In this test there are 12 exercises, 11 of them are worth 0, 1, or 2 points according to the correctness of the answer. There is one longer exercise, broken down into 5 shorter questions, which is more complex; if answered correctly it is worth up to 14 points.

1. Which kind of ionizing radiation is more damaging to tissues, alpha particles or protons? How is this related to the Bethe formula?

2. Consider 5000 eV electrons that stop in water. After one electron stops in water, you estimate that it produced 94.1 ± 1.2 copies of a certain species (one of those listed in the Species column in the table). Can you identify the species?

Table 13.3 *G* Values (Number per 100 eV) for Various Species in Water at 0.28 μs for Electrons at Several Energies

	Electron Energy (eV)							
Species	**100**	**200**	**500**	**750**	**1000**	**5000**	**10,000**	**20,000**
OH	1.17	0.72	0.46	0.39	0.39	0.74	1.05	1.10
H_3O^+	4.97	5.01	4.88	4.97	4.86	5.03	5.19	5.13
e^-_{aq}	1.87	1.44	0.82	0.71	0.62	0.89	1.18	1.13
H	2.52	2.12	1.96	1.91	1.96	1.93	1.90	1.99
H_2	0.74	0.86	0.99	0.95	0.93	0.84	0.81	0.80
H_2O_2	1.84	2.04	2.04	2.00	1.97	1.86	1.81	1.80
Fe^{3+}	17.9	15.5	12.7	12.3	12.6	12.9	13.9	14.1

3. What is the approximate size of a human cell? What is its mass assuming it to be nearly spherical?

4. What is the difference between somatic and germ cells?

5. What is catalase? How does its activity differ from that of superoxide dismutase?

6. What is the difference between eukariotes and prokaryotes? Are bacteria prokaryotes or eukaryotes?

7. What is range of validity of the linear-quadratic model? Is it correct to utilize the linear-quadratic model in a fractionated radiotherapy with a total dose of 120 Gy? (explain)

8. What is a ribosome? How many subunits make up a complete ribosome?

9. What is the difference between endogenous and exogenous damage? Name two sources of exogenous damage.

10. What is the difference between single-strand breaks and double-strand breaks in DNA? Which one is more likely to induce a mutation?

11. Define apoptosis. Define clonogenic death.

12. Consider a disk of tumor cells that has radius R_T, fixed thickness, and fixed cell density n. We irradiate the disk with a circular beam with axis centered on the disk, such that the dose is spread uniformly over a circle with radius R_B and has the value D when R_B=R_T, i.e.,

$$D(R) = D_B \frac{R_T^2}{R_B^2}$$

1. Recall the definition of Equivalent Uniform Dose

2. Find the formula for the Equivalent Uniform Dose on the disk of tumor cells, assuming that $R_B > R_T$, and that the survival probability is given by the simple Poisson model $S(D) = e^{-D/D_0}$.

3. Find the formula for the Equivalent Uniform Dose on the disk of tumor cells, assuming that $R_B < R_T$, and that the survival probability is given by the simple Poisson model $S(D) = e^{-D/D_0}$.

4. Explain how results 2 and 3 can be used to determine the optimum beam size that kills the most cells in the tumor.

5. Can you produce a formula for the Tumor Control Probability as a function of the beam radius using results 2 and 3?

Solutions

1. Alpha particles are more damaging than protons. This can be understood from the Bethe formula, where the average energy deposited per unit length is proportional to the square of the particle charge. In this case we expect the average energy deposited per unit length by alpha particles to be four times as large as that deposited by protons.

2. From the table, we find that the average numbers of each species are

OH	H_3O^+	e^-_{aq}	H	H_2	H_2O_2	Fe^{3+}
37.0	251.5	44.5	96.5	42.0	93.0	645.

When we take the estimate 94.1 ± 1.2, we see that it differs from the expected average for H_2O_2 by less than one standard deviation. The result for H is also marginally compatible, as it differs from the estimate by little more than 2 standard deviations.

3. The approximate size of a human cell is about 10 μm. This implies a volume of about 4×10^{-15} m^3. Assuming a density close to that of water, we find that the mass of one cell is about 4×10^{-9} g.

4. Germ cells are either a sperm or an egg, all other human cells are called somatic cells.

5. Catalase converts the hydrogen peroxide into water and oxygen (O_2).
Superoxide dismutase (SOD) converts the superoxide anion O^- into atomic oxygen (O) or hydrogen peroxide H_2O_2.

6. Prokaryotes: cells lack a nucleus and are usually very simple organisms. Archaebacteria and Eubacteria are Prokaryotes.
Eukaryotes: cells have a nucleus. Protists, Fungi, Plants and Animals are Eukaryotes.

7. The validity of the linear-quadratic model ranges from a little less than 1 Gy to about 6 Gy. It is correct to use the lq model in fractionated radiotherapy whatever the total dose, because fractions are always less than 6 Gy.

8. Ribosomes are sophisticated molecular machines made up of more than 70 proteins and 4 strands of RNA, divided into two subunits. They assemble all the cell's proteins.

9. The damage associated with chemicals produced by the cell itself is called *endogenous damage*. The damage produced by external agents is called *exogenous damage*.

10. In a single-strand break only one of the DNA strands is damaged, while in double-strand breaks both strands are damaged. The double-strand breaks are harder to repair and the are more likely to induce mutations.

11. Apoptosis, is synonymous with programmed cell death, which implies the existence of a genetic program of cell death. Apoptosis is believed to account for most cell death during development and in normal adult tissue turnover, and it can also be induced experimentally by various biological, chemical, or physical agents. Clonogenic death occurs when cells lose the ability to proliferate.

12.

1. For any dose distribution, the corresponding Equivalent Uniform Dose EUD is the dose in Gy, which, when distributed uniformly across the target volume, causes the survival of the same number of clonogens.

2. In this case the beam radius is larger than the tumor radius, therefore the dose is uniform throughout the tumor disk and its value is

$$D_B \frac{R_T^2}{R_B^2}$$

3. In this case the beam radius is smaller than the tumor radius, the tumor is irradiated only in its central part. The number of cells in the central part is

$$\pi n R_B^2$$

while the number of cells in the external annulus which is not irradiated is

$$\pi n R_T^2 - \pi n R_B^2 = \pi n (R_T^2 - R_B^2)$$

The surviving fraction in the central disk is

$$\mathrm{S_{disk}} = \exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right)$$

while the surviving fraction in the non-irradiated external annulus is $\mathrm{S_{ann}} = 1$.

The total number of surviving cells is

$$\pi n R_B^2 \mathrm{S_{disk}} + \pi n (R_T^2 - R_B^2)\mathrm{S_{ann}} = \pi n R_B^2 \exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right) + \pi n (R_T^2 - R_B^2)$$
$$= \pi n \left[R_B^2 \exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right) + (R_T^2 - R_B^2)\right]$$

This number corresponds to a uniformly spread dose EUD, and to the mean number of surviving cells

$$\pi n R_T^2 \exp\left(-\frac{\mathrm{EUD}}{D_0}\right)$$

so that, by the definition of Equivalent Uniform Dose, we find

$$\pi n R_T^2 \exp\left(-\frac{\mathrm{EUD}}{D_0}\right) = \pi n \left[R_B^2 \exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right) + (R_T^2 - R_B^2)\right]$$

or also

$$\exp\left(-\frac{\mathrm{EUD}}{D_0}\right) = \left[\frac{R_B^2}{R_T^2}\exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right) + \left(1 - \frac{R_B^2}{R_T^2}\right)\right]$$

By taking logarithms, we find the Equivalent Uniform Dose as a function of the scaled radius $r = R_B/R_T$

$$\mathrm{EUD} = -D_0 \ln\left[\frac{R_B^2}{R_T^2}\exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right) + \left(1 - \frac{R_B^2}{R_T^2}\right)\right]$$

4. The EUD is a function of the beam radius and the optimum beam size is obtained by maximizing the EUD. In this very simple case one finds that the optimum beam size is just the tumor radius.

5. Since the cells in the annulus are not killed by radiation as long as the beam radius is smaller than the tumor radius, the TCP is 0 for $R_B < R_T$. In the case $R_B > R_T$, the mean number of surviving cells is

$$\pi n R_T^2 \exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right)$$

and therefore, from the Poisson formula, we find that the probability that no cell survives – i.e., the TCP – is

$$\mathrm{TCP} = \exp\left[-\pi n R_T^2 \exp\left(-\frac{D_B}{D_0}\frac{R_T^2}{R_B^2}\right)\right]$$

and this quantity is maximum for minimum beam radius, i.e., $R_B = R_T$.