AbstractID: 2538 Title: Outcome prediction models in radiotherapy: methods for improvement and future uses

Historically, the ability to predict a patient's outcome to a course of radiation therapy has been very limited. Knowledge of a patient's likely response to a given therapy was quantified by the maximum slope of the sigmoidally-shaped patient population dose response curve: steep slopes correspond to precisely known individual dose thresholds, whereas shallow slopes correspond to poorly quantified individual dose thresholds. In the 3-D treatment planning era, the situation has been fundamentally altered: it is no longer adequate to characterize dose distributions by a single number, as the effect of any distribution, especially on normal tissues which are often non-uniformly irradiated, may depend in a complex way on the spatial distribution. It has been recognized for more than 60 years that irradiated organ volume can dramatically affect response. Efforts to quantify the 'volume-effect' began in earnest in the late 1980's, but have recently gained much more momentum and effectiveness due to the advent of 3-D treatment planning. In most investigations to date, the dose-volume histograms of irradiated organs or tissue structures are analyzed to determine the dose parameters which most correlate with outcome. Remarkably, most organ responses appear to fall (very roughly) into just two categories: in Group I, complication risks rise according to the volume given a dose above a relatively high-dose threshold (typically 50-60 Gy). These organs include the spinal cord, brain stem esophagus, rectum, and small bowel. In this group, organ function is related to organ structure. In Group II, complication risk is correlated with the mean dose or something similar; functional ability is partially impaired even at relatively low doses. This response group includes parotid glands, brain, liver, and lung. Simplified dose-response models were developed by Kutcher, Burman, Brahme, Niemierko and others which reflected this range of response behavior. However, those analyses are far from utilizing the full potential of image-based 3-D treatment planning, based as they are only on cumulative dose-volume-histogram (DVH) data. Moreover, they ignore other potential clinical risk factors, such as diabetes, age, etc. In this talk we will estimate the trajectory of evolving dose-volume-outcomes models, including the need to search for potential variations in functional sensitivity vs. anatomical location, the inclusion of patient and disease risk factors, the need for advanced modeling techniques, and the future use of other biomarkers (imaging or gene analysis-based) in combined models. Methods to deal with the crucial need to accelerate inter-institutional data collection, modeling, and public archiving will be discussed. Lastly, we will discuss the inevitable move towards treatment planning based on outcomes models (e.g., maximizing the probability of tumor control with acceptable complication risks), and how we can get there from here.