AbstractID: 11855 Title: A Simple Kinetic Model with a Mechanistic Basis for Tumor Survival Curves

Purpose: To develop a simple kinetic model for tumor survival curves which is able to describe their behavior for high and low LET clinical applications and at the same time can provide a relation to the mechanisms for DNA damage and repair.

Method and Materials: Analytical and numerical solution of a nonlinear set of equations

$$\frac{dN}{dt} = \left[-\alpha_0 \ln\left(\frac{N}{N_\infty}\right) - (1+\gamma)\kappa_{RAD}(t) \right] N + \kappa_{REP} N_R$$

$$\frac{dN_R}{dt} = \kappa_{RAD}(t)(N - N_R) - \kappa_{REP} N_R$$

$$\frac{dN_{NR}}{dt} = \kappa_{RAD}(t)(N_R + \gamma N)$$

where N is the number of clonogenic cells with undamaged DNA, N_R is the number of cells with reversible DNA damage and N_{NR} is the number of cells with irreversible DNA damage. At the same time α_0 and N_∞ are Gompertz model parameters and κ_{REP} is the probability per unit time for DNA repair. The probability per unit time for radiation reversible damage of DNA is given by $\kappa_{RAD}(t)$, as well as $\gamma\kappa_{RAD}(t)$ is the probability per unit time for radiation irreversible DNA damage. A study of limit cases for the solution behaviour is made for several cases in order to find the relation between the linear-quadratic model parameters and those of the proposed kinetic model, which is going to make easier its clinical application.

Results: The proposed model is able to describe the proper behavior at low and high LET for V-79 cells in late S phase. The values obtained for the new set of parameters and clinical applications related to fractionation are discussed.

Conclusion: It is possible to develop simple microscopic models based on DNA damage and repair mechanisms in order to describe tumor survival curves. DNA damage has to be considered in two steps, one reversible and another irreversible. Its relation with the linear-quadratic model can be helpful in order to implement its clinical application.

Conflict of Interest (only if applicable): None