

AbstractID: 1311 Title: Modeling Subclinical Tumor Cell Burden within the Clinical Target Volume and Its Dose Response to Radiation Therapy

The concept of clinical target volume (CTV) is often used in intensity modulated radiation therapy (IMRT) to specify anatomic regions harboring subclinical disease. A distinction has been made between CTV as a perceived direct microscopic extension of gross tumor volume (GTV) and that resulting from stochastic formation of metastases (often treated prophylactically). The former entity is dictated by the limiting resolution of diagnostic imaging. For the latter, we propose here a biophysical model based on the kinetics of metastatic formation in order to interpret radiation dose-response relationships for the subclinical disease. Specifically, the metastases control probability (MCP) was formulated as a function of radiation dose and metastatic cell burden (MCB), which in turn was derived from the kinetics of primary tumor growth and subsequent metastatic colony formation and growth. By first empirically assuming a *log-uniformly* distributed MCB and excluding patients without subclinical metastasis, our model predicted a sigmoid-shaped MCP curve with a slope that is flatter than the control probability for GTV, in agreement with published clinical observations. However, using a mechanistic model, an explicit stochastic expression for the metastasis-free subset was obtained by subjecting all patients to undergo a Poisson process of metastatic establishment. Numerical simulations confirmed that the sigmoid MCP curve has a shallower slope if a *log-normally* distributed metastatic rate or a Gaussian distributed metastatic colony growth rate is considered. This mechanistic model of metastatogenesis appears to be a versatile tool for clinical application, and may help in formulating appropriate therapeutic strategies for subclinical metastases using IMRT.