

“Two Stage Clonal Expansion Models of Carcinogenesis for Acute, Continuous, and Multiple Exposure with Applications to Radiation”

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ABSTRACT

Extended two-stage clonal expansion models of carcinogenesis are proposed to suit acute, continuous and multiple exposures respectively. Within the piece-wise constant parameter framework, these models will provide analytical formulas for the survival and hazard functions of the model under different conditions. To verify the proposed models, the JANUS dataset of mouse experiment (conducted by Argonne National Laboratory) will be used for acute and multiple acute exposure cases. However, for verification under continuous condition, a different data set, beagle dog data (conducted by Inhalation Toxicology Research Institute (ITRI) and Battelle Pacific Northwest Laboratory (PNL)) will be used to investigate the association between radiation and cancer, in terms of cumulative hazard, with the biokinetics of radionuclides incorporated in the model.

The derivation of analytical formulas for the survival and hazard functions of the models, instead of recursive / numerical forms, will greatly facilitate estimation of the parameters by simplifying the maximum likelihood estimation, and investigation of the properties of survival and hazard functions.

Although the applications in this study will focus on radiation carcinogenesis, the improved models are not limited to such applications. Investigations of the risks of cancer induced by exposure to chemicals will benefit.