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"A Bayesian semiparametric model for radiation dose-response estimation"
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Study Findings

This study proposed a new statistical approach using a semiparametric model* to estimate the dose-response relationship under a framework of Bayesian statistics* —one of the primary objectives of radiation risk analysis—with increased accuracy. Without assuming a specific parametric model,* such as the linear non-threshold model,* this approach can estimate various dose-response curves with uncertainty more accurately and therefore is expected to be particularly useful in evaluating the risk associated with low-dose exposure.

*Semiparametric model: falls between a parametric model and a nonparametric model, which assumes no specific form with respect to dose response

*Bayesian statistics: generalizes the conventional statistics by introducing a "prior probability" based on common senses or experiences and enables us to conduct data analysis more flexibly. The term "Bayesian semiparametric model" in the title indicates a semiparametric model under this framework of Bayesian statistics.

*Parametric model: describes how risk increases with dose (x) with a set of parameters (β), such as the linear non-threshold dose model (βx)

*Linear non-threshold model: assumes risk to be monotonically increasing in proportion to the increasing dose

Explanation

Characterizing the dose-response relationship and estimating acceptable exposure levels are the primary goals of risk assessment. In analyses of health risks associated with exposure to radiation, while there is clear agreement that moderate to high radiation doses cause harmful effects in humans, information is limited for understanding the possible biological effects at low doses, e.g., less than 100 mGy, which is the dose range relevant to most radiation exposures today. While a simple parametric model, such as the linear non-threshold model, is interpretable and supported by some biological considerations, risk analysis based on a simple parametric structure can be misleading in evaluating the risk and its uncertainty associated with low-dose exposure. In particular, a linear model with a fixed value at the lowest dose (e.g., zero response at zero dose) can only accommodate linear confidence bounds that narrow to a point at the low-dose end. This study proposed a new approach using a semiparametric model that is flexible in regard to the shape of both the mean response and the confidence bounds and evaluated its performance in comparison with the conventional approach of parametric models.

1. Study purpose

The main purpose of this study was to show that a semiparametric dose-response model that assumes no specific parametric function form can be an alternative approach that is appropriate for evaluation of risk associated with radiation exposure, especially at low doses.

2. Study methods

This study considered a semiparametric dose-response model that has a connected piecewise-linear, dose-response function with a correlation structure among the random slope coefficients defined over closely spaced dose categories, which was applied to radiation-dose-response estimation. Using simulations under several plausible dose-response relationships, we evaluated the performance of the proposed approach compared to those of the conventional parametric approach in terms of bias, efficiency, and precision of uncertainty estimation. Also, the proposed approach was applied to analysis of solid cancer incidence in the Life Span Study (LSS) cohort of atomic-bomb survivors (1958–1998), and the estimated dose-response curves with interval estimates were compared to those obtained by other approaches.

3. Study results

Our simulation study demonstrated that the conventional approach using parametric models could be problematic in bias and underestimation of uncertainty when a non-linearity was assumed in the dose response at a low dose range. In contrast, the proposed approach produced results that were overall less biased and more accurate in uncertainty estimation. In analysis of the LSS data, compared to the conventional linear non-threshold model, the proposed approach estimated smaller risks with wider interval estimates at low doses, which indicated no clear evidence of an increased risk up to 100 mGy of exposure (Figure).

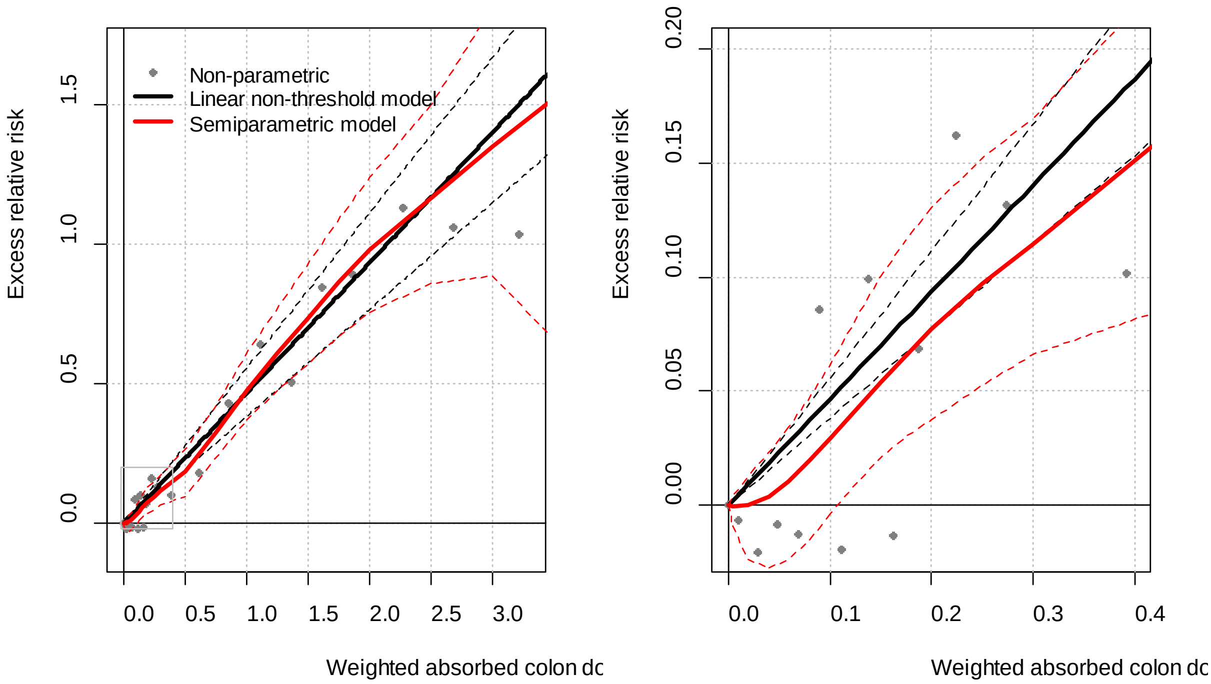

Figure: Excess relative risk (ERR) for all solid cancer in the Life Span Study cohort (1958–1998) in relation to radiation exposure, estimated by the linear non-threshold model (black) and the semiparametric model (red) over the entire dose range (left) and at 0–0.4 Gy (right). Dashed curves are 95% confidence (or credible) intervals. All estimates are gender-averaged ERRs at age 70 after exposure at age 30.

Study Significance

With relatively few assumptions and modeling options to be made by the analyst, the semiparametric model proposed in this study can be flexibly fitted to data generated by various shapes of dose-response curves with uncertainty appropriately handled at any dose range and therefore is expected to be particularly useful in characterizing risk at a low dose range and accurately estimating acceptable exposure levels.

The Radiation Effects Research Foundation has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for more than 60 years. RERF's research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International

Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

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