Historically, RT fields/doses were selected based on clinical experience and intuition. Clinicians generally recognized the imprecision of these empiric guidelines, as they did not reflect the underlying three-dimensional anatomy, physiology, and dosimetry. A great promise afforded by 3D imaging was an improved quantitative relationship between 3D doses/volumes and outcomes. When 3D dosimetric information became more widely available (late 80s-early 90s), 3D guidelines were needed. In 1991, multiple investigators pooled the available, albeit sometimes limited, information regarding leading to the often-quoted "Emami paper" (IJROBP 1991).

During the last 20 years, additional 3D dose/volume/outcome data has become available. A central goal of QUANTEC is to summarize this information in a clinically useful manner. For each organ, the literature providing meaningful dose/volume/outcome data is reviewed. Clinical/treatment variables that may impact the application of the data is discussed. Where available, NTCP-model parameters are provided. We hope this information will improve patient care by providing clinicians and treatment planners with the tools necessary to determine the "optimal" 3D dose distribution for each individual case.

Nevertheless, the information provided herein is not ideal, and care must be taken to apply it correctly. Unfortunately, the data are incomplete for essentially almost every organ. The user must recognize the limitations inherent in extracting/pooling literature data. For some complications, some studies summarize their findings in terms of models that can be used to estimate risk. Extreme care should be taken when such models are applied clinically, especially when clinical dose/volume parameters are beyond the range used to generate the model. Models that rely on DVH data discard all spatial information (and hence inherently assume that all regions of an organ are functionally equally important), and often do not consider variations in fraction size (a particular concern with the increasing use of hypo-fractionated schedules). Similarly, the increasing use of RT combined with concurrent chemotherapy, with rapidly evolving drugs/doses, questions the validity of historic data to modern times.

For essentially all patients with curative cancers, a marginal miss is a more serious complication than is a normal tissue injury. Care must be taken not to compromise target coverage to reduce the normal tissue risks. A clinical balance is needed. Further, palliation in patients with recurrent/metastatic/incurable disease, with limited expected survival, often requires one to exceed "tolerances", as concern for late effects may not be applicable (e.g. RT fields for locally advanced lung cancer may include large volumes of lung and heart and withholding RT due to the risk of pericarditis, or pneumonitis, may not be "therapeutically rational"). These concerns are most applicable to our youngest generation of recently-trained radiation oncologists. Such individuals have become accustomed to having 3D dosimetric information available for every case, and rely on such data for many of their clinical decisions. These physicians may be uncomfortable in clinical settings wherein large radiation fields need to be applied in a relatively rapid fashion (i.e. without 3D dosimetry) in order to provide effective palliation.

## **Educational Objectives**

- To understand the rationale, methodology and background of QUANTEC (QUAntitative Normal Tissue Effects in the Clinic)
- To broadly understand the clinical organ-specific findings in QUANTEC

- To understand the differences between the QUANTEC review and the prior Emami review.
- To recognize the limitations of QUANTEC and the opportunities for improvement in predicting normal tissue toxicity from radiation therapy