Abstract:

The risks of late effects from galactic cosmic rays (GCR) and solar particle events (SPE) are potentially a limitation to long-term space travel. The late effects of highest concern have significant lethality including cancer, effects to the central nervous system (CNS), and circulatory diseases (CD). For cancer and CD the use of age and gender specific models with uncertainty assessments based on human epidemiology data for low LET radiation combined with relative biological effectiveness factors (RBEs) and dose- and dose-rate reduction effectiveness factors (DDREF) to extrapolate these results to space radiation exposures is considered the current “state-of-the-art”. The revised NASA Space Risk Model (NSRM-2014) is based on recent radio-epidemiology data for cancer and CD, however a key feature of the NSRM-2014 is the formulation of particle fluence and track structure based radiation quality factors for solid cancer and leukemia risk estimates, which are distinct from the ICRP quality factors, and shown to lead to smaller uncertainties in risk estimates. Many persons exposed to radiation on earth as well as astronauts are lifetime never-smokers, which is estimated to significantly modify radiation cancer and CD risk estimates. A key feature of the NASA radiation protection model is the classification of radiation workers by smoking history in setting dose limits. Possible qualitative differences between GCR and low LET radiation increase uncertainties and are not included in previous risk estimates. Two important qualitative differences are emerging from research studies. The first is the increased lethality of tumors observed in animal models compared to low LET radiation or background tumors. The second are Non-Targeted Effects (NTE), which include bystander effects and genomic instability, which has been observed in cell and animal models of cancer risks. NTE’s could lead to significant changes in RBE and DDREF estimates for GCR particles, and the potential effectiveness of radiation mitigator’s. The NSRM-2014 approaches to model radiation quality dependent lethality and NTE’s will be described.

CNS effects include both early changes that may occur during long space missions and late effects such as Alzheimer’s disease (AD). AD effects 50% of the population above age 80-yr, is a degenerative disease that worsens with time after initial onset leading to death, and has no known cure. AD is difficult to detect at early stages and the small number of low LET epidemiology studies undertaken have not identified an association with low dose radiation. However experimental studies in mice suggest GCR may lead to early onset AD. We discuss modeling approaches to consider mechanisms whereby radiation would lead to earlier onset of occurrence of AD. Biomarkers of AD include amyloid beta (Aβ) plaques, and neurofibrillary tangles (NFT) made up of aggregates of the hyperphosphorylated form of the micro-tubule associated, tau protein. Related markers include synaptic degeneration, dendritic spine loss, and neuronal cell loss through apoptosis. Radiation may affect these processes by causing oxidative stress, aberrant signaling following DNA damage, and chronic neuroinflammation. Cell types to be considered in multi-scale models are neurons, astrocytes, and microglia. We developed biochemical and cell kinetics models of DNA damage signaling related to glycogen synthase kinase-3β (GSK3β) and neuroinflammation, and considered multi-scale modeling approaches to develop computer simulations of cell interactions and their relationships to Aβ plaques and NFTs. Comparison of model results to experimental data for the age specific development of Aβ plaques in transgenic mice will be discussed.