AbstractID: 7858 Title: Biological/clinical Outcome Models in RT planning

The use of mathematical models to summarized clinical or biological endpoints with respect to the distribution of dose throughout an organ or tissue has great appeal. At its best, the overall cumulative effects of all parts of a heterogeneously irradiated object could be summarized in terms of a clinically relevant outcome such as a tumor control probability (TCP) or a normal tissue complication probability (NTCP). Further, it could be anticipated that a treatment planner would want to incorporate such information directly into the optimization of treatment planning parameters.

Despite this appeal, integration of these concepts into mainstream treatment planning has been slow in coming. Parameterization of the models is conceptually simple, requiring input data consisting primarily of dose, volume and outcome information from groups of patients. However, uncertainties in accumulated total effective dose and differential irradiated volumes together with heterogeneities in biological responses can make these determinations difficult. At best, it has been possible to obtain broad "population" based model parameters for some organs and tumors for "groups of similarly-treated patients". In general, as used today, these models are not within themselves (i.e., without additional stratification factors) "predictive" of outcome for "individual" subjects, nor can their use be generally extrapolated to the treatment of populations with techniques that vary greatly from those originally used.

However, disclaimers aside, the appeal remains great, and real progress has been made. In this session we will present some of the basic concepts associated with the models. Examples will be given as to how the models accommodate the responses of different tumor types and so-called serial and parallel normal tissues. We will show how (as currently used) implementation of the models in evaluation or planning generally first requires reduction of a complex dose distribution (or DVH) into an equivalent "uniform" total (or partial) object dose.

Examples where the biological models appear to work well to describe the response of groups of patients will be provided. Specifically, the use of NTCP models for planning the treatment of tumors surrounded by volume effect normal tissues will be demonstrated, as will the use of EUD to allow rational heterogeneous irradiation of target volumes.

Some technical details associated with the implementation of biological models into IMRT planning systems will be discussed. Since mathematical structures of biological models are nonlinear, an optimization algorithm that can explicitly handle nonlinear objective and constraint functions is important. We will describe various ways of incorporating the models into optimization problems.

This session will be concluded with a short survey of existing software tools that utilize the biological models for dose-response data analysis, plan evaluation, and IMRT plan optimization.

Educational Objectives:

1. Understand the basis and statistical nature of standard NTCP and TCP models.
2. Recognized that dose distribution reduction remains a basic component of their implementation and understand how this is accomplished.
3. Appreciate that as currently used, most results apply to "populations" of "similarly treated" patients
4. Understand numerical issues of implementing and using the biological models within optimization systems