

## FC Rad Onc (SA) Part I - Radiobiology & Cancer Biology

| TOPIC                               | KNOWLEDGE UNIT  |   |  |   |   |  |   |
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| <b>Questions 1 and 2 (50%)</b>      |   |   |  |   |   |  |   |
| <b>Radiation interaction</b>        | Radiation interaction with matter, direct/indirect effects, free radicals, interaction with H <sub>2</sub> O [Hall Chapt. 1]  | DNA critical target, evidence, types of DNA damage [Hall Chapt. 2&3]  |  | Chromosomal aberrations, molecular markers of damage, cell lethality [Hall Chapt. 2]  |   | Cellular damage response – repair [Hall Chapt. 5], cycle arrest [Hall Chapt. 22], apoptosis [Hall Chapt. 3, 18], radiation-induced signal transduction/early response genes [Hall Chapt. 18] |   |
| <b>Radiosensitivity</b>             | Factors determining inherent radiosensitivity, oncogene/genetic control of radiosensitivity, radiosensitivity of cancer stem cells [Hall Chapt. 3]  |   | Radiosensitisers, oxygen [Hall Chapt. 6], chemotherapy [Hall Chapt. 27], hypoxic cell radiosensitisers [Hall Chapt. 26], high LET [Hall Chapt. 3], hyperthermia [Hall Chapt. 28] |   |   | Radioprotectors, radiation mitigators, radionuclide eliminators, dietary supplements [Hall Chapt. 9]   |   |
| <b>Cell survival</b>                | Cell death after irradiation, clonogenicity, apoptosis, necrosis, autophagy, senescence [Hall Chapt. 3&18]  | Cell survival curves, curve shape derived parameters & intro to LQ/multi-target model, fractionated survival, D0, D10 [Hall Chapt. 3]                                   |  | Hyperradiosensitivity/induced radioresistance in the low dose region, [Joiner Chapt. 14], bystander effect [Hall Chapt. 3], abscopal effects [Hall Chapt. 19] |   | Probability of tumour cure and number of surviving clonogens [Hall Chapt. 3], exponential tumour cell growth [[Hall Chapt. 23, Joiner Chapt. 5]  |   |
| <b>Cell cycle</b>                   | Phases and length, DNA histogram, techniques, checkpoints, cyclins/kinases and molecular control, p53 & Rb, p21, p16 [Hall Chapt. 4]  |   |  | Radiosensitivity in the cell cycle (age response), mechanisms, reassortment during fractionation, induction of partial synchrony by radiation [Hall Chapt. 4] |   |  |   |
| <b>Repair</b>                       | DNA repair, dsb repair (HR/NHEJ), misrepair, mismatch repair, BER, NER [Hall Chapt. 2]  | Repair affecting cell survival, PLD repair, SLD repair, repairable damage, non-repairable damage, lethal damage, techniques to demonstrate repair types [Hall Chapt. 5] |  | SLD repair during fractionation/LDR, rates of repair of cells/tissues [Hall Chapt. 6]   | Dose-rate effect, influence of 4Rs, brachytherapy, inverse dose-rate effect [Hall Chapt. 6]                           |  | Exploitation of repair differences for therapeutic gain, relevance of $\alpha/\beta$ , examples of tumours that may have high repair capacity [Hall Chapt. 7] |
| <b>Radiation type</b>               | Differential biological effects and survival curves [Hall Chapt. 3,4,5,6,7], photons, neutrons, alphas, heavy ions, physical and biological properties that contribute to response [All modalities: Hall Chapt. 25] |   |  |   |   | RBE, factors affecting, variation of RBE with LET/OER, overkill [Hall Chapt. 7]  |   |
| <b>Oxygen effect</b>                | Oxygen as a radiosensitiser, mechanisms, oxygen fixation hypothesis, oxygen level [Hall Chapt. 4, 6]  | OER [Hall Chapt. 6], effect of LET [Hall Chapt. 6], cycle phase [Hall Chapt. 4]   | Relevance to tumours, acute /chronic hypoxia, evidence [Hall Chapt. 6]   | Hypoxic fraction, techniques to demonstrate tumour hypoxia [Hall Chapt. 6]  | Hypoxia in human tumours [Hall Chapt. 6], addressing hypoxia in the clinic, hypoxic radiosensitisers [Hall Chapt. 26] | Reoxygenation, mechanisms, time-frame, relevance to fractionation [Hall Chapt. 6]  | Hypoxia inducible factor, mechanisms, role in cancer, role in RT [Hall Chapt. 26], hypoxia and chemoresistance/ tumour progression [Hall Chapt. 6]            |
| <b>Tumour kinetics and response</b> | Tumour growth rates, limits of detection, Gompertzian growth [Hall Chapt. 22]   | Tpot, Teff, growth fraction, cell turnover, cell loss, labelling index, mitotic index, cell line,   |  | In vivo tumour models, methods of assessing radiation response, growth delay assay, excision assay, spheroids [Hall Chapt. 21]                                |   | Tumour cure/control, dose-response, clinical TCD <sub>50</sub> and TCD <sub>50</sub> assay [Hall Chapt. 21],   |   |

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|   |   | immortalisation, Hayflick [Hall Chapt. 22]   |   |  |  |   | relationship to surviving clonogens, gamma factor [Joiner Chapt. 5]   |   |  |
| <b>Normal tissue</b>                      | Radiation pathology of organs [Hall Chapt. 19,20], whole body irradiation & syndromes, hematopoietic, GIT, cerebrovascular, prodromal, LD50, pulmonary syndrome, cutaneous injury [Hall Chapt. 18]  | Radiation pathogenesis, early/late responding tissues, turnover, latent period, recovery [Hall Chapt. 19,20]   | Casaret's classification, Michalowski's classification [Hall Chapt. 20], animal models [Hall Chapt. 19], anatomical & functional endpoints [Hall Chapt. 19,20], | Tolerance [Hall Chapt. 20], TD, factors affecting [Hall Chapt. 20, 21], dose-response curves, uncomplicated cure, therapeutic advantage [Hall Chapt. 19], Emami et al, QUANTEC [Hall Chapt. 20], retreatment [Hall Chapt. 24], | Functional subunits, tissue architecture (series/parallel), concept of tissue rescue unit [Hall Chapt. 20]                                     | Volume-dependence of organs [Hall Chapt. 20], seriality, functional reserve, DVH-based tolerance limits, Lyman-Kutcher-Burman [Joiner Chapt. 7]   | Dependence of normal tissues on fractionation and overall treatment time, $\alpha/\beta$ values [Joiner Chapt. 9], determination of $\alpha/\beta$ from fractionated data [Hall Chapt. 19, Joiner Chapt. 9] |   |  |
| <b>Questions 3 and 4 (50%)</b>            |   |  |   |  |  |   |   |   |  |
| <b>Clinical Fractionation</b>             | Rationale, 4Rs [Hall Chapt. 5,6,23], therapeutic advantage, historical – Strandquist/Ellis, types of fractionation [Hall Chapt. 23]   | Influence of overall time & fractionation, repopulation & repair, relevance of $\alpha/\beta$ values and LQ, latent period [Hall Chapt. 23]                                  |   | Repopulation/accelerated repopulation in normal tissues and tumours, rates, counteracting [Hall Chapt. 23]   |  | Isoeffect curves, relationship between total dose and dose per fraction, early/ tumour/late-responding tissues, 'spaghetti' plot [Hall Chapt. 23] |   |   |  |
| <b>Biological equivalence estimations</b> | Concepts, EQD2 [Joiner Chapt. 23], BED [Hall Chapt. 23], influence of repair & the $\alpha/\beta$ , range of validity of LQ. [Hall Chapt. 23, Joiner Chapt. 10]   | Overall time [Hall Chapt. 23], time factor, kick-off time [Hall Chapt. 23], tumours vs normal tissue   |   | Variations of equations, HDR, LDR, PDR, multiple daily fractions, incomplete repair, tissue repair rates [Joiner Chapt. 9]   |  |   | Clinical problems, equivalent regimens, methods for calculating unknown (d/# or n), gaps [Joiner Chapt. 10]   |   |  |
| <b>Chemotherapy agents</b>                | Types (alkylating agents, antibiotics, anitmetabolites, vinca alkaloids, taxanes, topoisomerase inhibitors), targeted agents, immune checkpoints and therapies, hormonal therapies, PARP inhibitors, synthetic lethality, molecular susceptibility [Hall Chapt. 27] |  | Mechanisms, cell cycle dependency, reasons for chemoresistance, properties of cancer stem cells [Hall Chapt. 27]  |  | Interaction with radiotherapy [Hall Chapt. 27]   |   | Hypoxic cell cytotoxics [Hall Chapt. 26, 27]  | Secondary malignancies [Hall Chapt. 27] |  |
| <b>Other normal tissue effects</b>        | Fertility, irradiation of germ cells, male versus female, heritable effects, heritable radiosensitivity syndromes, epigenetic effects, evidence [Hall Chapt. 11]  | Radiation carcinogenesis, evidence, latent period, risk estimates and guidelines, DDREF, age/sex/dose dependence, secondary malignancies after radiotherapy [Hall Chapt. 10] |   |  | Embryo & foetus, critical periods, animals vs humans, irradiation of the pregnant human female, cancer from in utero exposure [Hall Chapt. 12] |   | Cataractogenesis [Hall Chapt. 13]   |   |  |
| <b>Hyperthermia</b>                       | Mechanisms of cell kill, thermotolerance, differential effects in normal tissue and tumour, radiosensitisation, chemosensitisation  |  |   |  |  |   |   |   |  |
| <b>Cancer biology 1</b>                   | Carcinogenesis, multistep nature: initiation, promotion, progression [Hall Chapt. 18]   | Hallmarks of cancer, associated mechanisms, molecular biology [Hall Chapt. 18, Hanahan and Weinberg 2011]  | Genetic basis, oncogenes, tumour suppressor genes [Hall Chapt. 18]  | Growth factors & signal transduction pathways [Hall Chapt. 18]   |  |   | Immortality & senescence [Hall Chapt. 18]   |   |  |
| <b>Cancer biology 2</b>                   | Apoptosis, pathways [Hall Chapt. 18]  | Angiogenesis, angiogenic switch,   | Invasion & metastasis [Hall Chapt. 18]  | Emerging hallmarks: altered metabolism, loss of immune surveillance [Hanahan and Weinberg 2011]  |  | Enablers of cancer: genomic instability, inflammation [Hall   | Cancer stem cells   | Tumour progression [Hanahan             |  |

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|  |  | tumour blood vessels, influence of HIF [Hall Chapt. 18] |  |  | Chapt. 18, Hanahan and Weinberg 2011] | [Hanahan and Weinberg 2011] | and Weinberg 2011] |
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- Hall and Giaccia, Radiobiology for the Radiologist 8<sup>th</sup> Edit., Wolters Kluwer 2019
- Joiner and van der Kogel, Basic Clinical Radiobiology 5<sup>th</sup> Edit., CRC Press 2019
- Hanahan and Weinberg, Hallmarks of cancer: the next generation, Cell, 144(5): 646-71