

AbstractID: 2540 Title: Dose-volume Modeling & Clinical Radiotherapy: the Art of Systematic Oversimplification

Science has been called “the art of systematic oversimplification” (Popper). Using this as a criterion, dose-volume modeling is a very scientific discipline! A flurry of more or less mechanistic models has been proposed but despite their conceptual appeal these models are obviously oversimplified representations of what we know about the radiation pathogenesis of side-effects of radiotherapy. From an empirical point of view, most clinical data sets do not provide sufficient structural resolution to allow validation of – or even discrimination between – any of these. Perhaps it is symptomatic that the most widely used, and in some sense most successful, dose-volume model is the “post-modern” model proposed by Lyman 20 years ago. Notwithstanding these philosophical concerns, dose-volume modeling has established itself as an exciting research field and a very useful tool in this age of conformal and intensity-modulated radiotherapy. Arguably, the use of these oversimplified models has greatly expanded and intensified the systematic collection and analysis of dose-volume data. It is tempting to draw a parallel to the use of the linear-quadratic model: originally this was closely linked to the target-cell hypothesis, a point of view that has all but disappeared now, where most researchers see the model as a pragmatic means of condensing empirical clinical data. Dose-volume models are currently used at two levels: to obtain a figure of merit for rival radiotherapy plans in daily routine planning and in the development of novel radiotherapy protocols to be tested in clinical trials. While current models have some credibility in the former application, they fail miserably in producing reliable, portable estimates of the absolute incidence of complications when applied in independent data sets or when extrapolated to considerably different dose distributions. This is not entirely the fault of the models: reliable estimates of the incidence of normal-tissue effects after radiotherapy are generally not available even in case of a uniform dose-distribution delivered to a critical structure. In the presentation, I will discuss dose-volume models from the perspective of evidence based medicine. How can these models be used in clinical trials design? And what are the most promising directions for future research? The possible effect of low-dose hyper-radiosensitivity and the challenge of incorporating the effect of cytotoxic drugs into dose-volume models will be discussed.

Educational Objectives:

1. To understand the strengths and weaknesses of current dose-volume models from the perspective of evidence based medicine.
2. To identify directions for future research on the clinical application of dose-volume models