Estimation of Accelerated Failure Time due to Radiation for All Solid Cancer and CVD Deaths among A-bomb Survivors

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Introduction: In radiation epidemiology studies for the health effects of radiation in the cohorts such as the atomic-bomb (A-bomb) survivors, radiation workers (occupational exposure), and the exposed at nuclear accidents (Chernobyl and Fukushima), because the risk per unit dose (per 100, 200 mSv or 1 Sv) is small, the large cohort is required to estimate the risk with enough accuracy. The radiation risk estimation is made often in terms of the relative risk (RR) or the accelerated failure time (AFT) that has more direct interpretation than the RR.

Methods: Two measures for the radiation risk in survival analysis are the excess relative risk (ERR) and the failure time acceleration rate (FTAR). Physical interpretations of these terms are that RR (=1+ ERR) is the product factor of log-survivor function due to a unit radiation dose and FTAR is defined as the shrinkage rate of survival time per a unit radiation dose. Because piecewise exponential model is a piecewise AFT model, the ERR from piecewise exponential (grouped Poisson) model can be transformed to the FTAR. The transformation formula (Nakashima & Neriishi 2014) from ERR to FTAR in a piece of major/primary-time-scale is expressed as $FTAR = ERR/(1+ERR)$. For the A-bomb survivors cohort data, the expected acceleration time (EAT) until a fixed time point T_1 is estimated with an inner product of the mean major-time-scales and FTARs, $\hat{F}TAR_{i,j} = \hat{E}RR_{i,j}/(1+\hat{E}RR_{i,j})$, with the effect modifier category indices $i=(i_1,i_2,i_3)$ of sex (i_1), age at exposure (ageX) category (i_2), major-time-scale category (i_3) & radiation dose category j with j = 1 for control (0 Gy) group, and the mean time $\bar{t}_{i,+,j=1}$ is the mean major-time-scale (person-years) for the cells with suffices $(i, j=1)$ until the fixed time point T_1. An integral expression is possible for the EAT formula.

Results: For all solid cancer & CVD (circulatory diseases) grouped Poisson ERR mortality analyses using the Life Span Study (LSS) follow-up cohort grouped data (from 1950 to 2003) available at the homepage library of the Radiation Effects Research Foundation (RERF), sex, ageX & (attained) age are the dose effect modifiers for all solid cancer (Ozasa et al. 2012), and no dose effect modifier for CVD (Shimizu et al. 2014). The sex averaged EATs of two causes of death using the whole data (until 2003) at mean ageX = 27.8y (years) & mean age = 27.8 + 55 = 82.8y (until the year of 2000 = T_1) was estimated separately as 8.0y (95%CI: 6.3, 9.5y) at 1 Gy for all solid cancer and 2.6y (1.0, 4.1y) at 1 Gy for CVD. From the fitted EATs in dose intervals, the 95%CI lower bound of EAT for CVD death in the dose range below 1.5 Gy were negative indicating non-significant acceleration due to radiation in this dose range. The EAT estimates for both causes of death showed the more acceleration for the exposed younger.

References: Nakashima E & Neriishi K (2014) *IBC2014*, Florence, Italy; Ozasa et al. (2012) *Rad. Res.* 177:229-243; Shimizu et al. (2014) *BMJ* 2010.