Exercise 1. Cell survival curves (Credit 2)

a) DNA is the main target of ionizing radiation, and DNA can be damaged through direct and indirect action. Explain these two mechanisms and indicate which types of ionizing radiation causes direct and indirect action.

b) Draw typical cell survival curves for cells damaged through direct and indirect action both in the presence and absence of oxygen, i.e. 4 survival curves.
Explain why the cell survival curves are different.
Draw typical cell survival curves for cells that are killed through mitotic cell death and cells that are killed through apoptotic cell death.
Explain the difference.
Use the linear quadratic model and give the equation for survival of cells undergoing both mitotic and apoptotic death using.

c) Cell survival curves can be mathematical described by the multitarget - single hit model.
Explain the parameters that give information about
-the initial slope of the curve
-the exponential part of the curve
-the size of the shoulder
-How can the number of targets be determined?
Deduce the mathematical relationship between the parameters describing the exponential part of the curve, the size of the shoulder and the number of targets.
Explain how many targets are responsible for the initial slope of the curve.

Exercise 2. Radiobiological aspects (Credit 2)

a) Define the relative biological effectiveness (RBE).
Maximum RBE is obtained for LET=100 keV/μm. Explain why.

b) Explain how a split-dose experiment can obtain information about repair of sublethal damage, reassortment (also called redistribution), and repopulation.

c) The dose-rate is being reduced until a very low dose-rate. Explain how the cell survival curve changes with the change in dose-rate.

d) Hypoxic cells are a major problem in radiotherapy. Explain 4 different ways to overcome this problem..

Exercise 3. Optimizing radiotherapy (Credit 2)

a) Explain the therapeutic index in radiotherapy and how this index can be increased by biological modifiers.

b) The patients are normally given fractionated therapy as 30 doses of 2 Gy for 6 weeks. Sometimes the fractionation regimen is changed to accelerated treatment or hyperfractionation or hypofractionation. Explain these 3 fractionation regimens. Explain for which type of cancer you would like to use them and why. Explain the effect these 3 fractionation regimens have on normal tissue.

c) Proton therapy is a promising treatment. Explain the advantages and disadvantages using this treatment modality compared to conventional photon radiotherapy.

Exercise 4. Calculation (Credit 1)

a) Standard fractionation is 2 Gy per fraction, 5 fractions per week for 6 weeks. For a rapidly growing tumor this gave a BED = 120 Gy
We want to increase the dose per fraction to 3 Gy. How many fractions are needed to maintain the same BED? Discuss briefly how you would deliver these fractions.

b) A normal organ with $\alpha/\beta=3$ Gy is located close to the tumor. Compare BED for the two fractionation regimen in a). Comment on which of the treatments are most optimal for the normal organ

c) In clinical practice the equivalent dose in 2 Gy fractions (EQD2) is used rather than BED. Give the equation that shows the relationship between BED and EQD_2.
For rapidly growing tumors, BED needs to be adjusted to take into account the proliferation of tumor cells. Deduce the equation for BED that is adjusted for the proliferation.

Exercise 5: Multiple choice (Credit 1)

You have 3 possible solutions. Mark the correct answer by setting x in front of the correct answer. You have to hand in the two sheets with multiple choice together with the other answers. Write your candidate number on the sheets.

a) In the Compton process incoming photons interact with
   - The nucleus
   - bound electrons
   - "free" electrons

b) Charged particles causes
   - Direct ionization
   - Indirect ionization through the Compton process
   - Indirect ionization through the photoelectric process

c) DNA double strand breaks can be repaired by homologous recombination repair. This takes place in
   - G1
   - G2
   - Mitosis

d) Which of the following statements is wrong for apoptosis
   - Apoptosis is the most common mechanism of radiation-induced cell death
   - Radiation-induced apoptosis is highly cell-type dependent
   - Apoptosis causes fragmentation of the nucleus

e) Brachytherapy is characterized by
   - The dose rate is low close to the source
   - Substantial repair of sublethal damage
   - The dose is well defined around the source

f) In clinical practice radionucleotide therapy is mainly based on
   - Isotopes coupled to DNA
   - Isotopes coupled to antibodies
   - Isotopes coupled to nanoparticles

g) Deterministic effect is characterized by
   - There is no threshold for the effect
   - Severity increases with the dose
   - The probability of occurrence is dose-independent

h) Normal tissue response to radiation is characterized by
   - Proliferating cells having low radiosensitivity
   - No threshold needs to be reached
   - Cell organization in the tissue

i) Late effects on normal tissue depends mainly on
   - Size of fractionated dose
   - Overall treatment time
   - Dose rate

j) Structurally defined functional units are characterized by
   - Clonogenic cells can migrate from one functional structural units to another
   - Having high radiation tolerance
   - Being independent of its neighbor functional structural units

k) Hypoxia-inducible factor in the presence of oxygen will
   - Be degraded
   - Promote angiogenesis (formation of new blood vessels)
   - Promote cell proliferation

l) Advantages of chemotherapy is
   - High specificity toward cancer cells
   - Reaches metastases
   - Can be repeated many times without inducing resistance toward cancer cells

m) The target for hyperthermia is
   – DNA
   – Proteins
   – Both DNA and proteins

n) Hyperthermia is most sensitive to cells in
   - G1
   - S-phase
   - Late G2/mitosis