

AbstractID: 3127 Title: Tumor Resensitization during Fractionated Radiotherapy: Modeling and Fitting data from animal experiments

**Purpose:** To further develop the modeling of tumor dynamics, we propose a mechanism of tumor resensitization based on reoxygenation, leading to the derivation of a time-dependent expression for the radiosensitivity,  $\alpha(t)$ , that can be incorporated into tumor control probability (TCP) models used to fit fractionated dose response data.

**Method and Materials:** To model the process of reoxygenation, we first assume that a tumor's radiosensitivity is dictated by the oxygenation level of an inner core of tumor cells, which is initially hypoxic, and thus radioresistant. Using an equation to describe the diffusion of oxygen to this inner core from outer tumor layers, and by presuming a relationship between  $\alpha$  and the oxygen concentration, an expression for  $\alpha(t)$  can be derived. This expression is then incorporated within a TCP model that already includes tumor cell repopulation and repair. We fit a published set of experimental animal TCP curves corresponding to several different fractionation regimes using both the modified (with resensitization) and unmodified (without resensitization) versions of the TCP model. To investigate the importance of the  $\beta$  mechanism, we also fit a version of the model *with* resensitization in which the linear-quadratic (LQ) parameter  $\beta$  was set to zero.

**Results:** The modified model *with* resensitization, and with a non-zero  $\beta$  component, produced statistically superior fits. Specifically, only this model was able to describe an "inverse" dose-fractionation behavior present in the data, which indicated that less dose was required to achieve a given tumor control with five fractions than with three.

**Conclusion:** Resensitization and the  $\beta$  mechanism may be important in the description of the dose-response for a small number of fractions. Since it may in the future be possible to alter radiotherapy schemes after monitoring the tumor response in the first few treatments, consideration of such factors may prove clinically useful.