γ-H2AX kinetic profile in mouse lymphocytes exposed to the internal emitters cesium-137 and strontium-90

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Study Goal: In the event of a dirty bomb scenario or an industrial nuclear accident, volatile radionuclides such as 137Cs and 90Sr may be dispersed into the atmosphere as a component of fallout. The goal of the present study was to examine the effect of uniform (137Cs) and non-uniform (90Sr) protracted internal radiation exposure on DNA damage in mouse peripheral blood lymphocytes in vivo following the injection of a single radionuclide exposure.

Abstract: Radioactive isotopes of Cesium-137 (137Cs) and Strontium-90 (90Sr) are considered to be some of the most dangerous radionuclides released into the environment in terms of their high radioactivity, long-lived effects (physical half-lives of about 30 years) and the ease in which they are taken up into the food chain. Their biochemical and physical properties contribute to their unique temporal pattern and biological behavior. To study the effects of prolonged exposure to ingested radionuclides, we have performed long-term (30 day) internal-emitter mouse irradiations using soluble-injected 137CsCl and 90SrCl2 radioisotopes. The effect of ionizing radiation on the induction and repair of DNA double strand breaks (DSBs) in peripheral mouse lymphocytes in vivo was determined using the y-H2AX biodosimetry marker. Using a serial sacrifice experimental design, whole-body radiation absorbed doses for 137Cs (0 to 10 Gy) and 90Sr (0 to 49 Gy) were delivered over 30 days following exposure to each radionuclide. The committed absorbed doses of the two internal emitters as a function of time post exposure were calculated based on their retention parameters in the studied mice and their derived dose coefficients for each specific sacrifice time. In order to measure the kinetic profile for y-H2AX, peripheral blood samples were drawn at 5 specific timed dose points over the 30-day study period and the total y-H2AX yields per nucleus were determined in isolated lymphocytes by indirect immunofluorescence. A mechanistically-motivated model was used to analyze the temporal kinetics of y-H2AX fluorescence. Exposure to either radionuclide showed two peaks of y-H2AX: one within the first week, which may represent the death of mature, differentiated lymphocytes, and the second at approximately three weeks, which may represent the production of new lymphocytes from damaged progenitor cells.

Conclusion: A key finding was that a significant y-H2AX signal was observed for several weeks after the start of a single radionuclide exposure. The continual bombardment of gamma and beta particles to induce new DNA damage, the constant changing of dose and dose rates, the effects of cell cycle repair and apoptosis all add to the complexity of the radiation-induced cellular effects posed by the inhalation or ingestion of an internal emitter.

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