LETTERS TO THE EDITOR


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This letter is regarding the article by Grant et al. entitled “Solid Cancer Incidence among the Life Span Study of Atomic Bomb Survivors: 1958–2009” published in Radiation Research (1). This article describes the findings of the third analysis of solid cancer incidence among the Life Span Study (LSS) cohort of atomic bomb survivors in Hiroshima and Nagasaki. In this publication, which includes an additional 11 years of follow-up since the previous reported analysis, Grant et al. report a linear dose-response relationship for cancer incidence in females and a linear-quadratic one for males. The authors also claim that they found a linear increase in excess relative risk (ERR) for dose range as low as 0–100 mGy. Although the paper addresses a very challenging issue, it has some major shortcomings.

One concern regarding the results presented in this article is that solid cancer incidence rate presented in Table 3 of the original article (1) shows a threshold dose of 100–200 mGy for increased cancers as seen in the plot (Fig. 1) but the authors used a linear no-threshold model to fit the data and extract the excess relative risks (ERRs).

Additional reason to not use the linear dose-response model for analyzing the LSS data is vast amount of evidence for the reduction of cancers after exposure to low levels of radiation, contradicting the linear model (2). Although several publications have claimed to support the linear no-threshold model or low-dose radiation carcinogenicity (3–5), careful scrutiny has shown major flaws in them rendering their conclusions untrustworthy (6–10). In addition, though solid cancer mortality data in the LSS cohort appeared to be consistent with a linear dose-response relationship in the reports published until recently (11), the update of the data by Ozasa et al. in 2012 (12) showed a significant curvature in the dose-response relationship in the 0–2 Gy range that was inconsistent with the assumed linear model used in the data analysis, and the authors were not able to explain the significant curvature in the data. An analysis that takes into account the likely negative bias in the baseline cancer mortality rates (used in the LSS data analysis) has shown that these data are consistent with radiation hormesis (13). Hence, the use of the linear dose-response model for the analysis of the LSS data is not at all justified. In addition, the dose-threshold analysis of Ozasa et al. (from which they concluded that zero dose was the best estimate of threshold dose) was flawed because it used a restricted functional form for the shape of dose-response, and the use of a more general dose-response shape resulted in the conclusion that a finite dose-threshold could not be excluded (14).

One general concern regarding the use of the cancer incidence data for estimating health effects of radiation is that cancer incidence rates can increase as a result of cancer screening programs skewing the results, and many of the detected cancers may not be real cancers as they would not cause any harm to the subjects.

One issue with the use of the atomic bomb survivor data for estimating health effects of radiation is that A-bomb survivors are known to face higher stress due to their cancer concerns. Japanese scientists, in a study aimed at investigating whether having been in the vicinity of the Nagasaki atomic bomb explosion (in the absence of substantial exposure to radiation) affected the mental health of local inhabitants, found that it could be associated with poorer mental health more than 50 years after the event (15). Chronic stress is known to suppress the immune system and increase cancer risk (16), and the survivors closer to the bomb explosion had higher levels of stress potentially contributing to their higher rates of cancers (17). Furthermore, since radiation dose from diagnostic imaging has increased considerably during the past few decades, radiation dose from radiological examinations for many of the survivors in the lowest dose cohorts could far exceed the radiation dose they received from the atomic bomb explosions, introducing additional uncertainty to any dose-response relationship determined in the low-dose region.

An issue of concern with the data presentation is the absence of error bars in Fig. 4 of their publication, which makes it harder to evaluate the shape of dose response. The large fluctuations in ERR between adjacent data points indicate error bars may be large, implying the data may be compatible with threshold and hormesis models, in addition to the linear model depicted. Furthermore, splitting of the data into male and female parts has reduced the statistical power making it harder to determine the shape of dose response from the analysis presented. For determining the shape of dose response in A-bomb survivors, the cancer mortality data published by Ozasa et al. (12) appear to be the most appropriate data if corrections are applied for the deficiencies in their analysis, and such analysis has shown there was reduction of cancers from low radiation exposures (13).

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REFERENCES