

Radiation Oncology Radiobiology

Detailed High-Yield Reference | ABR Core Exam Prep

This reference expands each core radiobiology concept with the governing formula or model, key variables, clinical application, a worked example, and a high-yield pitfall, organized by topic area.

DNA Damage, Repair, and Cell Death

DNA Damage Types and Repair Pathways

Formula / Concept	Radiation induces single-strand breaks, double-strand breaks (DSBs), base damage, and DNA-protein crosslinks; DSBs are the most biologically critical lesion. Repair occurs via non-homologous end joining (NHEJ, active throughout the cell cycle, error-prone) or homologous recombination (HR, restricted to S/G2 phase, high-fidelity).
Key Variables	Lesion type; repair pathway; cell cycle phase at the time of damage.
Clinical Application	Explains why cells in S/G2 phase, with a sister chromatid available for HR, can repair DSBs more accurately than cells relying on NHEJ, contributing to cell-cycle-dependent radiosensitivity.
Worked Example	A cell irradiated in G1 phase relies predominantly on NHEJ to repair a double-strand break, an error-prone process that can leave small deletions or translocations, whereas the same lesion occurring in S/G2 phase can be repaired with higher fidelity via homologous recombination using the sister chromatid as a template.
High-Yield Pitfall	NHEJ, not HR, is the dominant repair pathway in G1 phase and throughout most of the cell cycle in mammalian cells — HR is restricted to S/G2 phase because it requires a sister chromatid template.

Modes of Radiation-Induced Cell Death

Formula / Concept	Mitotic catastrophe (death during or after a failed attempt at mitosis with unrepaired damage) is the dominant mode of radiation-induced death in most solid tumors; apoptosis predominates in certain radiosensitive tissues (lymphocytes, spermatogonia); necrosis and senescence are additional pathways, particularly at high doses per fraction.
Key Variables	Tissue/cell type; dose per fraction; p53 status.
Clinical Application	Explains why lymphoid malignancies and normal lymphocytes are exquisitely radiosensitive at low doses, while many solid tumor cell types must pass through mitosis before dying, contributing to the delayed clinical response often seen with fractionated radiotherapy of solid tumors.
Worked Example	A lymphoma cell undergoes rapid apoptosis within hours of a modest radiation dose, while an epithelial carcinoma cell exposed to a similar dose may continue to appear viable for days until it attempts and fails mitosis, illustrating why radiographic tumor shrinkage in epithelial tumors often lags behind treatment delivery.
High-Yield Pitfall	Apparent radioresistance on early post-treatment imaging does not necessarily indicate treatment failure — many solid tumors die via the delayed process of mitotic catastrophe rather than rapid apoptosis.

Cell Cycle Radiosensitivity

Formula / Concept	Radiosensitivity varies through the cell cycle: G2/M phase is generally most radiosensitive, late S phase is generally most radioresistant, and G1 is intermediate.
Key Variables	Cell cycle phase; presence of a G2/M checkpoint arrest after irradiation.
Clinical Application	Provides part of the radiobiological rationale for fractionation (the redistribution 'R'), since cells surviving one fraction and progressing into more sensitive phases become more susceptible to subsequent fractions.
Worked Example	A population of asynchronously cycling tumor cells irradiated with a single fraction shows relative sparing of cells that happened to be in late S phase at that moment; as those cells progress into G2/M before the next fraction, they become more susceptible, illustrating the redistribution effect central to fractionated treatment.
High-Yield Pitfall	Cell-cycle-dependent radiosensitivity differences are most relevant to rapidly cycling cell populations — they are far less relevant to slowly proliferating or quiescent late-responding tissues, where repair-based mechanisms dominate the response to fractionation.

Cell Survival Models

Linear-Quadratic (LQ) Model

Formula / Concept	$SF = e^{-(\alpha D + \beta D^2)}$
Key Variables	α = linear component of cell killing; β = quadratic component of cell killing; D = absorbed dose for the irradiation under consideration. In fractionated-regimen equations, d usually denotes dose per fraction.
Clinical Application	The standard framework for comparing different fractionation schedules and calculating biologically effective dose.
Worked Example	At low doses per fraction, the linear (αD) term dominates cell killing, while at higher doses per fraction the quadratic (βD^2) term becomes proportionally more significant — part of the radiobiological rationale for why hypofractionated regimens produce a different balance of tumor versus normal tissue effect than conventional fractionation.
High-Yield Pitfall	The LQ model is generally considered most accurate in the conventional dose-per-fraction range (roughly up to 6-10 Gy per fraction); its accuracy at the very high doses per fraction used in some SBRT/SRS regimens is debated, and alternative models have been proposed for that regime.

Alpha/Beta Ratio

Formula / Concept	The dose at which the linear and quadratic components of cell killing contribute equally.
Key Variables	Low α/β (approximately 3 Gy) characterizes late-responding normal tissue; high α/β (approximately 10 Gy) characterizes acutely responding tissue and most tumors.
Clinical Application	Central to fractionation decisions — tissues or tumors with a low α/β ratio are relatively more sensitive to changes in dose per fraction, part of the rationale for hypofractionation in tumors with an unusually low α/β ratio.
Worked Example	Prostate cancer is thought to have an unusually low α/β ratio, closer to that of late-responding normal tissue than typical tumors, which is part of the radiobiological rationale for using moderately hypofractionated or extreme hypofractionation (SBRT) regimens in prostate cancer.
High-Yield Pitfall	Not all tumors have α/β near 10 Gy. Prostate cancer is the clearest, most clinically important example of a tumor with a relatively low estimated α/β ratio; low values have also been reported for selected other tumor types, though estimates vary considerably by histology, dataset, and endpoint.

Surviving Fraction at 2 Gy (SF2)

Formula / Concept	The surviving fraction predicted by the LQ model at D = 2 Gy.
Key Variables	Cellular α and β values.
Clinical Application	Used experimentally as a benchmark of intrinsic cellular radiosensitivity, and historically explored as a potential predictive assay for individual patient or tumor radiosensitivity, though not routinely used in standard clinical practice.
Worked Example	Two tumor cell lines exposed to the same 2 Gy dose might show very different surviving fractions if their intrinsic radiosensitivity differs, illustrating how SF2 has been explored as a laboratory correlate of clinical radioresponsiveness.
High-Yield Pitfall	SF2 and similar in vitro clonogenic radiosensitivity assays have not been established as reliable, routinely used predictive tools for individualizing patient treatment in standard clinical practice, despite ongoing research interest.

Single-Hit Multi-Target Model

Formula / Concept	$SF = 1 - (1 - e^{-D/D_0})^n$
Key Variables	D_0 = dose to reduce survival to 37% on the exponential portion of the curve; n = extrapolation number, reflecting the width of the initial shoulder.
Clinical Application	A historically important model preceding the linear-quadratic model; the 'shoulder' on a cell survival curve reflects accumulation and repair of sublethal damage at low doses.
Worked Example	A survival curve with a wide initial shoulder (large n) suggests a greater capacity to accumulate and repair sublethal damage before cell killing dominates, a concept that helped establish the biological rationale for fractionation before the LQ model became the dominant framework.
High-Yield Pitfall	The multi-target model does not accurately describe the low-dose region of the cell survival curve as well as the linear-quadratic model does, a major reason the LQ model has largely superseded it in modern clinical and research use.

BED and Fractionation

Biologically Effective Dose (BED)

Formula / Concept	$BED = nd [1 + d/(\alpha/\beta)]$
Key Variables	n = number of fractions; d = dose per fraction.
Clinical Application	Allows comparison of the biological effect of different fractionation schedules on a common scale, essential when converting between conventional and hypofractionated/SBRT regimens.
Worked Example	A hypofractionated regimen and a conventionally fractionated regimen delivering very different total physical doses can be shown to have a similar (or different) biological effect once converted to BED, which is why BED, not total physical dose alone, is used to compare across differing fractionation schemes.
High-Yield Pitfall	Basic BED calculations assume complete repair between fractions and do not inherently account for overall treatment time or repopulation unless a specific time-correction term is added, which can lead to inaccurate comparisons for regimens with substantially different overall treatment durations.

EQD2 (Equivalent Dose in 2 Gy Fractions)

Formula / Concept	$EQD2 = D \times [(d + \alpha/\beta) / (2 + \alpha/\beta)]$
Key Variables	D = total dose; d = dose per fraction; α/β = tissue-specific ratio.
Clinical Application	Used clinically, especially in brachytherapy planning (such as cervical cancer), to sum doses from different fractionation schemes (external beam plus brachytherapy) on a common, clinically intuitive 2 Gy-equivalent scale.
Worked Example	In cervical cancer treatment combining external beam radiation with brachytherapy, EQD2 is used to sum the biological effect of both components onto a single combined scale, allowing clinicians to compare cumulative dose against normal tissue tolerance limits, which are also typically expressed in EQD2 terms.
High-Yield Pitfall	EQD2 conversions depend heavily on the assumed α/β ratio for the tissue in question — using a tumor's α/β ratio when the calculation should reflect late-responding normal tissue (or vice versa) produces a clinically misleading result.

Time-Corrected BED and Accelerated Repopulation

Formula / Concept	$BED = nd[1 + d/(\alpha/\beta)] - (\ln 2/\alpha \times T_p) \times (T - T_k)$
Key Variables	T_k = kickoff time when repopulation begins to accelerate; T_p = potential doubling time; T = overall treatment time.
Clinical Application	Explains why unplanned treatment breaks or prolonged overall treatment time can reduce local control in rapidly proliferating tumors, such as head and neck squamous cell carcinoma.
Worked Example	A head and neck cancer patient whose treatment course is prolonged by unplanned breaks beyond the typical kickoff time may experience accelerated tumor repopulation that reduces the effective biological dose delivered, a major reason minimizing treatment breaks is emphasized clinically in rapidly proliferating tumors.
High-Yield Pitfall	Not all tumors exhibit clinically significant accelerated repopulation within a typical treatment course — the time-correction factor is most relevant for rapidly proliferating tumors such as head and neck squamous cell carcinoma, and less relevant for slower-growing tumor types.

Half-Life of Sublethal Damage Repair

Formula / Concept	Repair half-times are tissue-dependent and commonly on the order of roughly 0.5-4 hours, although repair may involve multiple kinetic components.
Key Variables	Tissue-specific repair kinetics; interfraction interval.
Clinical Application	Relevant to determining the minimum safe interfraction interval, particularly for regimens delivering more than one fraction per day, such as hyperfractionation or some HDR brachytherapy schedules.
Worked Example	An interfraction interval of about 6 hours is commonly used for twice-daily external-beam schedules to permit substantial normal-tissue repair, though this is a practical convention rather than a value derived from a single universal repair half-time.
High-Yield Pitfall	Six hours is a practical convention, not a universal biological threshold — repair kinetics can be biexponential, and some late-responding tissues have slower repair components. Incomplete repair increases biological effect, especially in late-responding tissues.

The Four (Five) Rs of Radiobiology

R	Concept	Clinical Relevance
Repair	Sublethal damage repair between fractions	Basis for allowing adequate interfraction interval; spares late-responding normal tissue.
Repopulation	Surviving clonogens proliferate during treatment	Rationale for avoiding unplanned treatment breaks and for accelerated fractionation in some tumors.
Redistribution	Cells move through the cell cycle into more radiosensitive phases	Fractionation reassorts surviving cells, increasing the sensitivity of subsequent fractions.
Reoxygenation	Previously hypoxic tumor cells may become better oxygenated between fractions because of changes in tumor perfusion, oxygen consumption, and tumor regression	Improves radiosensitivity of previously hypoxic clonogens over the treatment course.
Intrinsic Radiosensitivity	Inherent cell/tissue sensitivity (the 5th R)	Varies by histology and underlying molecular/genetic factors.

Oxygen Effect, LET, and RBE

Oxygen Enhancement Ratio (OER)

Formula / Concept	$OER = \text{Dose (hypoxic)} / \text{Dose (aerobic)}$ for the same biological effect.
Key Variables	For low-LET radiation such as x-rays and gamma rays, OER is typically about 2.5-3 at doses in the conventional experimental range; OER can be dose-dependent and tends to decrease at very low doses.
Clinical Application	Explains why hypoxic tumor regions are relatively radioresistant, part of the rationale for strategies such as hyperthermia, hypoxic cell sensitizers, or altered fractionation aimed at improving outcomes in hypoxic tumors.
Worked Example	A hypoxic region within a bulky tumor requires a higher physical radiation dose to achieve the same cell killing as a well-oxygenated region, illustrating why tumor hypoxia is considered an adverse prognostic and radioresistance factor.
High-Yield Pitfall	The oxygen effect is most pronounced across conventional therapeutic dose ranges and diminishes at very low doses — an important nuance when considering the relevance of hypoxia across different fractionation and dose regimens.

Relative Biologic Effectiveness (RBE)

Formula / Concept	$RBE = \text{Dose (reference radiation)} / \text{Dose (test radiation)}$ for the same biological effect.
Key Variables	Reference is typically 250 kVp x-rays or Co-60; RBE varies by radiation type, dose per fraction, and endpoint studied.
Clinical Application	Used to convert physical dose delivered by non-photon modalities (protons, neutrons, heavy ions) into a photon-equivalent biological dose for prescribing and comparing treatment plans.
Worked Example	A given physical dose of neutron radiation produces substantially more biological damage than the same physical dose of photon radiation, reflected in a much higher RBE for neutrons compared with the RBE of approximately 1.1 conventionally used for protons.
High-Yield Pitfall	RBE is not a fixed constant for a given radiation type — it varies with dose per fraction, tissue/endpoint studied, and position within the beam (such as the distal Bragg peak edge in particle therapy), so a single RBE value is always a simplification.

Linear Energy Transfer (LET)

Formula / Concept	Energy deposited by ionizing radiation per unit path length traveled through tissue.
Key Variables	Higher LET produces denser, more clustered ionization; RBE generally increases with LET up to an optimal point.
Clinical Application	Higher LET radiation produces more densely clustered ionization tracks that are more difficult for cells to repair, contributing to higher RBE up to an optimal LET, beyond which 'overkill' reduces additional benefit.
Worked Example	Carbon ion therapy exploits higher LET, particularly within the Bragg peak, to produce densely ionizing tracks that are less dependent on oxygen for their damaging effect, part of the rationale for considering heavy ion therapy in relatively hypoxic or radioresistant tumors.
High-Yield Pitfall	RBE does not increase indefinitely with LET — beyond an optimal LET, 'overkill' occurs, where additional ionization density is delivered to cells that are already lethally damaged, providing no further biological benefit relative to the physical dose delivered.

Dose-Response Modeling

Tumor Control Probability (TCP)

Formula / Concept	A sigmoidal dose-response curve, often modeled with a Poisson or logistic function, describing the probability of eradicating all clonogens at a given dose.
Key Variables	Clonogen number; intrinsic radiosensitivity; hypoxic fraction; curve steepness.
Clinical Application	Used conceptually to understand why dose escalation can improve tumor control up to a point of diminishing returns, and why tumor heterogeneity (in radiosensitivity, hypoxia, or clonogen number) affects the steepness of the dose-response curve.
Worked Example	A tumor with a larger clonogen burden generally requires a higher dose to achieve the same TCP, shifting the dose-response curve toward higher dose rather than making it inherently flatter. Heterogeneity in radiosensitivity, hypoxia, clonogen number, and other biologic factors across a tumor population is what tends to broaden and reduce the apparent steepness of the clinical TCP curve.
High-Yield Pitfall	More clonogens do not inherently mean a flatter TCP curve — clonogen burden primarily shifts the required dose higher; population heterogeneity in radiosensitivity, hypoxia, and clonogen number is the major determinant of population dose-response slope, and TCP models describe population-level probabilities, not certainties for any individual patient.

Normal Tissue Complication Probability (NTCP)

Formula / Concept	A sigmoidal dose-response curve, often modeled with the Lyman-Kutcher-Burman (LKB) model, describing the probability of a defined complication at a given dose and volume.
Key Variables	Dose; irradiated volume; organ-specific parameters (steepness, tolerance dose).
Clinical Application	The LKB model and its variants incorporate not just dose but also irradiated volume, allowing clinicians to estimate complication risk for a specific treatment plan and compare competing plans.
Worked Example	Two treatment plans delivering the same maximum dose to an organ at risk can have different estimated NTCP values if they irradiate different volumes of that organ, illustrating why volume, not dose alone, matters in NTCP estimation for parallel organs.
High-Yield Pitfall	NTCP models are generally derived from and most validated for specific endpoints (such as a defined grade of pneumonitis or a specific radiographic finding) — applying an NTCP model outside the endpoint or dataset it was derived from can produce misleading risk estimates.

Therapeutic Ratio and Therapeutic Window

Formula / Concept	The separation between the TCP and NTCP dose-response curves; a wider separation reflects a more favorable relationship between the probability of tumor control and the probability of normal-tissue complication.
Key Variables	Relative position and steepness of the TCP and NTCP curves.
Clinical Application	The central organizing concept behind virtually all technique, fractionation, and dose-escalation decisions in radiation oncology, since the goal of most treatment changes is to widen, or at minimum preserve, this ratio.
Worked Example	A more conformal treatment technique that reduces dose to surrounding normal tissue while maintaining tumor dose widens the therapeutic ratio without requiring any change in the intrinsic biological radiosensitivity of either the tumor or the normal tissue.
High-Yield Pitfall	A wider separation between TCP and NTCP curves on a graph does not by itself guarantee clinical success in an individual patient — population-level dose-response curves describe probabilities, not certainties, for any single patient.

Normal Tissue Architecture and Tolerance

Parallel vs. Serial Organ Architecture

Formula / Concept	Serial organs (such as spinal cord) behave like a chain, where damage to any single functional subunit can cause organ-level complication, making maximum point dose the most relevant metric; parallel organs (such as lung, liver, kidney) are composed of many independently functioning subunits, making irradiated volume (mean dose or V_x) more relevant than any single point dose.
Key Variables	Functional subunit organization (serial vs. parallel); organ-specific tolerance data (historical Emami data, updated by QUANTEC guidelines).
Clinical Application	Explains why spinal cord constraints are expressed as a maximum point dose, while lung constraints are expressed as a mean dose or percent volume receiving a threshold dose (such as V20).
Worked Example	A small, high-dose hot spot within the spinal cord carries a very different risk implication than a similarly sized hot spot within the lung, since the spinal cord's serial architecture means even a small segment of severe damage can cause a clinically significant deficit, while the lung's parallel architecture can tolerate a small region of high dose without necessarily causing clinically apparent dysfunction.
High-Yield Pitfall	Serial-versus-parallel is a useful teaching model, not an absolute dichotomy — even serial organs are generally best characterized by near-maximum dose to a small volume rather than a literal mathematical point dose, and many organs have mixed architecture. Use clinically validated DVH constraints rather than assuming every serial organ is governed by a single point dose.

Particle Therapy Radiobiology

RBE in Proton and Heavy Ion Therapy

Formula / Concept	Clinical proton therapy conventionally assumes an RBE of 1.1 relative to photons across most of the treatment field. Actual proton RBE is variable and tends to increase as LET rises toward the distal edge and distal fall-off of the Bragg peak; heavier ions (such as carbon) have substantially higher and more spatially variable RBE due to increased LET.
Key Variables	LET; position within the Bragg peak (proximal, plateau, distal edge); particle type.
Clinical Application	The generic proton RBE of 1.1 is used clinically to convert physical proton dose to a biologically weighted dose (Gy(RBE)), though the assumption of a constant RBE is a simplification that may underestimate biological effect near the distal fall-off, relevant to critical structure sparing at the beam's distal edge.
Worked Example	A critical structure near the distal end of a proton beam, where LET rises toward the distal edge and distal fall-off just before the particles stop, may experience a greater biological effect than the conventionally assumed 1.1 RBE model predicts, meaning normal tissue immediately beyond the intended target may receive a somewhat higher biological dose than the physical dose alone would suggest.
High-Yield Pitfall	The clinical 1.1 proton RBE is a pragmatic constant, not a universal biological value — actual RBE varies with LET, dose, tissue, and endpoint, and generally rises toward the distal edge and distal fall-off of the Bragg peak; variable-RBE models remain an active area of research.

Combined Modality and Special Topics

Chemoradiation Synergy

Formula / Concept	Concurrent chemoradiation can act through direct radiosensitization (inhibiting DNA repair or cell cycle checkpoints), spatial cooperation (treating micrometastatic disease outside the radiation field), or independent additive cytotoxicity.
Key Variables	Drug mechanism (radiosensitizer versus independently cytotoxic agent); sequencing (concurrent versus sequential).
Clinical Application	Explains why concurrent, rather than sequential, chemoradiation generally produces superior local control in many disease sites, at the cost of increased acute toxicity.
Worked Example	Cisplatin given concurrently with radiation in head and neck cancer is thought to act partly as a radiosensitizer by interfering with DNA repair processes, contributing to improved local control compared with radiation alone, though at the cost of increased acute mucosal and hematologic toxicity.
High-Yield Pitfall	Not all chemotherapy agents used in combination with radiation act as true radiosensitizers — some contribute primarily through independent cytotoxicity or treatment of micrometastatic disease outside the radiation field (spatial cooperation), a distinction relevant to understanding why certain combinations are chosen for certain clinical scenarios.

Retreatment and Reirradiation

Formula / Concept	Cumulative BED or EQD2 from an initial course and a reirradiation course can be estimated by summing the contributions from each course. Clinical interpretation may also incorporate an assumed degree of time-dependent tissue recovery, but no universally validated recovery correction exists for most normal tissues.
Key Variables	Time interval since initial treatment; tissue-specific recovery, which is generally assumed rather than precisely known for most tissues; cumulative BED.
Clinical Application	Guides clinical decision-making about the feasibility and dose limits of reirradiation, particularly for serial organs like the spinal cord, where the consequences of cumulative damage are severe.
Worked Example	For spinal-cord reirradiation years after an initial course, clinicians may consider evidence of partial time-dependent recovery, but additional dose is selected conservatively because the magnitude and timing of that recovery remain uncertain.
High-Yield Pitfall	Do not assume complete recovery or apply a universal percentage recovery — reirradiation constraints are tissue-, interval-, endpoint-, and technique-dependent, and no universally validated recovery correction exists for most normal tissues.

Second Malignancy Risk

Formula / Concept	At low doses, radiation-induced cancer risk is often approximated using a linear-no-threshold model for radiation-protection purposes. At the much higher and heterogeneous doses encountered in radiotherapy, second-malignancy risk is more complex and depends on dose, fractionation, irradiated volume, age at exposure, tissue type, and genetic susceptibility.
Key Variables	Dose; irradiated volume; age at exposure; underlying genetic syndromes (such as Li-Fraumeni or retinoblastoma gene carriers).
Clinical Application	Informs technique selection in pediatric and young adult patients, where minimizing integral dose and low-dose bath to normal tissue is prioritized given the long latency period and extended lifetime risk window.
Worked Example	For a pediatric CNS tumor, proton therapy can substantially reduce integral dose and dose beyond the target compared with many photon plans, potentially reducing estimated late second-malignancy risk, since protons substantially reduce (though do not entirely eliminate) the low-dose bath to surrounding normal tissue from range uncertainty, secondary particles, and beam arrangement.
High-Yield Pitfall	Second-cancer risk after radiotherapy cannot be described by one simple dose-response function across the full therapeutic dose range; models carry substantial uncertainty, and risk is a stochastic, latent effect that can take years to decades to manifest, particularly relevant in pediatric radiation oncology.

Pediatric Radiosensitivity

Formula / Concept	Growing tissues, particularly bone and growth plates, the developing brain, and certain endocrine organs, are more radiosensitive than their adult counterparts and are especially vulnerable to growth and developmental effects at doses with minimal consequence in a fully developed adult.
Key Variables	Age at treatment; developmental stage of the irradiated tissue; dose to growth plates or developing organs.
Clinical Application	Drives more conservative dose constraints and greater emphasis on minimizing integral dose to normal developing tissue in pediatric radiotherapy compared with adult protocols.
Worked Example	Radiation to a growth plate in a young child can cause asymmetric bone growth or growth arrest, a long-term effect that would not occur from a similar dose delivered to a skeletally mature adult, illustrating why pediatric treatment planning gives special consideration to growth plate location.
High-Yield Pitfall	Adult normal tissue tolerance doses cannot be directly extrapolated to pediatric patients — growing tissues have distinct radiosensitivity and late-effect profiles that require separate consideration in treatment planning.

Hyperthermia as a Radiosensitizer

Formula / Concept	Mild heating of tumor tissue, typically to the low 40s Celsius, enhances radiation effect through improved tumor oxygenation via increased blood flow, inhibition of DNA repair, and direct cytotoxicity to cells in radioresistant phases (such as S phase) or hypoxic regions.
Key Variables	Temperature achieved; duration of heating; timing relative to radiation delivery.
Clinical Application	Used as an adjunct to radiation in select clinical scenarios, such as recurrent chest wall disease or certain soft tissue sarcomas, where it can improve local control when added to radiation.
Worked Example	Hyperthermia delivered shortly before or after a radiation fraction to a chest wall recurrence can improve local tumor control compared with radiation alone, in part by transiently improving oxygenation in hypoxic tumor regions that would otherwise be relatively radioresistant.
High-Yield Pitfall	The radiosensitizing benefit of hyperthermia is time-dependent relative to the radiation fraction — heating given too far in advance of or after the radiation dose loses much of its synergistic effect, so timing and sequencing are clinically important.

Bystander Effect and Adaptive Response

Formula / Concept	The bystander effect describes biological effects (such as DNA damage or cell death) occurring in cells that were not directly irradiated but are in proximity to or communication with irradiated cells, mediated by signaling molecules; the adaptive response describes a phenomenon in which a very small priming dose can, in some experimental systems, reduce the biological effect of a subsequent larger dose.
Key Variables	Cell-to-cell communication/signaling; priming dose (for adaptive response); time interval between doses.
Clinical Application	These phenomena remain primarily research and radiobiology concepts, illustrating that radiation effects are not confined solely to directly traversed cells, with implications for understanding low-dose radiation risk models.
Worked Example	In laboratory experiments, unirradiated cells cultured in media transferred from irradiated cells can show DNA damage responses similar to directly irradiated cells, illustrating that soluble signaling factors can propagate radiation effects beyond the cells physically traversed by radiation.
High-Yield Pitfall	Bystander and adaptive response phenomena are well described in laboratory/experimental systems but remain of uncertain and debated clinical magnitude in human radiotherapy — they should not be assumed to have a defined, quantifiable clinical dose-modifying effect in routine practice.

This reference summarizes widely used field-standard radiobiology models for board review and is not a substitute for a full radiobiology text. © Hasan Murshed, MD, MS — drhasanmurshed.com