5 Radiation Biology

5.1 Definitions and Relations

The material below is mainly related to cell survival and clinical therapeutic applications are not included. The cell survival models are introduced without any discussion of the biology behind them.

Cell survival

Cell survival can have different meanings depending on the context. *Differentiated cells* that do not divide can be regarded as dead when they lose their specific function. *Proliferating cells* that are dividing cells can be regarded as dead when they lose their reproductive capacity. They may divide a couple of times, but they have lost their *clonogenic* capacity.

Cells that die when trying to divide are undergoing a so called *mitotic death*. Another type of death is *apoptosis*, also called programmed cell death. This type of death leads to changes in the function of the cell as nuclear fragmentation, chromatin condensation and chromosomal DNA fragmentation. Both types of cell death will lead to the loss of cell reproduction.

Plating efficiency

A common way to measure cell survival is to grow single cells in a nutritional liquid on dishes. These cells will then grow into large colonies that can be seen by the naked eye if the cells still have their reproductive capacity. By calculating the number of colonies for cells irradiated with different absorbed doses and under different conditions, it is possible to obtain cell survival curves. It is then important to have a reference dish with unirradiated cells. *Plating efficiency* is defined as the percentage of cells that grow into colonies.

$$PE = \frac{\text{Number of colonies counted}}{\text{Number of cells seeded}} \tag{5.1.1}$$

Surviving fraction is then defined as

$$SF = \frac{\text{Number of colonies counted}}{\text{Number of cells seeded} \cdot PE} \tag{5.1.2}$$

Cell survival models

Exponential dose response model. Cell survival data are often plotted as the logarithm of the surviving fraction. This means that a linear curve indicates an exponential relation between absorbed dose and survival.

$$SF = \frac{N}{N_0} = e^{-D/D_0} \tag{5.1.3}$$

where SF is the ratio of the number of surviving cells N to the initial number of cells N_0. D is the absorbed dose and D_0 is the absorbed dose that reduces the number of cells to 37% of the initial number. This is sometimes written as D_{37}. $1/D_0$ gives the slope of the curve. In Fig. 5.1 an exponential survival curve is included with D_0=0.96 Gy.

An absorbed dose of D_0 corresponds to on average one hit per cell. That not all cells are killed is due to statistics. Some cells will get more than one hit and some will not be hit. The distribution of hits is given by the binomial distribution, which for a large number of cells may be approximated by the Poisson distribution. The the probability to obtain n hits in a cell is then given by

$$P(n) = \frac{e^{-x}x^n}{n!} \tag{5.1.4}$$

where x is the average number of hits and n is the specific number of hits. If each hit results in a cell inactivation, then the probability of survival is the probability of not being hit, $P(0)$. Thus with x=1 and n=0

$$P(0) = \frac{e^{-1}1^0}{0!} = e^{-1} = 0.37 \tag{5.1.5}$$

D_0 is also often called the *mean lethal dose*.

Exponential cell survival is more common for densely ionizing radiation like neutrons and ions. Sometimes this curve is interpreted such that there is enough energy deposited in a hit to inactivate the cell (single-hit, single-target), and that there is no repair of the cells.
Survival curves with shoulder. Experimental survival curves often have a shoulder followed by an exponential decrease. Several mathematical models have been derived to fit the experimental data and there have been different suggestions on how to interpret these results from a more fundamental point of view. This is under debate and will not be included here. However, there is probably some relation between the response and the energy deposited by each track within some or several important targets (DNA, cell nucleus,...). The possibility to repair the initial damages is also of importance for the shape of the survival curves.

Single-hit multi-target model. The first interpretation of the shoulder was by using the “single-hit multi-target” model. In this model it is assumed that to inactivate the cell there is a need for one hit in n targets. The survival fraction will then be given by

$$SF = 1 - (1 - e^{-D/D_0})^n \tag{5.1.6}$$

where D_0 is the dose to reduce cell survival to 37% along the log-linear slope of the curve. n is the extrapolation number, that is the value of the y-axis when D=0. The interpretation of hits and targets is probably not correct, but the equation may describe the shape of the survival, in particular at high doses.

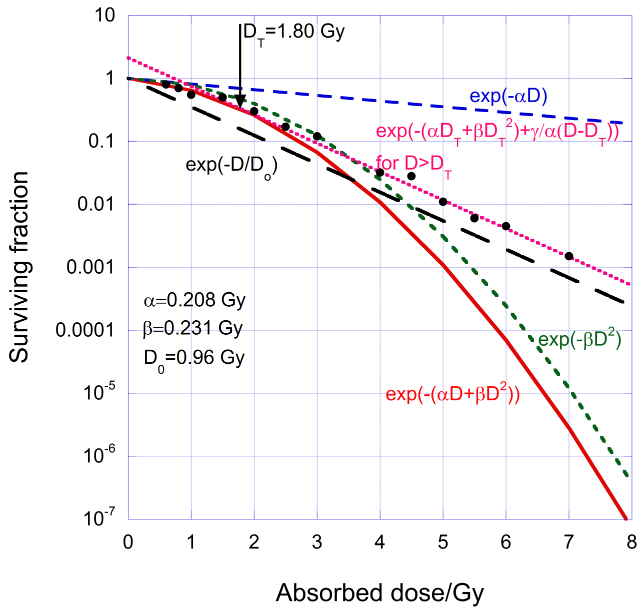

Figure 5.1: Different cell survival curves compared with experimental data for mammalian cells (Puck and Markus, 1956). The LQ-model shows a good agreement for low doses below 2-3 Gy. With increasing doses the difference between experiment and the LQ-model increases. In the figure the separate components $e^{-\alpha D}$ and $e^{-\beta D^2}$ are also included. The absorbed dose where these curves intersect gives the α/β-ratio (0.90 Gy). For large absorbed doses the experimental data can be fitted to a line in the lin-log diagram. The slope of this line is given by $1/D_0$, where D_0 (0.96 Gy) is the mean lethal dose for high absorbed doses. The LQ-L-model gives a good agreement with the experiments for the full dose range.For doses below D_T (1.80 Gy) the LQ-L-model agrees with the LQ-model.

Linear quadratic (LQ) model. The most common model used today in radiotherapy is the linear quadratic model.

$$SF = e^{-(\alpha D+\beta D^2)} \tag{5.1.7}$$

where α and β are fitting parameters that depend on the type of cells and radiation quality. α gives the slope of the initial part of the curve (See Fig. 5.1). The relation has sometimes been interpreted such that an inactivation can be produced by either a single track ($P = \alpha D$), or by two independent tracks ($P = \beta D^2$). However, this explanation does not include any discussion of repair and is not accepted today. This equation is the basis for many of the relations used to consider fractionation regimes in radiotherapy. However, one drawback of this curve is that the curvature increases continuously with absorbed dose. This not obtained experimentally and it is also difficult to find support from fundamental radiobiology. The difference between the model and experimental survival curves is rather small at absorbed doses around and below 2 Gy, which has been a normally used daily dose. See Fig. 5.1. However, recently it has become more common to use higher doses per fraction in radiotherapy and as such the difference between model and experiment is not acceptable. Lately there have thus been attempts to improve this model.

Linear quadratic linear (LQ-L) model. This model fits the first part of the LQ-model with a linear part at high doses (Astrahan, 2008). The model gives the transition between the two parts as

$$SF = e^{-(\alpha D+\beta D^2)} \text{ for} D < D_{\mathrm{T}} \tag{5.1.8}$$

and

$$SF = e^{-(\alpha D_{\mathrm{T}}+\beta D_{\mathrm{T}}^2+\gamma(D-D_{\mathrm{T}}))} \text{ for } D \geq D_{\mathrm{T}} \tag{5.1.9}$$

where γ is the cell kill per Gy in the final linear part of the curve at large absorbed doses.

The γ/α ratio can be calculated from the slope of the tangent at D_{T} and the α/β term

$$\gamma/\alpha = 1 + (2D_{\mathrm{T}}/(\alpha/\beta)) \tag{5.1.10}$$

The value of D_{T} may be obtained from experiments. This model can better describe cell survival curves over a large dose range (see Fig. 5.1).

Repairable conditionally repairable (RCR) model. The RCR-model (Lind et al, 2003) tries to include the repair of the cells into the model. The survival fraction in this model is given by

$$SF = e^{-aD} + bDe^{-cD} \tag{5.1.11}$$

where a, b and c are the parameters of the model. e^{-aD} corresponds to the undamaged cells. bDe^{-cD} corresponds to the fraction of cells that have been damaged and subsequently repaired. The model separates between two types of damage. One is the potentially repairable damage, that may also be lethal, and thus non-repaired or misrepaired. The other type is the conditionally repairable damage that may lead to an apoptotic response if not repaired. This expression for survival gives a good fit to experimental data over the full range of doses, from the very low, where there may be a hypersensitivity, to the exponential part at very high doses.

Fig. 5.2 shows a comparison between the LQ-model and the RCR model fitted to experimental cell survival data. The figure to the left shows that the RCR-model gives a lower survival at low doses than the LQ-model and thus provides a better means of simulating hypersensitivity. The figure to the right makes a comparison over a larger dose range and shows that the RCR-model gives a straighter line in the lin-log diagram than the LQ-model, which is in good agreement with experimental data. The

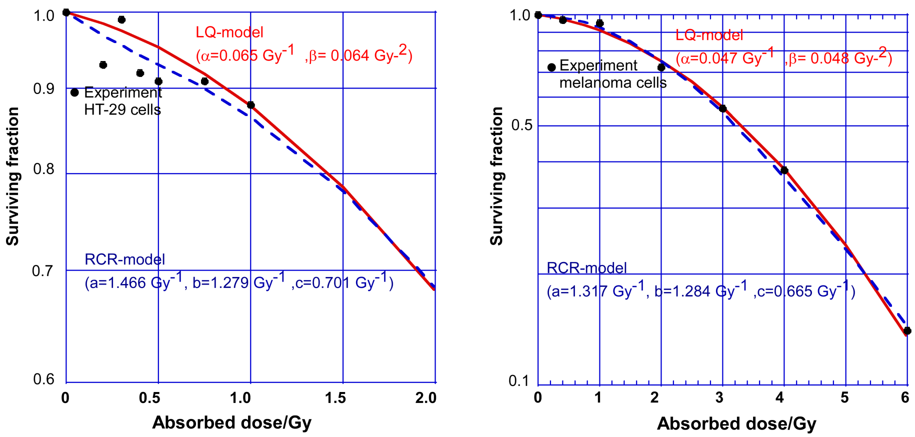

Figure 5.2: Survival fraction after irradiation with ^{60}Co for HT-29 cells (left figure) and human melanoma cells (right figure). The experimental data are fitted to the LQ model and the RCR model.

data in the figure are taken from Persson (Persson, 2002).

Oxygen enhancement ratio, OER.
Survival curves for cells exposed to radiation in the presence and absence of oxygen may be different. The ratio of doses under hypoxic and aerated situations to achieve the same biological effect is called oxygen enhancement ratio, OER.

$$OER = \frac{D_{\text{hypoxic}}}{D_{\text{aerated}}} \tag{5.1.12}$$

OER is dependent on radiation quality and is typical 2.5 to 3.5 for photons, 1.5 for neutrons and 1.0 for α-particles. Hypoxia is an important factor to consider in radiotherapy.

Relative biological effectiveness, RBE.
Different radiation qualities may have different effectiveness. The *relative biological effectiveness*, RBE, of some test radiation compared with a reference radiation is defined as

$$RBE = \frac{D_{\text{ref}}}{D_{\text{test}}} \tag{5.1.13}$$

where D_{ref} is the absorbed dose at the reference radiation quality at a certain biological endpoint and D_{test} is the absorbed dose at the test radiation quality at the same biological endpoint.

It is important to consider that RBE is defined for a certain biological endpoint, and may differ significantly when determining RBE at a cell survival for e.g. 50% or 10%. The radiation quality is often expressed in terms of LET (Linear Energy Transfer).

5.2 Exercises in Radiation Biology

Exercise 5.1. 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.

Exercise 5.2. Bacteria are irradiated by placing them in a radioactive solution with a β-emitting radionuclide. The number of surviving bacteria decreases with time (absorbed dose) approximately exponentially. This is assumed to confirm that the one-hit theory holds. 50% of the cells survive at an absorbed dose of 800 Gy. Estimate the sensitive volume in which the target theory assumes that one ionization kills the bacterium. The density of the bacterium = $1.35 \cdot 10^3$ kg m^{-3}, W_0= 110 eV. W_0 is the energy needed to inactivate the bacterium.

Exercise 5.3. A cell population is irradiated with 40.0 Gy (single irradiation). D_{10} (i e the absorbed dose that reduces the population to 10%) is 4.0 Gy, when the cells are irradiated at normal oxygen pressure.
a) Calculate the relative survival if it is assumed that the survival can be assumed to follow a single-hit, single target model without any repair.
b) Calculate the survival if 1% of the population is hypoxic (i.e. with low concentration of oxygen). D_{10} for hypoxic cells is supposed to be twice as large as for corresponding cells with normal oxygen pressure.

Exercise 5.4. A tumor has $1.0 \cdot 10^8$ cells. The tumor is irradiated with neutrons which means that one may assume that the survival curve is exponential. The D_0-value is 1.9 Gy. What absorbed dose is needed to obtain a probability of 1% that no cell survives? Assume that Poisson statistics may be used.

Exercise 5.5 The cell survival is often described by the linear quadratic model. A tumor with an α/β-ratio=10 Gy and β=$3.2 \cdot 10^{-2}$ Gy^{-2} is going to be treated. Normal cells will also be irradiated. These cells have an α/β-ratio = 3.0 Gy and β=$5.1 \cdot 10^{-2}$ Gy^{-2}. The treatment schedule implies 2.0 Gy every day for 30 days both for tumor cells and for normal cells. Calculate the survival of the two cell types. If the absorbed 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? Which is now the survival of the normal cells? If the absorbed dose instead is given in one treatment, which absorbed dose is needed to give the same tumor cell survival? Which is now the survival of the normal cells? Assume full repair between the treatments.

Exercise 5.6. Cells are irradiated with neutrons and in this case 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 RBE for a survival of 50% respectively 10% assuming that the reference quality is ^{60}Co photons.

Exercise 5.7. Cells are irradiated with neutrons and in this case their survival can be described using an exponential survival curve with D_0=1.5 Gy. When irradiating with photons the the survival curve has a shoulder and then an exponential part with a slope equal to the slope for the neutron irradiation. This curve is typical for what sometimes was described as a "single hit, multiple target model". When extrapolating the linear part of the curve to the absorbed dose, D=0, the extrapolation number n=3. Calculate the cell survival for a photon dose of 2.0 Gy. Which neutron dose would give the same cell survival? Assume that the patient is treated with photons in 30 fractions with 2.0 Gy per fraction. Calculate the cell survival in this situation assuming full repair between the fractions. If this survival should be obtained in a single dose, which absorbed dose is needed, for neutrons and photons?

Exercise 5.8. Chinese hamster cells irradiated with x rays show a cell survival according to Fig. 5.3. The data may be fitted with either the LQ model or the LQ-L model. Compare these two models with the experimental data, and plot them in a figure together with the experimental data. α=0.17 Gy^{-1}, β=0.06 Gy^{-2} and D_T=2α/β Gy. The cells are treated with a total absorbed dose of 20 Gy in fractions of a) 2 Gy and b) 10 Gy. Calculate the survival using the two models.

Exercise 5.9. Human melanoma cells are irradiated with ^{60}Co-γ-rays and ^{10}B ions with an LET of 160 eV nm^{-1}. The experimental survival curves are fitted with the LQ-model and the RCR-model. The parameters for the models are tabulated in Table 6.1.

Calculate RBE using the two models for a cell survival of 0.8 and 0.1.

Table 5.1: Parameters for the LQ- and the RCR models (Persson, 2002).

Radiation quality	LQ model	RCR model
^{60}Co	α = 0.047, β = 0.048	a=1.317, b=1.284, c=0.665
^{10}B	α = 0.712, β = 0.226	a=1.860, b=1.508, c=1.856

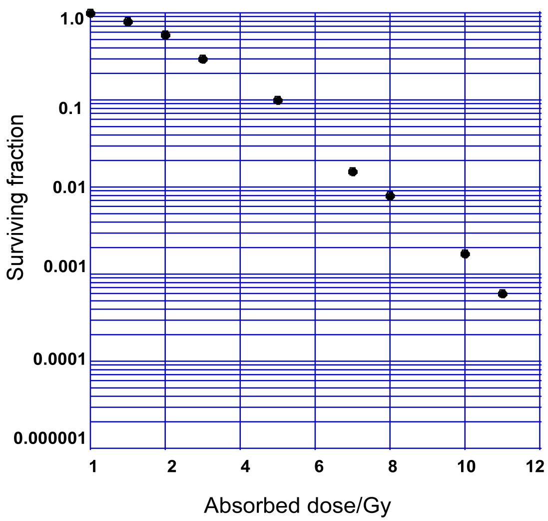

Figure 5.3: Cell survival for Chinese Hamster Cells.

5.3 Solutions in Radiation Biology

Solution exercise 5.1.
The plating efficiency (*PE*) is defined as

$$PE = \frac{\text{Number of colonies counted}}{\text{Number of cells seeded}} \tag{5.3.1}$$

The surviving fraction (SF) is obtained by

$$SF = \frac{\text{Number of colonies counted}}{\text{Number of cells seeded} \cdot PE} \tag{5.3.2}$$

The value of D_0 is obtained from

$$SF = e^{-D/D_0} \tag{5.3.3}$$

where SF is the surviving fraction, D is the absorbed dose and D_0 is the dose that reduces the survival to 37% of the initial number of cells.

Data:
Unirradiated cells: Number of cells seeded=100, number of colonies=75

Irradiated cells: Number of cells seeded=100, number of colonies=20

Data inserted gives

$$PE = \frac{75}{100} = 0.75$$

Surviving fraction

$$SF = \frac{20}{100 \cdot 0.75} = 0.267$$

This inserted in Eq. (5.3.3) together with D=2.0 Gy gives

$$0.267 = e^{-2.0/D_0}$$

This gives D_0= 1.51 Gy.

Answer: The mean lethal dose, D_0, is 1.5 Gy.

Solution exercise 5.2.
The energy E that is released in a volume v m^3 is given by

$$E = D\rho v \tag{5.3.4}$$

Number of "hits", n, in volume v is given by

$$n = \frac{D\rho v}{W_0} \tag{5.3.5}$$

where D is the absorbed dose and ρ the density of bacteria. W_0 is the energy needed to inactivate the bacterium.

For an absorbed dose D_0 (D_{37}) there is on average one hit (n=1) per bacterium if the survival curve is exponential. This gives

$$v = \frac{W_0}{D_0 \rho} \tag{5.3.6}$$

For these bacteria D_{50} is 800 Gy. The survival fraction for an exponential survival is given by

$$SF = e^{-D/D_0} \tag{5.3.7}$$

Data inserted gives

$$0.5 = e^{-800/D_0}$$

and

D_0= 1154 Gy

With ρ=1.35·10^3 kg m^{-3} and W_0=110 eV inserted in Eq. (5.3.6), v is given by

$$v = \frac{110 \cdot 1.602 \cdot 10^{-19}}{1154 \cdot 1.35 \cdot 10^3} = 1.13 \cdot 10^{-23}\ \text{m}^3$$

Answer: The active volume of the bacteria is $1.13 \cdot 10^{-23}$ m^3.

Solution exercise 5.3.
The survival fraction of cells is given by

$$SF = e^{-D/D_0} \tag{5.3.8}$$

With D_{10}=4.00 Gy for oxygenated cells, then D_0 is obtained from

$$0.1 = e^{-4.0/D_0}$$

Solving the equation gives $D_0 = -4.0/\ln 0.1$. Inserting this in Eq. (5.3.8) and setting D=40 Gy gives

$$SF = e^{10 \ln 0.1} = 10^{-10}$$

If the cells are hypoxic then D_{10}=8.00 Gy. The relative survival is then given by

$$SF = e^{5 \ln 0.1} = 10^{-5}$$

If in a population of cells, 1 % are hypoxic, then the total survival is given by

$$SF = 0.99 \cdot 10^{-10} + 0.01 \cdot 10^{-5} = 10^{-7}$$

The survival is dominated by the hypoxic cells.

Answer: The survival fraction is 10^{-10} for oxygenated cells and 10^{-7} for a population consisting of 99% oxygenated cells and 1% hypoxic cells.

Solution exercise 5.4.
The survival fraction of cells is given by

$$SF = N/N_0 = e^{-D/D_0} \tag{5.3.9}$$

where N is the average number of surviving cells after an absorbed dose of D Gy and N_0 is the number of cells before irradiation. Assume that the cell survival follows a Poisson distribution. Then the probability that n cells survive if there are N_0 cells initially and on average N cells survive is given by

$$P(n) = \frac{e^{-N} N^n}{n!} = \frac{e^{-N_0 e^{-D/D_0}} (N_0 e^{-D/D_0})^n}{n!} \tag{5.3.10}$$

The probability that no cell will survive is obtained by setting n=0. Thus

$$P(0) = \frac{e^{-N_0 e^{-D/D_0}} (N_0 e^{-D/D_0})^0}{0!} = e^{-N_0 e^{-D/D_0}} \tag{5.3.11}$$

Data:
D_0=1.9 Gy (mean lethal dose)
$P(0)$=0.01 (probability of no cell survival)
$N_0 = 10^8$ (number of initial cells)

Data inserted in Eq. (5.3.11) gives

$$0.01 = e^{-10^8 e^{-D/1.9}}$$

Taking the logarithm of the equation gives

$$\ln 0.01 = -10^8 e^{-D/1.9}$$

and D=32.1 Gy.

Answer: The absorbed dose needed to get a survival probability of 1% is 32 Gy.

Solution exercise 5.5.
Cell survival after one treatment for an absorbed dose D with the LQ-model is given by

$$SF = e^{-(\alpha D+\beta D^2)} \tag{5.3.12}$$

After N treatments the survival is

$$SF_N = [e^{-(\alpha D+\beta D^2)}]^N \tag{5.3.13}$$

Data:
D=2.0 Gy (absorbed dose)
N=30 (number of treatments)

Tumor cells
$\beta = 3.2 \cdot 10^{-2}$ Gy^{-2}, α/β=10 Gy $\Rightarrow \alpha = 0.32$ Gy^{-1}

Normal cells
$\beta = 5.2 \cdot 10^{-2}$ Gy^{-2}, α/β=3.0 Gy $\Rightarrow \alpha = 0.156$ Gy^{-1}

Data inserted in Eq. (5.3.13) gives

Tumor cells:

$$SF_{30} = [e^{(-0.32 \cdot 2.0 - 3.2 \cdot 10^{-2} 2^2)}]^{30} = 9.860 \cdot 10^{-11}$$

Normal cells:

$$SF_{30} = [e^{(-0.156 \cdot 2.0 - 5.2 \cdot 10^{-2} 2^2)}]^{30} = 1.679 \cdot 10^{-7}$$

The ratio of the survival tumor cells to normal cells is $9.860 \cdot 10^{-11}/1.679 \cdot 10^{-7}$=$5.87 \cdot 10^{-4}$.

If instead the absorbed dose per fraction is 1.0 Gy, the number of treatments for the same survival for tumor cells is given by

$$9.860 \cdot 10^{-11} = [e^{-(0.32 \cdot 1.0 + 3.2 \cdot 10^{-2} 1.0^2)}]^N = [e^{-0.352}]^N$$

and

$$N = \ln 9.860 \cdot 10^{-11}/(-0.352) = 65.45$$

Thus 65.45 treatments and 65.45 Gy are needed. This can compared with the absorbed dose 30x2 Gy = 60 Gy that was needed with an absorbed dose of 2.0 Gy per treatment.

The survival fraction of normal cells will in this situation be

$$SF_{65} = [e^{-(0.156 \cdot 1.0 + 5.2 \cdot 10^{-2} 1.0^2)}]^{65.45} = 1.224 \cdot 10^{-6}$$

The ratio of the survival tumor cells to normal cells is in this case $9.860 \cdot 10^{-11}/1.224 \cdot 10^{-6}$=$8.06 \cdot 10^{-5}$.

This gives a better ratio than for a treatment with 2.0 Gy per treatment as more normal cells will survive. However repopulation is not included in the calculations.

If the total absorbed dose is given in a single treatment, then with the same survival of the tumor cells, the absorbed dose will be given by

$$9.860 \cdot 10^{-11} = [-e^{-(0.32 \cdot D + 3.2 \cdot 10^{-2} D^2)}]$$

and

$$-\ln(9.860 \cdot 10^{-11}) = 0.32 \cdot D + 3.2 \cdot 10^{-2} D^2$$

giving

$$D = -\frac{0.32}{0.032 \cdot 2} \pm \sqrt{(\frac{0.32}{0.032 \cdot 2})^2 - \frac{\ln(9.860 \cdot 10^{-11})}{0.032}} = 22.3 \text{ Gy}$$

The survival fraction of normal cells will then be

$$SF = [e^{-(0.156 \cdot 22.3 + 5.2 \cdot 10^{-2} 22.3^2)}] = 1.81 \cdot 10^{-13}$$

The ratio of the survival tumor cells to normal cells is $9.860 \cdot 10^{-11}/1.81 \cdot 10^{-13}$=543. Thus in this case the survival of the normal cells is less than for the tumor cells.

Answer: The ratio between the survival of tumor cells and normal cells is $5.9 \cdot 10^{-4}$ with 2.0 Gy per treatment. With 1.0 Gy per treatment a total absorbed dose of 65.4 Gy is needed and the ratio between the survival of tumor cells and normal cells is $8.1 \cdot 10^{-5}$. For a single treatment an absorbed dose of 22.3 Gy is needed and the ratio between the survival of tumor cells and the normal cells is 543.

Solution exercise 5.6.

Neutrons:

The cell survival when irradiating with neutrons will give an exponential curve as the survival follows the single hit-single target model. Thus

$$SF = e^{-D/D_0} \tag{5.3.14}$$

With D_0=1.7 Gy the doses for 10% and 50% survival will be

$$0.1 = e^{-D_{10}/1.7}$$

and

$$0.5 = e^{-D_{50}/1.7}$$

respectively. This gives D_{10}=3.91 Gy and D_{50}=1.18 Gy.

Photons:

The survival follows the linear quadratic model. Thus the survival will be given by

$$SF = e^{-(\alpha D+\beta D^2)} \tag{5.3.15}$$

where α=0.15 Gy^{-1}, α/β=3.0 Gy and β=0.05 Gy^{-2}. This inserted in Eq. (5.3.15) gives the doses for 10 % and 50 % survival respectively.

$$0.1 = e^{-(0.15D_{10}+0.05D_{10}^2)}$$

and

$$0.5 = e^{-(0.15D_{50}+0.05D_{50}^2)}$$

Solving the equations give D_{10}=5.45 Gy and D_{50}=2.51 Gy

RBE is defined as the ratio of doses for the same effect or cell survival. Thus

$$RBE_{10} = 5.45/3.91 = 1.39$$

and

$$RBE_{50} = 2.51/1.18 = 2.13$$

Answer: RBE for 10% survival is 1.4 and for 50% survival 2.1.

Solution exercise 5.7.

Photons:

The cell survival is, assuming a single-hit multi-target model, obtained from the relation

$$SF = 1 - (1 - e^{-D/D_0})^n \tag{5.3.16}$$

where D_0=1.5 Gy (dose to reduce cell survival to 37% along the linear slope of the curve) and n=3 (extrapolation number).

Eq. (5.3.16) gives the survival fraction after an absorbed dose of 2.0 Gy

$$SF = 1 - (1 - e^{-2.0/1.5})^3 = 0.6006$$

With 30 fractions the survival fraction will be

$$SF = (1 - (1 - e^{-2.0/1.5})^3)^{30} = 2.284 \cdot 10^{-7}$$

If the absorbed dose is to be given in a single fraction, the absorbed dose for the same survival as from 30 fractions, will be obtained from

$$2.284 \cdot 10^{-7} = 1 - (1 - e^{-D/1.5})^3$$

D=24.6 Gy

This can be compared to 60 Gy needed in a 30 fraction treatment of 2 Gy.

Neutrons

The survival for neutrons is assumed to be exponential. Then the absorbed dose for a survival of 0.601 in one fraction is given by

$$0.601 = e^{-D/1.5}$$

D=0.765 Gy.

To obtain a survival fraction of $2.284 \cdot 10^{-7}$ for neutrons in a single fraction the absorbed dose needed is given by

$$2.284 \cdot 10^{-7} = e^{-D/1.5}$$

D=22.9 Gy.

Answer: The cell survival fraction for an absorbed dose of 2.0 Gy is 0.60 with photons. To obtain the same survival with neutrons an absorbed dose of 0.77 Gy is needed. The survival after 30 equal fractions with photons is $2.28 \cdot 10^{-7}$. To obtain the same survival in a single fraction, an absorbed dose of 25 Gy is needed for photons and 23 Gy for neutrons.

Solution exercise 5.8.
Assume that the survival follows the LQ model. The survival fraction will be given by

$$SF_{LQ} = e^{-(\alpha D+\beta D^2)} \tag{5.3.17}$$

where α=0.170 Gy^{-1} and β=0.06 Gy^{-2}.

The LQ-L model gives the survival fraction according to LQ model for doses below a dose D_{T} and for higher doses according to

$$SF_{LQ-L} = e^{-(\alpha D_{\mathrm{T}}+\beta D_{\mathrm{T}}^2+\gamma(D-D_{\mathrm{T}}))} \tag{5.3.18}$$

where

$$\gamma = \alpha[1 + (2D_{\mathrm{T}}/(\alpha/\beta))] \tag{5.3.19}$$

In this case, and it holds for many survival curves, $D_{\mathrm{T}} = 2\alpha/\beta$. Thus

$$\gamma = 0.17[1 + (2 \cdot 2)] = 0.85$$

Data inserted in Eqs. (5.3.17) and (5.3.18) gives the survival curves. The result is shown in Fig. 5.4. It is clear that for absorbed doses below around 5 Gy, both models agree with the experiments but for large absorbed doses the LQ-model underestimates the survival.

For a dose per fraction of 2.0 Gy, both models give the same result, and calculations can be made with the LQ model. An absorbed dose of 20 Gy in 2.0 Gy fractions will give a survival of

$$SF_{10} = (e^{-(0.170\cdot 2+0.06\cdot 2.0^2)})^{10} = 3.03 \cdot 10^{-3}$$

With a dose per fraction of 10 Gy, the two models will give different results.

<u>LQ model</u>
The survival will for a total dose of 20 Gy be

$$SF_{\mathrm{LQ},2} = (e^{-(0.170\cdot 10+0.06\cdot 10^2)})^2 = 2.05 \cdot 10^{-7}$$

<u>LQ-L model</u>
The corresponding survival will be with D_T=2·0.170/0.06=5.67 Gy.

$$SF_{\mathrm{LQ-L},2} = (e^{-(0.17\cdot 5.67+0.06\cdot 5.67^2+0.85(10-5.67))})^2 = 1.95 \cdot 10^{-6}$$

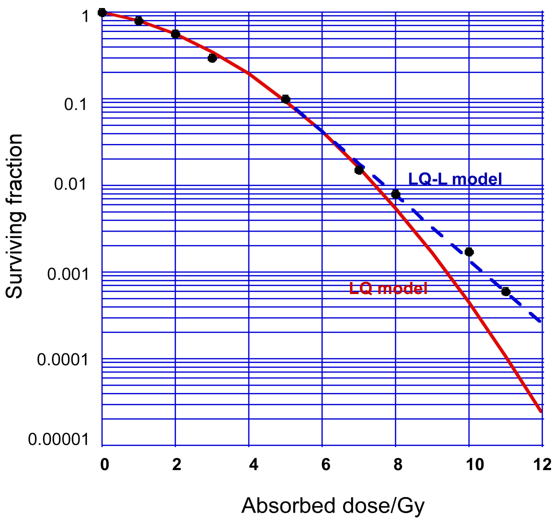

Figure 5.4: Cell survival for Chinese Hamster Cells. Experimental data and applied LQ model and LQ-L model respectively.

When treating patients with few fractions of large doses the LQ-model will give large differences compared to what is expected from cell survival data.

Answer: The survival with 10 fractions of 2.0 Gy is $3.03 \cdot 10^{-3}$ for both models. With two fractions of 10 Gy the survival is $2.05 \cdot 10^{-7}$ with the LQ- model and $1.95 \cdot 10^{-6}$ with the LQ-L model.

Solution exercise 5.9.
^{60}Co

<u>LQ model</u>

$$SF_{\mathrm{LQ}} = e^{-(\alpha D + \beta D^2)} \tag{5.3.20}$$

With α =0.047 Gy^{-1} and β =0.048 Gy^{-2}, the absorbed dose to achieve a survival rate of 80% is obtained by

$$0.8 = e^{-(0.047D + 0.048D^2)}$$

Solving the equation gives $D_{0.8}$=1.72 Gy.

A cell survival rate of 10% gives correspondingly $D_{0.1}$=6.45 Gy.

RCR model

$$SF_{\text{RCR}} = e^{-aD} + bDe^{-cD} \tag{5.3.21}$$

With a=1.317 Gy^{-1}, b=1.284 Gy^{-1} and c=0.665 Gy^{-1}, the absorbed dose to get a survival rate of 80% is obtained by

$$0.80 = e^{-1.317D} + 1.284De^{-0.665D}$$

Solving the equation numerically gives $D_{0.8}$=1.76 Gy.

A cell survival of 10% gives correspondingly $D_{0.1}$=6.70 Gy.

^{10}B ions

LQ model

With α =0.712 Gy^{-1} and β =0.226 Gy^{-2}, the absorbed dose to get a survival of 80% is obtained by

$$0.8 = e^{-(0.712D+0.226D^2)}$$

Solving the equation gives $D_{0.8}$=0.287 Gy.

A cell survival of 10 % gives correspondingly $D_{0.1}$=1.984 Gy.

RCR model

With a=1.860 Gy^{-1}, b=1.508 Gy^{-1} and c=1.856 Gy^{-1}, the absorbed dose to get a survival of 80% is obtained by

$$0.80 = e^{-1.860D} + 1.508De^{-1.856D}$$

Solving the equation numerically gives $D_{0.8}$=0.346 Gy.

A cell survival of 10% gives correspondingly $D_{0.1}$=1.986 Gy.

The RBE can now be determined

LQ model
$RBE_{0.8}$=1.72/0.287=6.0

$RBE_{0.1}$=6.45/1.984=3.3

<u>RCR model</u>
$RBE_{0.8}$=1.76/0.346=5.1

$RBE_{0.1}$=6.70/1.986=3.4

Answer: The RBE for 80% cell survival is 6.0 using the LQ-model and 5.1 using the RCR model. The RBE for 10% cell survival is 3.3 using the LQ-model and 3.4 using the RCR model.

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