AbstractID: 7789 Title: OPTIMISING RADIOTHERAPY USING NTCP MODELS: 17 YEARS in ANN ARBOR

Phase One clinical trials seek to determine the maximum tolerated dose (MTD) of the investigational treatment. Similarly, traditional radiation oncology dose escalation trials assign groups of patients to increasing dose levels until an unacceptable level of complications appear. This generally transpires on a sequential basis, regardless of tumor size or the distribution pattern of radiation dose to surrounding normal tissues (beyond the specification of a few well-accepted dose constraints such as maximum spinal cord dose). This can be a poor strategy for treatments limited primarily by complications to so-called volume-effect normal tissues which encompass the tumors, such as may be the case for tumors located in the liver or lung. A better scheme for Phase I/II dose escalation trials limited by these volume effect organs would attempt to treat sequential groups of patients with dose "distributions" that might be expected to lead to similar anticipated levels of complications (but of course with different tumor doses); with sequential escalation of each potential iso-complication level until an MTD profile is realized (which would inherently include the volume effect). The use of normal tissue complication probability (NTCP) models prospectively, in the treatment planning process, facilitates this type of normal tissue iso-complication based dose escalation.

Given the desire for iso-NTCP based dose escalation, clinical trials were developed and carried out at the University of Michigan for tumors located in the liver and lungs. In the 3-D conformal therapy era, these trials took place via recognition of one particular aspect of the effective volume (V_{eff}) dose volume histogram (DVH) reduction scheme (due to Kutcher and Burman) often employed in order to use the Lyman NTCP model for non-uniformly irradiated organs. That is, computation of a normal tissue V_{eff} for a particular dose distribution does not depend on the units of dose in the treatment plan (e.g., Gy, cGy/hr, or of greatest interest here, % dose). Given this, we recognized that treatment planning could proceed in the normal manner of that time (dose distributions generated in relative dose (%) with respect to an ICRU reference point prescription dose (most often the isocenter)), while at the same time attempts could be made to minimize the V_{eff} of the dose limiting normal tissue, with ultimate physical isocenter normalization dose (D_{norm} in Gy) prescribed after planning. That is, each V_{eff} has a corresponding D_{norm} leading to a fixed iso-NTCP level. Thus, reductions in V_{eff} generated during treatment planning, led to individualized increases in prescription isocenter dose after planning (a perceived benefit/goal for the treatment planner), all at fixed perceived level of NTCP. In the IMRT/optimization era, biological cost functions have been developed to accomplish these same goals.

This talk will summarize experiences in iso-NTCP dose escalation and planning at the University of Michigan for tumors in the liver and lungs; including current, ongoing, functional imaging based, adaptive treatment trials. Work supported in great part by NIH grant P01-CA59827

Educational Objective:

Understand the basis and ongoing use of iso-NTCP based dose escalation at the University of Michigan.