

ABR Radiation Oncology Study Guide:

Radiation and Cancer Biology

■ This exam tests your knowledge of the principles of cancer and radiation biology underlying the practice of radiation oncology. Included are questions on:

- basic cancer biology and the molecular biology of cancer
- the response to radiation at the subcellular and cellular levels
- the radiation responses of normal and malignant tissues
- radiation carcinogenesis
- hereditary effects as they relate to radiation protection

Categories for Cancer and Radiation Biology

■ Interaction of Radiation with Matter

- Definition of ionizing radiation and types
- Definition of LET and quality of radiation
- Generation of free radicals
- Direct and indirect action of radiation
- Role of oxygen

■ Molecular Mechanisms of DNA Damage

- Assays for DNA damage
- Neutral and alkaline elution, pulsed field electrophoresis, comet, plasmid-based assays
- Types of DNA lesions and numbers per cell/Gy
- Multiply damaged sites
- Single lethal hits and accumulated damage (inter- and intratrack)

■ Molecular Mechanisms of DNA Repair

- Types of repair
- Repair of base damage, single-strand and double-strand breaks
- Homologous recombination
- Nonhomologous end-joining

■ Chromosome and Chromatid Damage

- Assays
- Conventional and FISH
- Dose response relationships

- Use of peripheral blood lymphocytes in *in vivo* dosimetry
- Stable and unstable chromatid and chromosome aberrations
- Human genetic diseases that affect DNA repair, fragility, and radiosensitivity

■ Mechanisms of Cell Death

- Apoptotic death
 - Developmental and stress induced
 - Morphological and biochemical features of apoptosis
 - Molecular pathways leading to apoptosis
 - Radiation-induced apoptosis in normal tissues and tumors
- Necrotic death
 - Morphological, pathological, and biochemical features of necrosis
- Mitotic death following irradiation
 - Catastrophic vs apoptotic death
 - Cell division postradiation and time of clonogen death
- Radiation-induced senescence

■ Cell and Tissue Survival Assays

- In vitro clonogenic assays
 - Effects of dose, dose rate, cell type
- In vivo clonogenic assays
 - Bone marrow stem cell assays, jejunal crypt stem cell assay, skin clones, kidney tubules

■ Models of Cell Survival

- Random nature of cell killing and Poisson statistics
- Comparison of survival of viruses, bacteria, and eukaryotic cells after irradiation
- Single-hit, multitarget models of cell survival
- Two component models
- Linear quadratic model
- Calculations of cell survival with dose

■ Linear Energy Transfer

- RBE defined
- RBE as a function of LET
- Tissue type

■ Oxygen Effect

- Define OER
- Dose and dose per fraction effects

- OER vs LET
- Impact of O₂ concentration
- Time scale of oxygen effect
- Mechanisms of oxygen effect

■ Repair at the Cellular Level

- Sublethal damage repair
- Potentially lethal damage repair
- Half-time of repair
- Dose rate effects and repair
- Dose fractionation effects

■ Solid Tumor Assay Systems

- Experimental models
- TD50 limiting dilution assay
- Tumor regrowth assay
- TCD50 tumor control assay
- Lung colony assay
- In vitro / in vivo assay
- Spheroid systems

■ Tumor Microenvironment

- Tumor vasculature
- Angiogenesis
- Hypoxia in tumors
 - Measurement of hypoxia
 - Transient and chronic hypoxia
- Reoxygenation following irradiation
- Relevance of hypoxia in radiation therapy
- Hypoxia as a factor in tumor progression
- Hypoxia-induced signal transduction
- Cellular composition of tumors

■ Cell and Tissue Kinetics

- Cell cycle
- Measurement of cell cycle parameters by 3H-thymidine
- Measurement by flow cytometry, DNA staining and BrdU
- Cell cycle synchronization techniques and uses
- Effect of cell cycle phase on radiosensitivity
- Cell cycle arrest and redistribution following irradiation

- Cell cycle checkpoints, cyclins, cyclin dependent kinase inhibitors
- Tissue kinetics
 - Growth fraction
 - Cell loss factor
 - Volume doubling times
 - Tpot
- Growth kinetics of clinical and experimental tumors

■ Molecular Signaling

- Receptor/ligand interactions
- Phosphorylation/dephosphorylation reactions
- Transcriptional activation
- Gene expression profiling and radiation-induced gene expression
- Radiation-induced signals
 - DNA damage response
 - Non-DNA damage response
- Cell survival and death pathways

■ Cancer

- Cancer as a genetic disease
- Oncogenes
- Tumor suppressor genes
- Telomeric changes in cancer
- Epigenetic changes in cancer (e.g., hypermethylation)
- Multistep nature of carcinogenesis
- Molecular profiling of cancer
- Signaling abnormalities in carcinogenesis
- Effects of signaling abnormalities on radiation responses
- Prognostic and therapeutic significance of tumor characteristics

■ Total Body Irradiation

- Prodromal radiation syndrome
- Cerebrovascular syndrome
- Gastrointestinal syndrome
- Hematopoietic syndrome
- Mean lethal dose and dose/time responses
- Immunological effects
- Assessment and treatment of radiation accidents
- Bone marrow transplantation

■ Clinically Relevant Normal Tissue Responses to Radiation

- Responses in skin, oral mucosa, oropharyngeal and esophageal mucous membranes, salivary glands, bone marrow, lymphoid tissue bone and cartilage, lung, kidney, testis, eye, central and peripheral nervous tissues

■ Mechanisms of Normal Tissue Radiation Responses

- Molecular and cellular responses in slowly and rapidly proliferating tissues
 - Cytokines and growth factors
 - Regeneration
 - Remembered dose
 - Functional subunits
- Mechanisms underlying clinical symptoms
 - Latency
 - Inflammatory changes
 - Cell killing
 - Radiation fibrosis
 - Volume effects
- Scoring systems for tissue injury
 - LENT and SOMA

■ Therapeutic Ratio

- Tumor control probability (TCP) curves
 - Calculation of TCP
 - Factors affecting shape and slope of TCP curves
 - Influence of tumor repopulation/regeneration on TCP
- Normal tissue complication probability (NTCP) curves
 - Influence of normal tissue regeneration on responses
 - Response of subclinical disease
 - Causes of treatment failure
 - Factors determining tissue tolerance
 - Normal tissue volume effects
 - Dose-volume histogram analysis
- Effect of adjuvant or combined treatments on therapeutic rationals

■ Time, Dose, Fractionation

- The 4 R's of fractionation
- The radiobiological rationale behind dose fractionation
- The effect of tissue type on the response to dose fractionation
- Effect of tissue/tumor types on a/b ratios
- Quantitation of multifraction survival cures

- BED and isoeffect dose calculations

■ Brachytherapy

- Dose rate effects (HDR and LDR)
- Choice of isotopes
- Interstitial and intracavitary use
- Radiolabeled antibodies

■ Radiobiological aspects of alternative dose delivery systems

- Protons, high LET sources, BNCT
- Stereotactic radiosurgery/radiotherapy, IMRT, IORT
- Dose distributions and dose heterogeneity

■ Chemotherapeutic agents and radiation therapy

- Classes of agents
- Mechanisms of action
- The oxygen effect for chemotherapy
- Multiple drug resistance
- Interactions of chemotherapeutic agents with radiation therapy
- Photodynamic therapy
- Gene therapy

■ Radiosensitizers, Bioreductive Drugs, Radioprotectors

- Tumor radiosensitization
 - Halogenated pyrimidines, nitroimidazoles
- Hypoxic cell cytotoxins
 - Tirapazamine
- Normal tissue radioprotection
 - Mechanisms of action, sulfhydryl compounds, WR series, dose reduction factor (DRF)
- Biological response modifiers

■ Hyperthermia

- Cellular response to heat
- Heat shock proteins
- Thermotolerance
- Response of tumors and normal tissues to heat
- Combination with radiation therapy

■ Radiation Carcinogenesis

- Initiation, promotion, progression
- Dose response for radiation-induced cancers
- Importance of age at exposure and time since exposure
- Malignancies in prenatally exposed children
- Second tumors in radiation therapy patients
- Effects of chemotherapy on incidence
- Risk estimates in humans
- Calculations based on risk estimates

■ Heritable Effects of Radiation

- Single gene mutation
- Chromosome aberrations
- Relative vs absolute mutation risk
- Doubling dose
- Heritable effects in humans
- Risk estimates for hereditary effects

■ Radiation Effects in the Developing Embryo

- Intrauterine death
- Congenital abnormalities and neonatal death
- Microcephaly, mental retardation
- Growth retardation
- Dose, dose rate, and stage in gestation
- Human experience of pregnant women exposed to therapeutic dose

■ Radiation Protection

- General philosophy
- Stochastic and deterministic effects
- Relative weighting factors
- Equivalent dose-tissue weighting factor
- Effective dose, committed dose
- Collective exposure dose
- Dose limits for occupational and public exposure
- ICRP and NCRP