Evaluation of non-initial radiation exposure effect on solid cancer mortality among Hiroshima atomic bomb survivors: Poisson regression analysis using distance from the hypocenter and age at exposure as explanatory variables

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\textbf{INTRODUCTION} There are three large cohort studies on mortality risk among the atomic bomb survivors, which have been conducted independently by RERF, Hiroshima University and Nagasaki University. Recently, Ozasa et al. (Radiat. Res., 2012) reported that the sex-averaged excess relative risk (ERR) of all solid cancer was 0.42 per Sv for the subjects at an attained age of 70 years after exposure at the age of 30 as a result of LSS due to RERF. Tonda et al. (Radiat. Environ Biophys, 2012) tried to evaluate direct/indirect exposure effects on the cancer mortality using ABS cohort data managed at Hiroshima University. They suggested that there existed an impact on risk that could not be explained by only direct exposure. The purpose of this paper was to split the effects of direct/indirect exposures on ERR by using information of distance from the hypocenter to location at bombing (abbreviated in the following "exposure-distance").

\textbf{ERR model for initial radiation dose}

Hazard function: \( h(t) = h_0(t)(1 + \text{Excess Relative Risk}) \)

\[ ERR = \beta \times Dose \times \text{Effect Modifiers} \]

\[ \exp\left(\beta_1 \times \text{age} - 30 \right) \times \text{age}^{\beta_2} \times \text{sex}^{\beta_3} \]

Interpretation: \( \beta \) is ERR when Dose=1Sv, age=30, sex=70

\textbf{“Risk factor” approach for non-initial dose}

\[ ERR = (1 - \alpha) \times Dose + \alpha \times \text{Non-Initial Dose} \]

\[ NID = (\text{Distance}^{\alpha} - \text{Cutoff Point}^{\alpha}) \times \text{sex} \]

Optimization of Parameters

<table>
<thead>
<tr>
<th>AIC(p, K)</th>
<th>K: Distance(^{-\alpha})</th>
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</thead>
<tbody>
<tr>
<td>p</td>
<td>1</td>
</tr>
<tr>
<td>0.10</td>
<td>8.07</td>
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<tr>
<td>0.15</td>
<td>7.83</td>
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<tr>
<td>0.20</td>
<td>7.85</td>
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\textbf{MATERIALS & METHODS} From the ABS, we chose 53,493 subjects for analysis who satisfied the following conditions: (i) being alive and recognized as an atomic bomb survivor as of January 1, 1970 and (ii) having estimate of initial radiation dose (ABS93D). These subjects were followed until December 31, 2012. The endpoint is death from solid cancers (total number of deaths: 5,908).

We performed a Poisson regression analysis involving exposure-distance, age at exposure and initial dose. Initial radiation dose rapidly decreases before 1.5km, and from the point mortality risk might be explained by non-initial radiation dose. There are two statistical approaches for evaluating non-initial radiation effects. One is an use of interaction variable which expresses action or behavior of atomic bomb survivors with specific location and age, c.f., Ohtaki et al. (J. Hiroshima Med. Ass., 2014), Tonda et al. (J. Hiroshima Med. Ass., 2014), Satoh et al. (Nagasaki Med. J., 2014), Otani et al. (Nagasaki Med. J., 2012). A new approach is proposed by using a monotone decreasing function of exposure-distance and the risk factor can be described by sum of initial radiation and non-initial radiation.

\textbf{CONCLUSION} It was revealed from our analysis that there exists an impact on solid cancer risk that cannot be explained through initial radiation dose but some factors related to exposure for Hiroshima atomic bomb survivors. Since initial radiation dose of ground distance around 1.5 km was not high (at most 500mSv), they did not have serious damage. Therefore, men over 15 years old stayed in city center and worked more or looked for someone for a while after exposure. As the result, their cancer mortality risk increased by indirect exposure due to residual radioactivity.