Radiation Dose-Rate and DNA Damage

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In their article, Olipitz et al. (2012) examined signs of DNA damage after chronic exposure of C57Bl6 mice to low-level ionizing radiation (3 mGy/day). For 5 weeks, mice were irradiated continuously with 35.5 kV X-rays produced by the decay of iodine-125, yielding an accumulated dose of 105 mGy. The observed effects were compared with those from acute irradiation by X-ray machine at 1,700 mGy/day up to the same accumulated dose.

Olipitz et al. (2012) investigated signs of DNA damage using four histological methods. Most prominent of the methods was the expression of functional fluorescent protein as a result of recombination by homology-directed repair in pancreatic cells of transgenic FYDR (fluorescent yellow direct repeat) mice derived from the C57Bl6 strain. The other three methods were carried out using genetically unaltered C57Bl6 mice. The authors investigated DNA base damage in splenocytes; DNA double strand breaks in bone marrow erythrocytes; and the expression of select genes implicated in cell cycle arrest, tumor suppression, and apoptosis in white blood cells from blood samples.

Olipitz et al. (2012) used equal numbers of unirradiated mice as controls. However, sample sizes across the study ranged from 6 to 60 animals. Because of the wide range in animal numbers, nonparametric methods should have been used in statistical analyses. A multivariate analysis of variance comprising all observations in the study should have preceded any pairwise comparisons to allow the authors to evaluate the variability of observations within samples compared with the variability among samples (Mickey and Dunn 2009). Furthermore, the use of transgenic mice with one method and unaltered mice with the other three might have increased the variability in observation, reducing the chance of detecting statistically significant differences. The above weaknesses in experimental design and statistical analysis may have profoundly compromised the authors’ ability to discover statistically significant differences when the variance is lower, such as for micronuclei.

In his letter, Melzer correctly points out that data of Tanaka et al. (2009) show a statistically significant increase in chromosome aberrations in cells from mice exposed to 1 mGy/day up to a total of 1,000 mGy. However, after exposure to that same dose-rate for a longer period (up to 8,000 mGy), there was no statistically significant change in the number of chromosome aberrations. Furthermore, Tanaka et al. (2009) stated that regression coefficients (b4 and b6) in the equations for Dic by FISH at low dose rates of 20 mGy/day and 1 mGy/day at doses less than 8,000 mGy were not statistically significant.
linear dose–response relationship at 1 mGy/day was significantly different from the spontaneous level.

Melzer is correct that we cannot rule out the possibility that genetic changes might have been observed if the exposures had been carried out for a longer period. However, because cells have the capacity to repair radiation-induced DNA damage, it is possible that DNA damage would not accumulate with time.

Melzer is correct that a recent report suggested that exposure to radiation from CT (computed tomography) scans affects the risk of cancer in exposed children. An important difference is that CT scans are an acute exposure at a high dose-rate, which is very different from the low dose-rate conditions in our study. Nevertheless, we agree that it is very important to consider the fact that children have increased sensitivity to radiation damage.

One of Melzer’s final points is that inflammation might affect radiation sensitivity. Although we did not test the impact of inflammation in our study, it is important to note that inflammation is a highly genotoxic process itself, leading to levels of DNA damage orders of magnitude higher than levels we calculated in response to the low dose-rate we used. Finally, Melzer raises the issue of internal exposure by ingestion versus external sources. The body handles ingested radionuclides according to the chemical behavior of the element. Although we have examined the effect of radiation dose as delivered by internal or external photon- or beta-emitters, we did not consider the internal pattern of radionuclide uptake in our study.

The authors declare they have no actual or potential competing financial interests.

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