

i Department of Physics

Examination paper for TFY4315 Biophysics of Ionizing Radiation

Examination date: 04.06.2020

Examination time (from-to): 9:00 – 13:00

Permitted examination support material: All support material is allowed

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OTHER INFORMATION

If a question is unclear/vague – make your own assumptions and specify in your answer the premises you have made.

Saving: Answers written in Inspira are automatically saved every 15 seconds. If you are working in another program remember to save your answer regularly.

Cheating/Plagiarism: The exam is an individual, independent work. Examination aids are permitted. All submitted answers will be subject to plagiarism control. [Read more about cheating and plagiarism here.](#)

Citations: If you use information found in other sources (web, publications, books) then you need to cite the source.

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Weighting: The number of points is shown for each question in the exam. The maximum possible points in this exam are 80. These points will be added together with the points from the midterm/lab report (max 20) to a maximum of 100 points achievable. The grade is based on these points.

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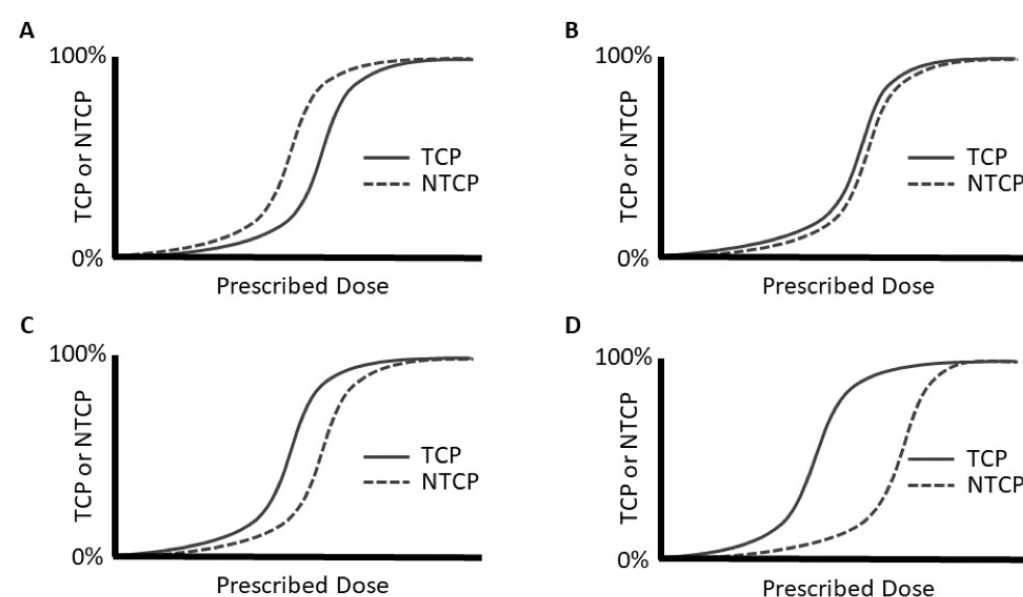
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Maximum marks: 0

2 Theory related to photon radiotherapy (15 points)

a) Explain what the tumor control probability (TCP), normal tissue complication probability (NTCP) and the therapeutic index are in radiotherapy.

b) How can the therapeutic index be increased by biologic response modifiers? Can you list three examples of biologic response modifiers and briefly describe their mechanism of action?



c)

You have started to work in the radiotherapy department and there you have gotten a new treatment planning system that uses TCP and NTCP to help select the best treatment plan. For one patient you have made four different plans to evaluate. Based on the TCP/NTCP curves (A-D), which of these plans would you choose to treat the patient with? Justify your result, both why you choose one of the plans and why you do not choose the others.

d) Cancer patients are commonly receiving fractionated radiotherapy delivered as 25 doses of 2 Gy for 5 weeks. However, sometimes the fractionation regimen is changed to accelerated treatment, hyperfractionated treatment or hypofractionated treatment. Explain the purpose and how the treatment would typically be delivered with each of these three fractionation regimens. Explain for which type of cancer you would like to use each of them and why. Explain the effect these three fractionation regimens have on normal tissue.

e) Two special fractionation regimens are named CHART and ARCON. Explain these regimens and in what situations these are used. Do you know any examples of studies where these have been successful?

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Words: 0

Maximum marks: 15

3 Theory related to proton radiotherapy (15 points)











a) Proton therapy is a promising treatment of cancer. Explain the advantages of using proton therapy compared to conventional photon-based radiotherapy. Do you know when Norway expects to get proton therapy?

b) Given that proton therapy has several advantages over photon-based radiotherapy, why are proton therapy not used even more (not only thinking about Norway but also world-wide)? Can you think of some reasons?

c) When delivering proton therapy it is being discussed to not use the standard fractionation anymore (for example 2 Gy times 25 doses) but rather go for larger doses and fewer fractions. What are the reasons why this approach may be more attractive for proton therapy?

d) What are regarded as the main research topics (unsolved challenges) related to the radiation biology of proton therapy? Name at least three different topics and discuss these briefly.

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Words: 0

Maximum marks: 15

4 Calculations (30 points)

- a) You are planning a fractionated radiotherapy treatment to be delivered in 1.5 Gy fractions. What is the total dose equivalent of this treatment for the late normal tissue reactions when you are comparing with a conventional schedule of 30 fractions of 2 Gy ? Assume the α/β is 3 Gy.
- b) An experimental data set for cell survival after radiation with different doses of X-rays is well fitted by the mathematical expression for a single-hit survival curve with an SF_2 of 0.37. What is the best estimate for the α parameter to describe the survival response?
- c) You are in the lab to study radiosensitivity of cell cultures. You have decided to use the clonogenic assay and after plating 2000 cells you irradiate these with an X-ray dose of 8 Gy. 14 days later you count 20 colonies. In parallel, 200 unirradiated cells made 40 colonies. What is the percent survival following the 8 Gy radiation dose?
- d) You are repeating the experiment from c) but now using carbon ions instead of X-rays. What is approximately the surviving fraction if you irradiate your cells with 5 doses of 0.5 Gy of carbon ions? You can assume that the surviving fraction of one dose is 0.4.
- e) You are planning a fractionated radiation of a patient with 25 daily fractions of 1.8 Gy. However, with respect to the complication probability of a critical normal tissue close to the tumor you have found that this treatment is biologically equivalent to a fractionated treatment with 17 daily fractions of 2.5 Gy. What is the α/β ratio of the critical normal tissue?
- f) A tumor has 10^6 clonogenic cells. The effective dose response curve is found for radiation dose fractions of 2 Gy per day. The curve has no shoulder and a D_0 of 2.5 Gy. What is the total radiation dose required to give a 37% probability of tumor cure? You can assume that the time between each fraction is sufficient for full repair of sublethal damage and that no cell proliferation occurs between the fractions.
- g) Based on the same variables as in f), what is the total radiation dose required to give a 37% probability of tumor cure if the tumor clonogens go through three cell divisions during the treatment? You can assume there was no loss of cells during the treatment.

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Maximum marks: 30

5 Which of these statements about photons is true?

Select one alternative:

- Photons used for radiotherapy should interact through the photoelectric effect
- Compton scattering results in production of Auger electrons
- X-rays travel faster than visible light
- Photons can be produced by annihilation (interaction between a positron and electron)

Maximum marks: 1

6 What is the minimum photon energy necessary to cause ionisation?

Select one alternative:

- 1 - 2.5 keV
- 100 - 250 eV
- 10 - 25 eV
- 10 - 25 keV

Maximum marks: 1

7 Which of these statements are NOT correct?

Select one alternative:

- Non-homologous end-joining is an error-prone repair pathway that involves DNA-PKCs-associated repair of DNA double strand breaks
- DNA repair by homologous recombination occurs primarily in the G1 phase of the cell cycle
- Following the production of DNA double strand breaks, ATM is converted from an inactive dimer to an active monomer form
- The DNA repair proteins MRE11, NBS1 and RAD50 localise at nuclear foci corresponding to presumed sites of DNA damage following exposure to DNA-damaging agents

Maximum marks: 1

8 What is the primary reason that high dose rate (HDR) brachytherapy is used for treatment of prostate cancer?

Select one alternative:

- Tumor response should be improved by using larger fraction sizes because of the lower α/β associated with prostate cancer compared to the surrounding normal tissues
- The probability of late normal tissue damage decreases with increasing fraction size
- The oxygen enhancement ratio is expected to be lower for HDR than for LDR brachytherapy
- Radiation safety is of less concern for radioisotopes used for HDR brachytherapy than for LDR brachytherapy

Maximum marks: 1

9 Regarding the effects of heat on cells, which of these statements is false?

Select one alternative:

- Hyperthermia does not affect the repair of radiation-induced DNA damage
- The initial shoulder of the hyperthermic survival curve suggests the repair of sublethal damage
- Cycling cells are more sensitive to heat than non-cycling cells
- Cells of low pH are sensitive to heat

Maximum marks: 1

10 Which statement about chronically hypoxic cells is true?

Select one alternative:

- Chronically hypoxic cells inhibits apoptosis in cancer cells
- Chronically hypoxic cells can be selectively targeted with certain bioreductive drugs
- Chronically hypoxic cells are resistant to hyperthermia
- Chronically hypoxic cells increases the metastatic potential of tumor cells

Maximum marks: 1

11 What is the name of an atom or molecule with an unpaired electron in the outer shell?

Select one alternative:

- Heavy ion
- Recoil proton
- Ion pair
- Free radical

Maximum marks: 1

12 Which of these statements about chromosome aberrations is false?

Select one alternative:

- An anaphase bridge is a chromatid aberration
- Ring chromosomes are induced as a linear function of dose for high LET radiation
- For a given dose of X-rays, the amount of dicentrics decreases with decreasing dose rate
- Symmetrical translocations are unstable chromosome aberrations

Maximum marks: 1

13 What is the main reason for cell death in most solid tumors after ionizing irradiation?

Select one alternative:

- Activation of apoptosis by the DNA damage response
- Oxidative damage to cellular proteins
- DNA damaged-induced senescence
- Mitotic catastrophe

Maximum marks: 1

14 Which of these types of ionizing radiation has the highest LET?

Select one alternative:

- 2.5 MeV alpha particles
- 150 MeV protons
- 75 MeV/nucleon argon ions
- 18 MeV/nucleon carbon ions

Maximum marks: 1

15 The oxygen enhancement ratio (OER) is different for different types of radiation. Which OER belongs to which type of radiation?

Please match the values:

	Protons	Alpha particle	Neutron	X-rays
OER = 2.5 - 3.0	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
OER = 2.5 - 3.0	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
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OER = 1.0	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Maximum marks: 1

16 For carbon ions the RBE for hypoxic cells compared to the RBE for oxygenated cells is:

Select one alternative:

- Lower
- Higher
- Dependent on the endpoint
- Equal

Maximum marks: 1

- 17 After exposure to ionizing radiation cells often undergo apoptosis. What is correct about cells undergoing apoptosis?

Select one alternative:

- They swell rapidly
- They elicit a strong inflammatory response
- They display enhanced expression of the gene encoding MSH2
- They exhibit nuclear fragmentation

Maximum marks: 1

- 18 Which of these pathways have shown to be involved in the cell death process after exposure to ionizing radiation?

Select one alternative:

- Autophagy
- Necrosis
- Mitotic catastrophe
- All the three others

Maximum marks: 1

- 19 Regarding hyperthermia, which of these statements about the Arrhenius analysis of mammalian cell death by heat is true?

Select one alternative:

- An Arrhenius curve plots the log of the slope ($1/D_0$) of the survival curve as function of the temperature
- The break point in the Arrhenius plot is different in cancer cells from rodents and humans
- The Arrhenius plot shows the temperature where the mechanism behind the cell death changes
- The break point in the Arrhenius plot is the temperature where the slope of the curve increases significantly

Maximum marks: 1

20 All these proteins are involved in non-homologous end joining of DNA double strand breaks, except:

Select one alternative:

- DNA ligase IV
- RAD52
- XRCC4
- KU70/KU80

Maximum marks: 1

21 Deposition of energy from proton beams is different compared to from photons. Energy from proton beams are mainly deposited:

Select one alternative:

- In the end of the track which forms the Bragg peak
- During the entire track which forms the Bragg peak
- In the middle of the track which forms the Bragg peak
- In the beginning of the track which forms the Bragg peak

Maximum marks: 1

22 At 150 μm distance from a tumor blood vessel can all these situations occur except one. Which one?

Select one alternative:

- Decreasing interstitial fluid pressure
- Decreasing glucose
- Decreasing pH
- Increased hypoxia

Maximum marks: 1

23 Which of these interactions with matter is the most important to produce a diagnostic X-ray image with high contrast?

Select one alternative:

- Pair production
- Coherent scatter
- Compton process
- Photoelectric effect

Maximum marks: 1

24 When it comes to tumor hypoxia, which statement is correct?

Select one alternative:

- Areas with chronic hypoxia in a tumor develop due to intermittent closure and opening of blood vessels
- When the tumor size increases the hypoxic fraction decreases
- Acutely hypoxic cells usually have a slower reoxygenation than chronically hypoxic cells
- If there is no oxygenation it is unlikely that all hypoxic cells are eliminated from the tumor during radiotherapy

Maximum marks: 1