Problem Set 5

1) Literature search:
Find a recent paper on the "Bystander Effect" and be prepared to briefly describe it in class on April 7 or 9.

2) An asynchronous population of 10^6 cells has the following cell cycle parameters:
$T_M = 1$ h; $T_{G1} = 15$ h; $T_S = 6$ h, and $T_{G2} = 2$ h.
a) What is the cell cycle time?
b) If the growth fraction is 1.0, how many cells are in the S phase?
c) Define growth fraction.
d) If the growth fraction is 0.5, how many cells are in mitosis?

3) The mean cell cycle time for the dividing cells in a tumor is 3 days (72 h).
a) If the growth fraction is 0.5 and there is no cell loss, what is the potential doubling time (T_{pot})?
b) Define cell loss factor.
c) List at least five ways that cells can be lost from a tumor.
d) From part a, if the cell loss factor is 0.8, what would be the potential doubling time?
e) For the tumor with parameters given in parts a and d, how would you predict that it would respond to radiation treatment? Explain your answer.

4) A researcher injects DU-145 human prostate cancer cells into the flank of a scid mouse on day 0. By day 5 the tumor measures 5 mm in diameter. Two weeks later, the tumor has grown to 2 cm in diameter.
a) What is the tumor volume doubling time?
b) When the tumor has reached the 2 cm diameter size, approximately how many cells will it contain? Do you think all the cells will be clonogenic? Why is it important to know how many cells are clonogenic?

5) A tumor consists of 10^8 clonogenic cells. The effective dose response curve, given in daily fractions of 1.8 Gy, has no shoulder and a D_0 of 3.3 Gy.   What total dose is needed to give a 90% chance of tumor cure?

6) Show that the difference between TCD_{10} and TCD_{90} is 3 x D_0.

7) The following Table gives the ED$_{50}$ values for myeloparesis (hind leg paralysis) in the rat following irradiation of a 2-cm region of cervical spinal cord.
a) Estimate the α/β ratio of the rat spinal cord for X rays and for neutrons.
b) What is the RBE of this neutron beam compared to x rays?

Treatment	Total Dose (Gy)
Single dose	
X rays	19.0
neutrons	13.6
Two fractions	
X rays	25.8
neutrons	14.7
Four fractions	
X rays	35.2
neutrons	15.5

8) Two different human prostate cancer lines are grown as solid tumors in scid mice. Cells from tumor line A have an SF$_2$ of 0.6, while cells from tumor line B have an SF$_2$ of 0.3 in clonogenic assays.
a) Excluding effects of tumor microenvironment and cell proliferation during fractionation, what would be the expected SF of each tumor line after 30 2-Gy fractions?
b) What is one tumor microenvironment factor that might change the radiation response from that calculated, and how would you expect it to alter the response (i.e., increase or decrease radiation sensitivity)?

9) A cancer patient is given a tracer injection of BrdUrd and 5 hours later a tumor biopsy is taken. Flow cytometry shows that 15% of cells have incorporated the BrdUrd, and analysis using the dual fluorescence method indicates a Relative Movement of 0.3.
a) Calculate the potential doubling time, T$_{pot}$.
b) If the growth fraction of this tumor is 0.35, calculate the tumor volume doubling time, and the cell cycle time.
c) If the cell loss factor of this tumor is 0.9, what would be the tumor volume doubling time?

10) The ED$_{50}$ for myeloparesis in the spinal cord (a late effect) is found to be 33 Gy when given in 10 fractions of 3.3 Gy each. How many fractions are needed to produce the same effect if the dose per fraction is lowered to 1.8 Gy? Assume that the overall treatment time is the same.

11) A fractionation schedule of 60 Gy given in 30 fractions of 2 Gy each produces an acceptable level of side effects in the normal brain (late effects).
a) Find a fractionation schedule using 1.65 Gy per fraction that gives the same level of late effects in the brain.
b) Which schedule would be more effective against a brain tumor? Why?