**A New Model of Short- and Long-term Effects of Exposure to Ionizing Radiation in Hematopoietic System of Human**

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In this report we present a new model of the hematopoietic system for humans exposed to chronic and acute ionizing radiation (IR). This model is capable of describing both short-term deterministic effects represented by the process of the loss and replacement of cells and long-term stochastic effects such as carcinogenesis. The model combines and further extends the ideas used in: i) models of hematopoietic system as formulated and developed by Mackey and colleagues, and ii) the carcinogenesis model of breaking barrier mechanisms recently developed by our group.

The generalized model of hematopoiesis relates the hematopoietic stem cell compartment with all lines of peripheral blood (red blood cells, white cells and platelets). Exposure to IR is described within the one-hit-one target theory, though the generalizations to include more sophisticated approaches as well as bystander effect are discussed. The concept of breaking barrier mechanisms is used to describe carcinogenesis represented as a dynamic trade-off between two antagonistic forces or processes, promoting or hindering carcinogenesis at its different stages (initiation, promotion, conversion).

The model was formulated in such a way that it represents the three levels of the organism's vital organization: i) a cellular level, where the dynamics of the processes of cell kinetics, reparation, and apoptosis, are defined, ii) a level of human organism, where covariates describing health states are measured, and iii) a population, where such characteristics as incidence and mortality rates associated with cancer are predicted.

One advantage of the suggested modeling approach is in the possibility of the natural combining of different measurements including age-specific hazard rate and measures, characterizing fractions of cells with breaking barriers. Another advantage is in the broad spectrum of areas of potential applications, including: i) further investigation of mechanisms of health effects induced by IR, i.e., carcinogenesis or reactions of radiosensitive tissues, ii) development of strategies of radiation protection through calculating risks for specific population groups, iii) investigation of normal tissue reaction during radiological treatment in radiation oncology, iv) biodosimetry, v) radiobiology, e.g., investigating IR induced genomic instability, and vi) development of methods of individual prognostication.

The model can be estimated using information on characteristics of hematopoiesis and cell damage by IR available in literature. Using the estimated model we performed simulation studies allowing for identification of dose characteristics of acute or chronic exposure for which disorders in hematopoietic systems occur in a



Article published by EDP Sciences and available at http://www.radioprotection.org or http://dx.doi.org/10.1051/radiopro:2008688

certain fraction of the exposed population.