THE ANALYSIS OF THE PATTERNS OF RADIATION-INDUCED DNA DAMAGE FOCI BY A STOCHASTIC MONTE CARLO MODEL OF DNA DOUBLE STRAND BREAKS INDUCTION BY HEAVY IONS AND IMAGE SEGMENTATION SOFTWARE

A. Ponomarev[1], F. Cucinotta[2]
[1]*3600 Bay Area Blvd., Life Sciences, USRA, Houston, TX 77058*
[2]*NASA Johnson Space Center, Human Research Program, Space Radiation Element, Mail Code SK37, Houston, TX 77058*

E-mail: artem.l.ponomarev@nasa.gov

Purpose: To create a generalized mechanistic model of DNA damage in human cells that will generate analytical and image data corresponding to experimentally observed DNA damage foci and will help to improve the experimental foci yields by simulating spatial foci patterns and resolving problems with quantitative image analysis.

Material and Methods: The analysis of patterns of RIFs (radiation-induced foci) produced by low- and high-LET (linear energy transfer) radiation was conducted by using a Monte Carlo model that combines the heavy ion track structure with characteristics of the human genome on the level of chromosomes. The foci patterns were also simulated in the maximum projection plane for flat nuclei. Some data analysis was done with the help of image segmentation software that identifies individual classes of RIFs and colocolized RIFs, which is of importance to some experimental assays that assign DNA damage a dual phosphorescent signal.

Results: The model predicts the spatial and genomic distributions of DNA DSBs (double strand breaks) and associated RIFs in a human cell nucleus for a particular dose of either low- or high-LET radiation. We used the model to do analyses for different irradiation scenarios. In the beam-parallel-to-the-disk-of-a-flattened-nucleus scenario we found that the foci appeared to be merged due to their high density, while, in the perpendicular-beam scenario, the foci appeared as one bright spot per hit. The statistics and spatial distribution of regions of densely arranged foci, termed DNA foci chains, were predicted numerically using this model. Another analysis was done to evaluate the number of ion hits per nucleus, which were visible from streaks of closely located foci. In another analysis, our image segmentaiton software determined foci yields directly from images with single-class or colocolized foci.

Conclusions: We showed that DSB clustering needs to be taken into account to determine the true DNA damage foci yield, which helps to determine the DSB yield. Using the model analysis, a researcher can refine the DSB yield per nucleus per particle. We showed that purely geometric artifacts, present in the experimental images, can be analytically resolved with the model, and that the quantization of track hits and DSB yields can be provided to the experimentalists who use enumeration of radiation-induced foci in immunofluorescence experiments using proteins that detect DNA damage. An automated image segmentaiton software can prove useful in a faster and more precise object counting for colocolized foci images.