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**“Cytogenetic reconstruction of gamma-ray doses delivered to atomic bomb survivors: Dealing with wide distributions of photon energies and contributions from hematopoietic stem/progenitor cells”**

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**Study Findings**

Chromosome aberration frequencies in blood lymphocytes are one marker used to biologically estimate radiation doses received by individuals. However, biodosimetry based on chromosome aberration frequencies has not been used in the case of A-bomb survivors for two reasons: one is that chromosome aberration frequency differs by gamma ray energy, and A-bomb gamma rays have a range of energies. The other reason is that survivors were exposed so long ago that some lymphocytes examined were hematopoietic stem/progenitor cells at the time of exposure of which their radiosensitivities are not well understood.

To overcome these hurdles, we compared tooth enamel radiation doses estimated using electron spin resonance (ESR) with doses in the same survivors estimated from chromosome aberration frequencies. (We assumed that all cells had been lymphocytes at the time of exposure and that the A-bomb gamma-ray spectrum was equivalent to that of <sup>60</sup>Co gamma rays.) This comparison, which factored in shielding differences between the teeth and bone marrow, showed close agreement between these two sets of biologically estimated doses.

Based on these study results, we concluded that unadjusted <sup>60</sup>Co gamma-ray equivalent doses estimated from chromosome aberration frequencies may be an accurate indication of A-bomb gamma-ray doses.

**Explanation**

Chromosome aberration frequencies in blood lymphocytes can be used in one method to estimate radiation doses received by individuals after exposure. Blood lymphocytes are irradiated *in vitro* with <sup>60</sup>Co gamma rays to obtain a dose-response curve between radiation dose and chromosome aberration frequency. The chromosome aberration frequencies are then determined to estimate exposure doses.

This procedure, however, has not been successfully used to estimate radiation doses received by A-bomb survivors for two reasons. One is that the wide distribution of energies released from the A-bombs makes model experiments impossible. Yet model experiments are needed to account for the fact that a given dose yields different chromosome aberration frequencies depending on the gamma-ray energy.

The second is that cells that were immature and differentiating at the time of exposure could have eventually entered into the lymphocyte pool after considerable time had passed. Immature cells could be more radiosensitive than blood lymphocytes but cannot be differentiated from old lymphocytes. When doses are estimated, all lymphocytes examined must therefore be assumed to have been mature lymphocytes at the time of exposure.

To overcome these hurdles, we estimated doses in about 100 A-bomb survivors from tooth

enamel, which is less dependent on photon energies, using ESR and from chromosome aberration frequencies. The latter estimates assume that all cells exposed to radiation were blood lymphocytes (differentiated mature cells) and that the effect of A-bomb gamma rays was the same as that of monoenergetic  $^{60}\text{Co}$  gamma rays.

### Study Results

Radiation doses estimated from tooth enamel using ESR were slightly larger than  $^{60}\text{Co}$  gamma-ray equivalent doses estimated from chromosome aberration frequencies. This difference is attributable to the larger shielding effect of bone on the bone marrow, where many lymphocytes reside, than the shielding effect of skin on teeth. We therefore used individual shielding data to estimate kerma doses before estimating organ doses. (Kerma dose refers to the dose present in the space the individual occupied at the time of exposure.) The two sets of dose estimates agreed closely.

Based on these study results, we concluded that unadjusted  $^{60}\text{Co}$  gamma-ray equivalent doses estimated from chromosome aberration frequencies may be an accurate indication of A-bomb gamma-ray doses.

### Study Significance

Our findings support the idea that radiation doses estimated from chromosome aberration frequencies are directly comparable to those physically estimated based on distance from the hypocenters and shielding of A-bomb survivors (DS02R1 doses). This understanding paves the way for use of chromosome aberration frequency data to determine whether physically estimated doses contain any systematic biases.

**The Radiation Effects Research Foundation** has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for around 70 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.

<sup>§</sup>*Radiation Research*, which is an official monthly journal of the Radiation Research Society, publishes original peer-reviewed papers and review articles on radiation effects and related issues in the fields of physics, chemistry, biology, and medicine. (Impact factor in 2016/2017: 2.539)