A research paper published in the *Journal of Radiological Protection*[§]

"A semiparametric approach to evaluate the potential for harm from low-dose radiation exposure"

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J Radiol Prot; 38(1):286-98, 2018/3
(doi: 10.1088/1361-6498/aaa57c)

Study Findings

While high levels of radiation exposure are widely recognized to cause adverse health effects, the lowest potentially harmful radiation dose has yet to be identified. Using a simulation approach,[*1] this study showed that a conventional approach based on a simple parametric dose-response model[*2] (e.g., a linear no-threshold model[*3]) can be unexpectedly inefficient, biased, and/or inaccurate in uncertainty evaluations at a low-dose range. Furthermore, we demonstrated that a semiparametric model[*4] assuming no specific form with respect to dose-response can be flexibly fitted to various plausible dose-response curves while appropriately handling risk-estimation uncertainty.

*[1] Simulation approach: by repeating computer-based experiment simulations, this method is used to verify risk values estimated by a given statistical model.

*[2] Parametric model: like the linear no-threshold model (βx), describes how risk increases with dose (x) using a set of parameters (β).

*[3] Linear no-threshold model: assumes that risk increases in proportion to increasing doses with no threshold.

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

Explanation

While high levels of radiation exposure are widely recognized to cause adverse health effects, defining the lowest potentially harmful dose remains a controversial issue. Given that epidemiological studies of a practical size are unlikely to provide sufficient statistical power* to detect small risks associated with low doses of radiation, it is necessary to accurately evaluate how uncertain these risk estimation results are. Using simulations that assume various dose-response relationships with a threshold dose (the lowest exposure at which risk is generated), we showed that a conventional approach based on simple parametric models (e.g., linear models with or without a threshold) can be unexpectedly inefficient, biased, and/or inaccurate in uncertainty evaluations in a low-dose range. In contrast, with no assumption of a specific function form, a semiparametric model can be flexibly fitted to various plausible dose-response curves while appropriately handling risk uncertainty. In particular, this approach can evaluate with relative accuracy the dose range in which a threshold might exist in dose-response relationships, while retaining sufficient statistical power to indicate a small increase in risk beyond the threshold. As a result, this approach is suitable for use in analyzing the risk of low-dose radiation exposure.

* Statistical power: probability that the existence of an effect or influence to be estimated can be correctly declared by a statistical test when such an effect or influence does exist; the probability increases when the amount of data or the effect to be estimated is large.

1. Study Purpose

The purpose of this study was to use simulations to compare the estimation performance of conventional approaches based on a parametric model and that of a semiparametric dose-response model, when a threshold is assumed to actually exist in dose-risk relationships.

2. Study Methods

This study considered a semiparametric model that conducts smoothing of a dose-response function connecting piecewise-linear functions defined over closely spaced dose categories, by handling the coefficients of piecewise functions as random slopes and allowing for autocorrelations between adjacent line sections. Both parametric and semiparametric approaches were used to estimate data simulated under dose-response relationships with various thresholds. Further, by repeating estimations using data simulated on the basis of various dose responses with threshold, we evaluated the performance of the proposed approach compared with that of the conventional parametric approach in terms of bias, efficiency, and precision of uncertainty estimation. Also, both approaches were applied to analysis of solid-cancer incidence in the Life Span Study (LSS) cohort of atomic bomb survivors (1958–2009), and the estimated dose-response curves with interval estimates were compared.

3. Study Results

In the conventional approach utilizing a parametric model, if non-linearity or thresholds existed in dose-response relationships in a low-dose range, bias and uncertainty were underestimated. In contrast, the semiparametric approach, with or without non-linearity or thresholds, produced estimation results with generally little bias, thus showing an ability to accurately evaluate uncertainty. Further, in the LSS data analysis, in comparison with results estimated by the conventional parametric model, the results by the proposed approach showed that the interval estimation in a low-dose range was wider, despite similar maximum likelihood estimation values, suggesting that no obvious risk increase was caused by exposure in a low-dose range.

Study Significance

The semiparametric model used in this study mostly obviates the analyst’s need for the assumption and option settings usually required to estimate radiation risk. In both high-dose and low-dose ranges, this model can reliably infer uncertainty in risk estimation while flexibly adapting to data from dose-response curves of various shapes. We therefore consider this approach effective in accurately estimating tolerable levels of radiation exposure as well as the characteristics of risk involved in low-dose exposure.

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