Correction of confidence intervals in excess relative risk models using Monte Carlo dosimetry systems with shared errors

Zhuo Zhang[1], Dale L. Preston[2], Mikhail Sokolnikov[3], Bruce A. Napier[4], Marina Degteva[5], Brian Moroz[2], Vadim Vostrotin[3], Elena Shiskina[5], Alan Birchall[6], Daniel O. Stram[1]

[1]Keck School of Medicine, USA; [2]Hirosoft International Corporation, USA; [3]Southern Urals Biophysics Institute, Russia; [4]Pacific Northwest National Laboratory, USA; [5]Urals Research Center for Radiation Medicine; [6]Global Dosimetry Limited, UK

In epidemiological studies, exposures of interest are often measured with uncertainties, which may be independent or correlated. Independent errors can often be characterized relatively easily while correlated measurement errors have shared and hierarchical components that complicate the description of their structure. For some important studies, Monte Carlo dosimetry systems that provide multiple realizations of exposure estimates have been used to represent such complex error structures. While the effects of independent measurement errors on parameter estimation and methods to correct these effects have been studied comprehensively in the epidemiological literature, the literature on the effects of correlated errors, and associated correction methods is much more sparse. In this paper, we implement a novel method that calculates corrected confidence intervals based on the approximate asymptotic distribution of parameter estimates in linear excess relative risk (ERR) models. These models are widely used in survival analysis, particularly in radiation epidemiology. Specifically, for the dose effect estimate of interest (increase in relative risk per unit dose), a mixture distribution consisting of a normal and a lognormal component is applied. This choice of asymptotic approximation guarantees that corrected confidence intervals will always be bounded, a result which does not hold under a normal approximation. A simulation study was conducted to evaluate the proposed method in survival analysis using a realistic ERR model. We used both simulated Monte Carlo dosimetry systems (MCDS) and actual dose histories from the Mayak Worker Dosimetry System 2013, a MCDS for plutonium exposures in the Mayak Worker Cohort. Results show our proposed methods provide much improved coverage probabilities for the dose effect parameter, and noticeable improvements for other model parameters.

USTUR-0483A-17