging, biology, physics, and computational sciences. These advances aim to maximize tumour control, minimize toxicity, and move toward personalized cancer care.

6.1 Adaptive Radiation Therapy (ART)

ART involves **modifying the treatment plan in real-time** based on anatomical or biological changes observed during therapy.

Tools: Cone-beam CT, MRI-guided RT, and deformable image registration.

Benefits: Accounts for tumour shrinkage, patient weight loss, organ motion (e.g., bladder, lung), and improves precision.

Example: Adaptive replanning in bladder and lung cancers has demonstrated reduced normal tissue doses and improved outcomes.

6.2 Radiogenomics and Biomarker-Based Personalization

Radiogenomics explores the link between genetic profiles and radiosensitivity**. Goal:** Predict which patients are more likely to benefit from RT or experience severe toxicity.[27]

Examples:

Fig. 1. **ATM, BRCA1/2 mutations** – increased radiosensitivity.

Fig. 2. **Hypoxia gene signatures** – resistance prediction.

Future: Tailored dose prescriptions and integration with precision oncology.

6.3 Combination Therapies

RT is increasingly combined with systemic therapies to exploit biological synergy:

Radio-immunotherapy: RT induces immunogenic cell death, enhancing immune checkpoint inhibitors (e.g., anti-PD-1, anti-CTLA-4).

RT + Targeted Agents: EGFR inhibitors (cetuximab), PARP inhibitors, and DNA-PK inhibitors can sensitize tumours.

RT + Chemotherapy: Remains standard in many cancers (e.g., concurrent chemo radiation in cervical and head & neck cancers).[29]

Challenge: Balancing enhanced efficacy with increased toxicity.

6.4 Artificial Intelligence (AI) and Machine Learning

AI applications in RT are transforming workflow:

Auto-segmentation of tumours and organs at risk.

Automated treatment planning with dose optimization.

Toxicity prediction models for personalized care.

Deep learning algorithms also support radionics – extracting quantitative features from medical images to correlate with outcomes.

Future: Fully autonomous treatment planning and real-time decision support.

6.5 Nanotechnology and Radio sensitizers

Nanoparticles act as radio sensitizers by enhancing radiation dose deposition within tumours while sparing normal tissues.[28]

Examples:

Gold nanoparticles (AuNPs) – increase local dose absorption.

Liposomal carriers – targeted delivery of radio sensitizers/chemotherapy.

Emerging approaches: Smart Nano carriers triggered by tumour microenvironment conditions (pH, hypoxia).

Clinical promise: Overcome hypoxia-related resistance and improve tumour specificity.

6.6 Other Emerging Directions

FLASH Radiotherapy: Ultra-high dose rates (>40 Gy/s) show reduced normal tissue toxicity while maintaining tumour control.

Theranostics: Combination of imaging and therapy using radiopharmaceuticals (e.g., Lutetium-177 DOTATATE, Actinium-225 conjugates).

MR-Linac Technology: Real-time MRI imaging integrated with RT delivery for superior soft-tissue visualization.[30]

7. CONCLUSION

Radiation therapy continues to be an indispensable modality in the multidisciplinary management of cancer, contributing significantly to both curative and palliative outcomes. Over the past decades, innovations in imaging, treatment planning, and delivery have markedly enhanced its precision, thereby reducing toxicity and improving tumor control. Despite challenges such as tumor hypoxia, radioresistance, and treatment-related side effects, ongoing research is addressing these limitations through advanced technologies and biological insights. The integration of molecular biology, radiogenomics, nanotechnology, and artificial intelligence is ushering in a new era of personalized radiation oncology. Combination strategies with immunotherapy and targeted agents further expand its therapeutic potential, transforming RT into a dynamic and adaptable treatment platform. Looking ahead, future directions such as adaptive radiotherapy, FLASH RT, MR-Linac systems, and theranostic radiopharmaceuticals are expected to redefine the landscape of cancer treatment. Ultimately, radiation therapy stands at the forefront of innovation in oncology, with the promise not only to improve patient survival but also to enhance quality of life, moving closer toward the goal of precision, safety, and long-term survivorship in cancer care.

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