i Front page

1 Exercise 1

Radiation absorption, damage and repair (20%)

a) Absorption of ionizing radiation in biological material can be classified as either directly or indirectly ionizing.

- Explain the difference between directly and indirectly ionizing radiation
- What types of radiation are associated with each type of radiation?

b) What is a free radical and why are they highly chemically reactive?
What are the main water radicals produced by radiation?

c) The indirect action of x-rays on biological material via radiolysis of water can be divided into physical, chemical and biological stages. Which characteristic processes are associated with each of these stages, and in what time intervals after radiation will they appear?

d) Radiation damage to mammalian cells can be divided into three subcategories; lethal, potentially lethal and sublethal. What are the differences between these subcategories?

e) Explain how sublethal damage repair, reassortment and repopulation can be found in split dose experiments.

Write your answer here:

Maks poeng: 20

2 Exercise 2

Cell survival after radiation - calculations (20%)

a) 100 unirradiated cells were seeded on a dish to determine the cell survival. After incubating for two weeks 75 colonies were obtained. On another dish 100 cells were seeded and irradiated with an absorbed dose of 2.0 Gy. After two weeks 20 colonies were counted. Calculate the D_0 value, assuming an exponential survival curve.

b) A cell population is irradiated with 40 Gy (single irradiation). D_{10} (i.e., the absorbed dose that reduces the population to 10%) is 4 Gy, when the cells are irradiated at normal oxygen pressure.

- Calculate the relative survival when it is assumed that the survival follows a single-hit, single-target model without any repair
- Calculate the survival when 1% of the population is hypoxic. D_{10} for hypoxic cells is twice as large as for corresponding cells with normal oxygen pressure

c) Cells are irradiated with neutrons and their survival can be described using a single-hit, single-target model with D_0 = 1.7 Gy. When irradiating with photons from a ^{60}Co source, the survival curve can be described using the linear quadratic model with α/β = 3.0 Gy and α = 0.15 Gy^{-1}. Calculate the RBE for neutrons for a survival fraction of 10%, assuming that the reference quality is ^{60}Co photons.

Write your answer here:

Maks poeng: 20

3 Exercise 3

Normal tissue damage - theory and calculations (20%)

a) In radiotherapy the damage to normal tissue should be limited as much as possible to avoid side-effects to the patient. Normal tissue damage to radiation is classified into early- and late responding effects.

- Describe the main property determining the radiosensitivity of normal tissue damage
- Draw a simple sketch of survival curves for early- and late responding normal tissue

b) The severity of normal tissue damage is also influenced by the organisation of the tissue, and can be described by functional structural units (FSU).

- Explain the difference in FSUs in kidney and skin in relation to the different radiosensitivity in these two normal tissues.

c) The cell survival is often described by the linear quadratic model.

A tumor with an α/β ratio = 10 Gy and $\beta = 3.2 \cdot 10^{-2}$ Gy^{-2} is going to be treated. Normal tissue cells will also be irradiated, these cells have an α/β ratio = 3.0 Gy and $\beta = 5.1 \cdot 10^{-2}$ Gy^{-2}.
The treatment schedule consists of 2.0 Gy every day for 30 days both for tumor cells and for normal tissue cells.

- Calculate the survival of both tumor and normal tissue cells. Assume full repair between the fractions.
- If the dose per fraction instead is 1.0 Gy, how many fractions are then necessary in order to obtain the same survival of the tumor cells? And what is now the survival of the normal cells?
- Which of the two treatment options would your recommend? Is there any limitations to the calculations (and conclusions)?

Write your answer here:

Maks poeng: 20

4 # Exercise 4

Lab and project work (20%)

a) Related to the project work on low dose-rate irradiation.

- Describe the concept of low dose-rate irradiation
- Explain the terms HRS and IRR
- At what dose levels does this effect occur?
- How is the cell cycle affected by low dose-rate irradiation in comparison to radiation with higher dose-rates?
- It has been shown that the sensitivity to radiation increases for hypoxic tumour cells receiving low dose-rate irradiation. What is believed to be the mechanism behind this observation?

b) Related to lab work on the linear accelerator.

- What is a depth dose curve? Sketch a typical depth dose curve for both photons and electrons and explain the main differences
- Approximately how far into water/tissue will electrons with energies 6 - 18 MeV reach? What kind of tumours are treated with electrons?
- What is the principles behind intensity modulated radiotherapy (IMRT)?
- What is the difference between IMRT and volumetric arc therapy (VMAT)?
- In the linear accelerator a flattening filter is often used. How is the delivered dose profile affected by this flattening filter? Is there any benefit of removing the flattening filter and in which cases is this done?

Write your answer here:

Maks poeng: 20

5 # Exercise 5

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

In terms of radiation-induced damage to mammalian cells, the most important radiolysis products of water are:

Choose one alternative

- hydrogen atoms
- hydrogen peroxide
- hydroxyl radicals
- superoxide radicals

Maks poeng: 1

6

Exercise 6

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Each of the following statements concerning radiation interactions with matter is true, EXCEPT:

Choose one alternative

- An annihilation reaction occurs when an electron interacts with a positron to produce two 0.511 MeV photons
- In the energy range generally used for radiation therapy, the Compton effect is the predominant interaction between photons and the matter through which they pass
- Pair production occurs for photon energies greater than 1.02 MeV
- The probability of the photoelectric effect occurring is inversely proportional to the atomic number of the absorbing medium

Maks poeng: 1

7

Exercise 7

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

The formation of DNA double strand breaks by increasing doses of radiation is best described as:

Choose one alternative

- Linear
- Quadratic
- Parabolic
- Linear-quadratic

Maks poeng: 1

8

Exercise 8

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Which of the following statements concerning the repair of radiation-induced DNA double strand breaks (DSB) is INCORRECT?

Choose one alternative

- In response to DNA-damaging agents, the RAD51 protein localizes in nuclear foci that represent sites of DNA repair
- BRCA1 is required for the formation of RAD51 nuclear foci
- Although the RAD50/MRE11/NBS1 (MRN) complex contributes to DNA repair, defects in either MRE11 or NBS1 do not result in a radiation sensitive phenotype
- The ataxia telangectasia mutated (ATM) protein is part of the initiation step in a signaling cascade that activates DNA strand break repair

Maks poeng: 1

9

Exercise 9

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Which of the following proteins moves to the sites of DNA double strand breaks in chromatin following irradiation?

Choose one alternative

- ATM
- NBS1
- SOD1
- TGF-beta 1

Maks poeng: 1

10

Exercise 10

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

The primary mechanism for the repair of DNA double-strand breaks during the G1 phase of the cell cycle is:

Choose one alternative

- base excision repair
- homologous recombination repair
- nucleotide excision repair
- nonhomologous end-joining

Maks poeng: 1

11

Exercise 11

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Which of the following statements regarding radiation-induced cell killing is INCORRECT?

Choose one alternative

- In some radiosensitive cell populations, cells can undergo an early interphase death within a few hours of irradiation
- Senescent or terminally-arrested cells die days to weeks post-radiation from necrosis
- Cycling cells in irradiated tissues may die due to mitotic catastrophe
- Morphological evidence of radiation damage can be seen immediately following irradiation in most cells

Maks poeng: 1

12

Exercise 12

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Concerning the linear-quadratic model to describe cell survival curves, all of the following statements are true, EXCEPT:

Choose one alternative

- The α/β ratio is the dose at which the linear and quadratic components of cell killing are equal
- A cell survival curve for high LET radiation typically has a large α/β ratio
- The α/β ratio for an intact normal tissue or tumor can be obtained from a series of multifraction experiments employing different doses per fraction
- At low doses, cell killing results primarily from more than one ionization track producing damage in separate chromosomes

Maks poeng: 1

13

Exercise 13

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Modifying which one of the following treatment parameters would cause the largest change in tumor response for high LET irradiation?

Choose one alternative

- total dose
- dose rate
- use of smaller-than-conventional fraction sizes
- use of a hypoxic cell sensitizer

Maks poeng: 1

14

Exercise 14

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

For mammalian cells, which of the following would yield the lowest OER?

Choose one alternative

- 160 MeV protons in the Bragg peak
- 270 MeV/μ carbon ions in the Bragg peak
- 10 MeV neutrons
- 250 kVp X-rays

Maks poeng: 1

15

Exercise 15

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Concerning the measurement of tumor oxygenation status, which of the following statements is TRUE?

Choose one alternative

- Tumor oxygenation status is likely to remain constant throughout treatment
- Cervical carcinoma patients whose tumors had pO_2 values >10 mmHg exhibited poorer outcomes than patients whose tumors had lower pO_2 values
- Patients whose hypoxic tumors reoxygenate only slowly or not at all during the course of treatment would benefit from the use of an accelerated treatment schedule
- Pimonidazole has proven useful for the detection of hypoxia in human tumors

Maks poeng: 1

16

Exercise 16

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

The repair of sublethal damage:

Choose one alternative

- increases as the time between two X-ray dose fractions is decreased
- is of greater importance for cells exposed to high LET compared with low LET radiation
- has a time course similar to that for DNA double strand break rejoining
- occurs in vivo, but not in vitro

Maks poeng: 1

17

Exercise 17

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

All of the following statements concerning tumor hypoxia are correct, EXCEPT:

Choose one alternative

- Hypoxia signaling is involved in the regulation of the epithelial–mesenchymal transition, invasion, intravasation, survival of circulating tumor cells, extravasation, formation of the premetastatic niche and growth from micrometastais to macrometastasis
- Hypoxia-inducible factors primarily regulate oxygen concentration in tumors, but exert little or no control over tumor invasiveness and metastasis
- A possible negative aspect of anti-angiogenic therapy is that it may increase tumor hypoxia, thereby increasing the harmful consequences resulting from this state
- Hypoxia-inducible factors are regulated by oxygen sensing prolyl hydroxylases

Maks poeng: 1

18

Exercise 18

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Which of the following statements concerning stem cells is FALSE?

Choose one alternative

- Most tumors are thought to contain a small population of putative “cancer stem cells” capable of self-renewal and differentiation, albeit poorly- regulated
- A stem cell is an undifferentiated cell that can produce daughter cells capable of either remaining stem cells, or committing to a pathway leading to differentiation
- Contrary to conventional thinking, it now appears that most, if not all, adult organs contain stem cells, or at least can produce stem cells in culture
- In both humans and rodents, stem cells rarely maintain telomerase activity, whereas their progeny, the progenitor cells, do

Maks poeng: 1

19

Exercise 19

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

One would expect to achieve the largest therapeutic gain using a:

Choose one alternative

- high LET ion beam with a tumor type having a large hypoxic fraction and little reoxygenation during treatment
- radiation protector that decreases the radiation response of both the tumor and normal tissues
- fractionated course of carbon ions that yields an RBE of 3.0 for the tumor and an RBE of 5.5 for the dose limiting normal tissue
- radiation sensitizer that increases response of tumors and dose limiting normal tissue by the same factor

Maks poeng: 1

20

Exercise 20

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

In a conventional fractionation pattern, a head and neck cancer is treated to a total of 70 Gy in 35 fractions, given one fraction per day, 5 days a week. What is the BED for the tumor (assuming an α/β of 10 Gy)?

Choose one alternative

- 55 Gy
- 84 Gy
- 60 Gy
- 70 Gy

Maks poeng: 1

21

Exercise 21

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

The greatest reduction in the risk of developing a late normal tissue effect following exposure to a particular dose of radiation can usually be achieved through:

Choose one alternative

- irradiation under high oxygen pressure
- the use of a protocol employing a series of small fractions, compared to fewer, larger, dose fractions
- an accelerated protocol
- use of agents that upregulate repair enzymes

Maks poeng: 1

22

Exercise 22

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Which of the following reasons represents the main advantage for the use of high energy protons compared with photons in cancer radiotherapy?

Choose one alternative

- Protons represent a high LET form of radiation
- Protons display a substantially reduced OER
- Protons provide a better physical dose distribution than photons
- Protons exhibiting a greater variation in cell cycle radiosensitivy comoared photons

Maks poeng: 1

23

Exercise 23

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Which of the following statements best describes hyperthermia-induced cell killing and thermotolerance?

Choose one alternative

- The more toxic a heat exposure, the greater the degree of thermotolerance induced in surviving cells
- The induction of thermotolerance is independent of the level of cell killing
- Thermotolerance decays in about 10 minutes after a mild heat treatment that only produces modest cell killing
- Thermotolerance develops secondary to mitochondrial damage

Maks poeng: 1

24

Exercise 24

Multiple choice (1%).
One correct answer. You get 1 point for correct answer, 0 for wrong answer.

Concerning time, dose and fractionation, which of the following statements is TRUE?

Choose one alternative

- Results of clinical trials have suggested that patients with tumors exhibiting Tpot values longer than 3 days would benefit from accelerated treatment
- If the interval between fractions is decreased to less than 6 hours, the incidence of late normal tissue effects may decrease due to incomplete repair
- If treatment time is extended beyond the point when an early responding normal tissue begins to exhibit compensatory proliferation, the total dose should be decreased to avoid enhancing the severity of early reactions
- Prolonging overall time within the normal radiotherapy range generally has a larger sparing effect on early compared with late reactions

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Maks poeng: 1

Document 1
Attached

NTNU

Department of Physics

Examination paper for TFY4315 Biophysics of Ionizing Radiation

Academic contact during examination: Kathrine Røe Redalen

Phone: 92437646

Examination date: 20.05.2019

Examination time: 09:00 – 13:00

Permitted examination support material: Code D

- **Simple specified calculator**
- **No printed or hand-written support material is allowed**

Language: English

Other information: Exam might be answered in English or Norwegian

Checked by:

_____

Date Signature