Radiation Carcinogenesis Risk as Influenced by Intercellular Interaction

Philip Hahnfeldt[1], Lynn Hlatky[1], Rainer K. Sachs[2]

[1]Center of Cancer Systems Biology, Caritas St. Elizabeth's Medical Center, Tufts Univ. School of Medicine, Boston, MA, USA; [2]Departments of Mathematics and Physics, University of California, Berkeley, CA, USA

Accurate assessment of radiation carcinogenesis is not only an important health objective, but offers mechanistic insight into the evolution of cancer in unexposed individuals. Historically, elucidation of the sequence of molecular events leading to carcinogenic transformation of the first tumor cell has been the basis for cancer risk assessment. But while the subsequent influence of tumor microenvironment on risk is crucial, it has not been explicitly included in standard radiation risk analysis. Our multi-stage tumor-environment interaction (MSTEI) model extends our deterministic rendering of the Two-Stage Clonal Expansion model – the widely-utilized stochastic standard – by considering intercellular interactions and late-stage progression in more detail. Beyond explaining epidemiologic incidence data for solid tumors, this model takes into account microenvironmental influences that may substantially modify or even terminate a cancer course considered inevitable under current biologically-based risk analysis. This inclusion is necessary in light of recent data showing that virtually all middle-aged individuals have microscopic, indolent tumors, while only a much reduced portion of them will ever present with clinical cancer.