AbstractID: 2965 Title: Theory of parameter correlation in a population tumor control model assuming high heterogeneity in the radiosensitivity

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Purpose: In this work we present a theoretical investigation of the parameter correlation in a population tumor control model assuming high population heterogeneity in the radiosensitivity.

Method and Materials: A number of authors have shown that ambiguity exists when radiobiological parameters are obtained by fitting population dose response data with a heterogeneous (population) tumor control model. The difficulty is that many different sets of parameter values can be used to construct TCP curves that are identical. These sets of parameters may be described as linear combinations of parameters. We use the Roberts and Hendry (1998 *IJROBP* **41** 689-699) closed formula to investigate this ambiguity.

Results: The Roberts and Hendry closed formula can be reduced to depend on two generalized parameters. For our analysis we introduce the following notation: TCP = $\Phi(\delta)$, $\delta = (\gamma - \kappa)/\sigma$, where $\kappa = (\alpha + \beta d - \lambda/d)D - \ln(k)$, $\sigma = \sigma_\alpha D$, and $\gamma = 0.577$ (Euler gamma constant). When the model is plotted in the κ–σ space, the iso-TCP lines are linear, and intersect at the point $\kappa = \gamma$, $\sigma = 0$. Parameter correlation occurs when combinations of $\alpha' = (\alpha + \beta d - \lambda/d)$, σ_α and $\ln(k)$ produce the same value of TCP for any value of the dose, D. This correlation can be proven by two methods: analytic or geometric. The specific form of the parameter correlation is: $\alpha' D_{50} - \ln(k) = \gamma$, ($D_{50}$ is the dose D where TCP(D)= 50%) and $\sigma_\alpha/\alpha' =$ constant.

Conclusion: When fitting a high heterogeneity TCP population model to clinical data, parameter correlation between the quantities ($\alpha + \beta d - \lambda/d$) and $\ln(k)$ exist. A linear relation characterized by a slope of $1/D_{50}$ represents this correlation.