AbstractID: 6584 Title: An analytic investigation of the effect of inter-patient heterogeneity on alpha/beta ratio estimates for tumors

Purpose: To analytically determine the relationship between the α/β ratio that would be obtained by fitting the individual (non-averaged) tumor control probability (TCP) model to clinical data and the α/β estimate from a fit of the population-averaged TCP model to the same clinical dose-response dataset.

Method and Materials: Recently, Carlone *et al*. (Med. Phys., 2006. 33(6): p. 1634-42) published fundamental forms of the population TCP model for the limits of dominant heterogeneity in radiosensitivity, and in clonogen number. In each case, the model is parameterized by γ_{50} and D_{50}. The individual Poisson TCP model has also been expressed in terms of these geometric parameters. Since the functional forms of these TCP models are similar, approximately the same γ_{50} and D_{50} values would be obtained for each model if they were fit to the same clinical dataset. This fact allows us to determine mapping relationships between parameter ratio estimates obtained from fits using the averaged or non-averaged TCP model. Mapping relationships are determined for the case of dominant heterogeneity in clonogen number, and in radiosensitivity.

Results: When heterogeneity in clonogen number dominates a clinical dataset, the individual and population-averaged α/β estimates are virtually identical. However, for the case where heterogeneity in radiosensitivity dominates, the individual α/β estimate will not be the same as the corresponding population α/β estimate.

Conclusion: Heterogeneity in radiosensitivity is believed to be the dominant form among clinical datasets. Hence, our analytic expressions suggest the individual α/β ratio estimate should be different from the population estimate. Because of this ambiguity, we suggest that modelling has limited value in α/β determination; only the clinical hypofractionation trials will have the ability to validate the hypothesis originally put forth by Brenner and Hall (IJROBP, 1999. 43(5): p. 1095-1101) that prostate cancer responds to fractionation as does a late responding tissue.