**A Comparative Modeling Study on Intestinal Crypt Dynamics of Steady State and After Radiation**

Shaowen Hu

KBRwyle, Houston, Texas, USA, shaowen.hu-1@nasa.gov

The epithelium lining the small intestinal tract of mammals consists of a layer of columnar cells folded into villi and crypt that are renewed every few days. High-dose radiation exposures could injure and deplete the proliferative cells at the bottom of crypt and induce gastrointestinal radiation syndrome. In this work we investigate comparatively two sets of mathematical models of crypt dynamics for the small intestinal of BDF1 mice. The spatial model considers multiscale biological processes occurring at the subcellular, cellular, and tissue levels of organization [1], while the compartmental model looks at three cellular groups that are in different stages of maturity and differentiation [2]. To obtain results of population kinetics and proliferation indices comparable to observations in unirradiated and acutely irradiated experiments, the spatial model needs to carefully consider and delicately interlink many factors such as crypt geometry, intercellular forces, cell division rules, stem cell niche structure, cell killing scheme, cell cycle parameters, etc. In addition, the parameters governing various processes at different levels need to be finely tuned as it is demonstrated that small perturbation of some parameters leads to drastically different results. Though complicated, the spatial model allows us to test the validity of basic biological rules at the cellular level and radiation response mechanisms at the subcellular level, and has the potential to further incorporate the radiation effects at other biological scales such as radiation induced genetic mutation, chromosomal aberration, DNA damage, and radiation track structure. On the other hand, the compartment model in this work uses only 10 experimentally measured cell kinetic and radiosensitivity parameters and applies limited assumptions of cellular regulation. Nevertheless, the simple model can simulate population kinetics and proliferation indices observed in chronically and acutely irradiated experiments, indicating an ideal approach to characterize the intestinal injury and gastrointestinal radiation syndrome in human. By quantitatively comparing simulation results with published research, both modeling approaches can enhance our understanding of the pathophysiologic effects of ionizing radiation on the small intestinal of mammals, and can be extended to model radiation induced tumorigenesis in colon and other organs.

**REFERENCES:**

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[2] Smirnova O.A., (2009) Blood and small intestine cell kinetics under radiation exposures: mathematical modeling. *Advances in Space Research* 44,1457–1469.