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Calculations of Mean Quality Factors and Their Implications for Organ-specific Relative Biological Effectiveness (RBE) in Analysis of Radiation-related Risk in the Atomic Bomb Survivors

Shota Shimizu,[a,1] Tatsuhiko Sato,[b] Sachiyo Funamoto,[a] Richard Sposto,[a] Harry M. Cullings,[a] Akira Endo,[b] Stephen D. Egbert,[c] Michiaki Kai[d]

[a] Department of Statistics, Radiation Effects Research Foundation, Hiroshima, Japan; [b] Japan Atomic Energy Agency, Tokai-mura, Japan; [c] Consultant, San Diego, California; [d] Nippon Bunri University, Oita, Japan

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Past and current estimates of relative biological effectiveness (RBE) from the cohort analyses of atomic bomb survivors suggested not only that RBE may be much higher than those assessed by the United Nations Scientific Committee on Effects of Atomic Radiation (UNSCEAR) and International Commission on Radiological Protection (ICRP), but also that RBE may differ by organ and organ depth. This is at least partly due to how the ratio of neutron to gamma-ray dose changes with organ depth because of the more rapid attenuation of neutrons in tissue. Additionally, the RBE estimates from Life Span Study (LSS) data depend on the total dose and the neutron/gamma ratio. To further examine this issue, we calculated the mean quality factor based on Linear Energy Transfer (LET) distributions for representative organs and exposure scenarios of A-bomb survivors using Particle and Heavy Ion Transport code System (PHITS) simulation and the radiation quality factor [$Q(L)$ relationship] defined by ICRP, as well as the Quality Factor (QF) function defined by the National Aeronautics and Space Administration (NASA). This is done in the context of the adult male phantom of the J45 series, which was created to precisely reproduce the anatomy of the Japanese population in 1945. We also investigate the depth dependence of the mean quality factors in the International Commission on Radiation Units and Measurements (ICRU) sphere irradiated by monoenergetic neutrons. Both the results from the human phantom, and from the ICRU sphere phantom suggest that the mean quality factors are approximately 15 and independent of the organ type, body depth, city and ground range when the contributions from the secondary γ rays are excluded from the neutron doses. We also discuss reasons that RBE estimates from cohort analyses are generally much larger than those based on the mean quality factors.

[1] Corresponding author: Shota Shimizu, Radiation Effects Research Foundation: Koeki Zaidan Hojin Hoshasen Eikyo Kenkyujo, Hiroshima City, Hiroshima Japan; email: sshimizu@rerf.or.jp.

INTRODUCTION

It is well known that neutrons produce higher biological effects than X and γ rays at the same absorbed dose (when total dose is small). Relative biological effectiveness (RBE), the ratio of absorbed doses that produce the same biological effect, has been stated to be 5–20 for neutron-induced cancer (*1*, *2*). Many studies have attempted to estimate neutron RBE observationally by using biological or epidemiological models with cancer data obtained in laboratory animals or human populations, respectively, using models that are linear or linear-quadratic functions of dose (*1–11*). Although there is limited information on RBEs for human carcinogenesis, the RBE values of neutrons are thought to be dependent on neutron energy because of the difference of secondary charged particles generated from neutron interactions.

Observed RBE values from well-defined exposure environments are the basis of the quality factor $Q(L)$ and the radiation weighting factor, w_R, to weight the radiation quality for dose assessment in radiation protection. The quality factor, $Q(L)$, was defined as a function of linear energy transfer (LET) [LET (L)] in water (*12*). In general, high LET radiations cause more DNA double-strand breaks per Gy due to differences in ionization density compared with low LET radiations. Thus, a survivable whole-body dose of high-LET radiation can increase the risk of future cancer incidence through induction of molecular and cellular damage (*13*). The radiation weighting factor, w_R, for neutrons was defined as a function of neutron energy. The numerical values of w_R were determined to be consistent with the mean radiation quality factor in the human body (*2*, *14*).

It has been suggested that there is reasonable agreement of the experimentally determined values of RBE with the functional dependence Q(L) (*14*). In general, the RBE should correspond to the quality of the incident radiation (i.e., the density of ionization of the incident radiation), with more densely ionizing radiations producing more cellular damage. In the case of neutrons, attenuation and nuclear reactions in a human body produce large differences in the radiation field throughout the body. It should be noted that

the neutron doses in LSS studies are delivered by protons and heavier charged particles produced by the neutron-scattered recoil and charged-particle capture emission (n, p), because neutrons do not directly ionize the atoms in tissue. It can be inferred that the physical reactions of neutrons in the body contribute to the charged-particle radiation field that with high-density deposition sites in the DNA strand, will consequently affect the RBE. The RBE of fission spectrum neutrons may depend on the depth and shape of the organ. Therefore, it would be useful to examine changes in Q(L) in various organs as an indicator for neutron RBE.

Several attempts have been made to estimate the neutron RBE from the Life Span Study (LSS) of atomic bomb (A-bomb) survivors (*3–10*), using detailed data on the age and shielding status of the exposed individuals. The early study showed a higher cancer risk related with radiation in Hiroshima than in Nagasaki, which was thought to be due to neutron effects (*3*). However, later revisions of dose calculations have made the neutron RBE estimates associated with the early study less reliable (*15*), as it is now known that the absorbed doses from neutrons are small compared to gamma radiation. On the other hand, recent studies (*6*, *7*, *9*, *10*) adopted a more modern dosimetry system, DS02 and its revised version DS02R1 (*16*, *17*), for assessing the dose to individual organs. Among them, the latest study (*9*) used updated dosimetry (DS02R1), to estimate the effective RBE of surrogate organ doses for a range of organs of varying depths, finding for each organ dose the neutron RBE that best fitted solid cancer incidence in the LSS data. These RBE estimates are not applicable for any specific organ, but rather the RBE of a single surrogate organ dose that is being used in analysis of a combination of cancers arising in various organs. This study suggested that the best estimate of the neutron RBE for colon dose in analysis of all solid cancer incidence was 80 [95% CI: 20–190]. These results are rather consistent with other investigations based on similar analyses of the LSS data (*4–8*), but they are much higher than the UNSCEAR and ICRP evaluations. Based on this result, Hafner *et al*. (*6*) indicated a reduction of 50% in the risk estimate for γ ray exposure if a neutron RBE of 110 is used as a surrogate organ dose in all solid cancer incidence study of A-bomb survivors instead of the neutron weighting of 10. The results by Cordova and Cullings (*9*) also show that the RBE for neutrons increases with the depth of the organ from which the surrogate dose is derived because of the way that the neutron/gamma ratio decreases with organ depth, which can be misinterpreted to mean that the true RBE for dose to a specific organ depends on the organ depth.

In this paper, we examine possible determinants of the dependence on organ and organ depth of the mean quality factor, which is closely related to the neutron RBE for A-bomb survivors using a computational approach based on analyses of secondary charged particles focusing on their LET. We performed Particle and Heavy Ion Transport code System PHITS (*18*) simulations using eight representative scenarios of A-bomb survivors using the adult male phantom of the J45 series (*19*, *20*), which were created for precisely reproducing the anatomy of the Japanese in 1945. The calculated LET distributions are converted to the mean quality factors using the Q(L) relationship defined by ICRP (*12*) as well as the QF function defined by NASA (*21*). In addition, we investigate the depth dependence of the mean quality factors in the ICRU sphere (*22*), which is a 30 cm tissue-equivalent phantom used to define area monitoring quantities in radiation protection.

MATERIALS AND METHODS

Procedure for Monte Carlo Simulation

PHITS version 3.31 was used in this study. PHITS has two methods for calculating absorbed doses due to neutron exposure, which are the kerma approximation and energy loss due to charged particles. In this study, the latter was employed by activating the event generator mode (*23*), which can identify all secondary charged particles including recoil nuclei.

In the PHITS simulation, the adult male phantom was irradiated by neutrons with energy and angular distributions for the representative exposure scenarios. The exposure scenarios are described in detail in the next section. Note that we also performed similar simulations by adopting an adult female phantom for exposure scenarios and found that the calculated data are almost independent of the phantom sex. Thus, the data obtained only from the male phantom are shown in this paper. The breast, brain, thyroid, marrow, lung, liver, and colon were the target organs selected in this study. It should be noted that secondary γ rays produced by neutron-induced reactions were not treated as attributable to neutron absorbed dose, because the DS02 system defines the neutron dose in terms of neutron kerma. Thus, it is assumed that the dose due to secondary gamma rays are categorized into photon dose in the DS02 system.

Phantom and Source Data from DS02

The adult male phantom of the J45 series was constructed based on a hybrid phantom developed at the University of Florida and National Cancer Institute (*24*) by adjusting its physical characteristics to that of the 1945 Japanese phantom with an average weight of 54.0 kg. Eight representative exposure scenarios of the A-bomb survivors were considered in this study. Their source information was obtained from the output of the dosimetry system DS02 for the respective outdoor free field and indoor shielding fluences at 1,000 and 1,500 m in Hiroshima and Nagasaki. Note that the outdoor free field fluence is the data for each city and each distance obtained when there is no shielding, i.e., free in air and 1 m above ground, and the indoor shielding fluence is the data for each city and each distance obtained from the shielding parameters of the exposure situation when survivors were exposed inside of a japanese style wooden building (*16*).

Quality Factors Based on ICRP and NASA

In this study, the mean quality factor was calculated to characterize the neutron RBE of the A-bomb survivors and to be compared to RBE. The Q(L) relationship proposed by ICRP (*12*) and $QF_{\gamma\text{-Acute}}$ proposed by NASA (*21*) were adopted for the quality factors. The numerical values of each quality factor are shown in Fig. 1 as a function of LET. The $QF_{\gamma\text{-Acute}}$ values for protons, carbon ions, and oxygen ions are independently plotted in the figure because ion-species dependence can be considered in the concept. Note that $QF_{\gamma\text{-Acute}}$ represents the quality factor when the acute γ-ray exposure was selected as the reference radiation.

The neutron mean quality factor based on the ICRP's definition, $\overline{Q_{\mathrm{ICRP}}}$, can be calculated as follows:

$$\overline{Q_{\mathrm{ICRP}}} = \frac{\int_0^\infty Q(L)D(L)dL}{\int_0^\infty D(L)dL} \tag{1}$$

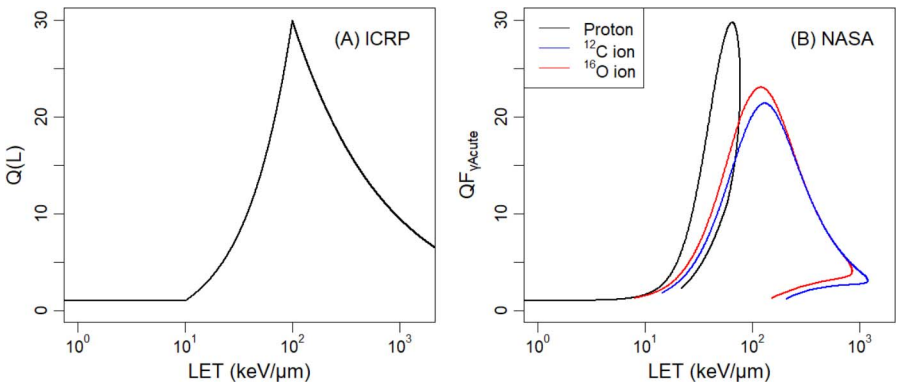

FIG. 1. Radiation quality factors expressed as a function of linear energy transfer (LET) in water as defined by International Commission on Radiological Protection (ICRP) (panel A) and the National Aeronautics and Space Administration (NASA) (panel B).

where L is the LET [keV/μm] in water and $D(L)$ is the absorbed dose due to charged particles with LET $= L$. Similarly, the neutron mean quality factor based on NASA's definition, $\overline{Q_{\mathrm{NASA}}}$, is calculated by

$$\overline{Q_{\mathrm{NASA}}} = \frac{\sum_Z \int_0^\infty QF_{\gamma\mathrm{Acute}}(Z,E)D(Z,E)dE}{\sum_Z \int_0^\infty D(Z,E)dE} \quad (2)$$

where $D(Z, E)$ is the absorbed dose due to charged particles with atomic number Z and energy E. Note that the NASA quality factor can be evaluated not only by its mean value but also by its uncertainty, but in this study, only the mean value is discussed.

It should be noted that the ICRP currently recommends the use of the radiation weighting factor, w_R, for calculating the effective dose, but w_R is designated to be used only for radiological protection purposes and it should not be applied to biological discussions (*2*, *14*).

Calculation of Mean Quality Factor for Mono-energetic Neutrons

For investigating the organ depth dependence of neutron RBE, we calculated neutron $\overline{Q_{\mathrm{ICRP}}}$ at three locations in the ICRU sphere phantom irradiated by mono-energetic neutrons with energies from 10^{-8} to 10 MeV. It would be useful to examine the impact of neutron-capture reactions by comparing between scenarios with and without secondary gamma-ray contribution to $\overline{Q_{\mathrm{ICRP}}}$. Figure 2 shows the simulation setup for this calculation. For representing the organs at shallow, middle, and deep depths inside the human body, target spheres with a radius of 0.5 cm were placed at 0.5, 7.5, and 15.0 cm, respectively, aligned along the central axis of the ICRU sphere for calculating $D(L)$. That is different from the human phantom simulations, where secondary γ rays and associated electrons were transported using the Electron Gamma Shower version 5 (EGS5) mode (*25*) to derive the neutron mean quality factor including body-secondary photon doses.

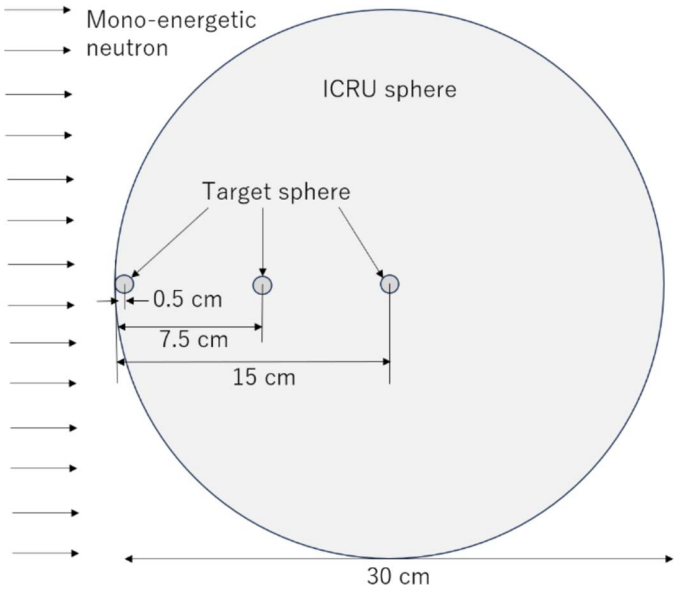

FIG. 2. Simulation setup for calculating $\overline{Q_{\mathrm{ICRP}}}$ in the International Commission on Radiation Units and Measurements (ICRU) sphere irradiated by mono-energetic neutrons.

RESULTS

Figure 3 shows the comparison of $\overline{Q_{\mathrm{ICRP}}}$ calculated by Eq. (1) and $\overline{Q_{\mathrm{NASA}}}$ calculated by Eq. (2) for various organs. The statistical uncertainties of these data are negligibly small, less than 1% in most cases. The calculated data were for the outdoor exposure scenario at 1,000 m in Hiroshima and with the phantom standing and facing the direction of the hypocenter. Figure 3 shows that $\overline{Q_{\mathrm{NASA}}}$ values are higher than the corresponding

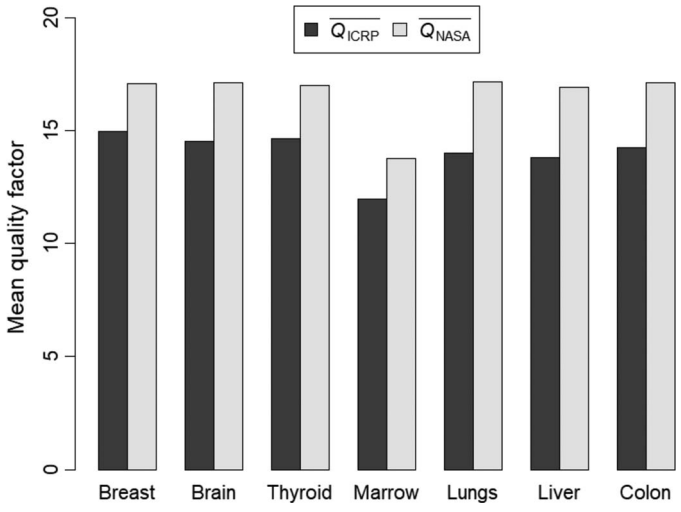

FIG. 3. Comparison between the calculated $\overline{Q_{\mathrm{ICRP}}}$ and $\overline{Q_{\mathrm{NASA}}}$ values for each organ. The calculated data are for the outdoor exposure scenario at 1,000 m in Hiroshima.

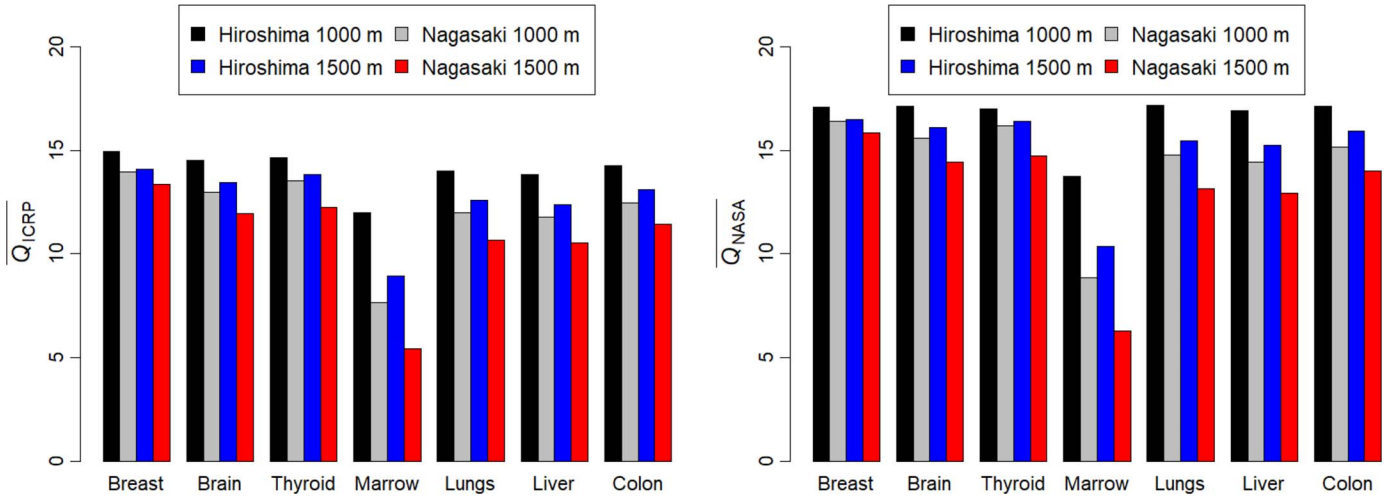

FIG. 4. Dependences of $\overline{Q}_{ICRP}$ and $\overline{Q}_{NASA}$ on the city and the distance from the hypocenter for the outdoor exposure scenario, by organs.

$\overline{Q}_{ICRP}$ values for all organs. Calculation of mean quality factors showed almost constant values across all organs, although the marrow is lower than other organs. This tendency was the same for other exposure scenarios. Only the results will be described for $\overline{Q}_{ICRP}$ as they were consistent.

The dependences of $\overline{Q}_{ICRP}$ and $\overline{Q}_{NASA}$ on the city and the distance from the hypocenter are shown in Fig. 4 for the outdoor exposure scenario. It was found that $\overline{Q}_{ICRP}$ tended to be higher in Hiroshima and at 1,000 m in comparison to the corresponding data in Nagasaki and at 1,500 m. This tendency is consistent with the past analysis based on the radiation weighting factor (*26*). However, their differences were generally insignificant (less than 20%) except for the marrow case. Figure 5 shows the percentage differences between $\overline{Q}_{ICRP}$ calculated for the outdoor and the indoor exposure scenarios. They ranged between 0 and 14%, indicating that $\overline{Q}_{ICRP}$ was slightly lower when inside of a structure.

Figure 6 shows $\overline{Q}_{ICRP}$ at the depths of 0.5, 7.5 and 15 cm in the ICRU sphere irradiated by mono-energetic neutrons. Figure 6 depicts the data with and without considering the sphere secondary γ-ray contributions, respectively. It can be seen in Fig. 6 (left panel) that $\overline{Q}_{ICRP}$ with considering the secondary γ-ray contributions decreased with depth except for neutron energies over a few MeV. In contrast, $\overline{Q}_{ICRP}$ without considering the secondary gamma-ray contributions were almost independent of the depth except for the valley and peak regions observed around 10 keV and 1 MeV, respectively. In general, a larger difference between the data shown in Fig. 6 results including the secondary dose contribution.

Figure 7 shows the neutron fluences for four representative outdoor exposure scenarios adopted in this study. As discussed in previous studies (*26*, *27*), the spectral shapes of the neutron fluences change little at distances greater than 1,000 m, though the high-energy spectra becomes slightly harder in Nagasaki than in Hiroshima, and at 1,500 m than at 1,000 m, respectively (*26*).

DISCUSSION

In this study we calculated neutron mean quality factors, $\overline{Q}_{ICRP}$ and $\overline{Q}_{NASA}$, for different organs using the newly developed J45 phantom, and for different organ depths based on the ICRU sphere. Our results show that the neutron energy spectrum differ slightly for different organs, and for different distances and shielding, mean quality factors are for the most part similar across these different scenarios, showing little variation among organs except for marrow (see Supplementary Fig. S1; https://doi.org/10.1667/RADE-24-00199.1.S1).[2] Our results also show that the neutron mean quality factor is highly dependent on organ depth when the secondary gamma ray contribution is included in the neutron dose, because body shielding is much greater and variable for neutron dose than for gamma rays (Fig. 6, left panel) is for the most part independent of depth when this contribution is not included, which (Fig. 6, right panel) is the case for the neutron doses used in analyses of the RERF cohorts. Hence, our results imply that there should be little variation in Q the mean quality factors across organs or organ depths in analyses of data from atomic bomb survivors.

As shown in Fig. 3, both the $\overline{Q}_{ICRP}$ and $\overline{Q}_{NASA}$ values obtained from this study are much lower than the corresponding RBE data (RBE_{LSS}) obtained from the analyses of LSS data (*4–9*). The calculated neutron mean quality factors are approximately 15 across organs, while the colon RBE estimate as a surrogate organ for all solid cancer incidence was, for example, 80 in the most recent analysis (*9*). Note that our results are in agreement with the corresponding mean radiation weighting factor, approximately 20–23, obtained from the past study (*26*), considering the relationship between w_R and the effective quality factor q_E given in equation (4.7) of ICRP Publication 92 (*14*).

[2] Editor's note. The online version of this article (DOI: https://doi.org/10.1667/RADE-24-00199.1.S1) contains supplementary information that is available to all authorized users.

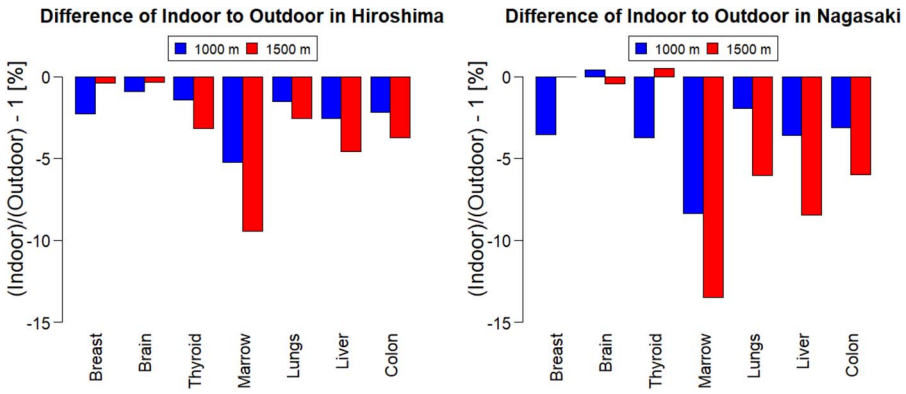

FIG. 5. Percentage differences between $\overline{Q_{\mathrm{ICRP}}}$ values calculated for the inside compared to the outside.

The main reason for the intrinsic difference between $\mathrm{RBE_{LSS}}$ and the mean quality factor computed here is that they are based on entirely different determinants. The quality factor functions estimate for an organ derived in this work relates to the neutron fluence in that organ and therefore to the cancers that would arise in that organ. The RBE estimates obtained for the LSS (*9*) use organ-specific doses in the denominator but use all solid cancers combined in the numerator because there were not statistically enough cancers in individual organs to obtain useful estimates, among other considerations. The LSS-based estimates use organ-specific neutron and gamma ray doses, but do not use any aspect of the organ-specific neutron and gamma ray spectra.

In terms of the numerical aspect, the quality factor functions used by ICRP are assumed not to exceed 30 (*12*), which means that by adopting these functions, the mean quality factors computed in this paper are also bounded below this value. The detailed procedure for deriving the $Q(L)$ relationship has not been documented in any ICRP publication, but it is probably based on the $Q(y)$ relationship given in ICRU Report 40 (*28*). The numerical value of $Q(y)$ was determined by assessing the experimental RBE data with emphasis on the results for incidence of chromosome aberrations in vitro, which are mostly below 30 (*26*). The accuracy of $Q(L)$ was also confirmed by comparing it with the RBE of total chromosomal exchanges (*27*). However, it should be noted that chromosome aberrations are an initial endpoint of biological damage. In addition, $Q(L)$ was originally introduced for the radiological protection purpose, and adequacy of the use of $Q(L)$ for the RBE estimate remains unclear. On the other hand, $\mathrm{QF_{\gamma\text{-}Acute}}$ is designed to be used for the regulatory risk for solid tumors, though it is mostly based on the RBE data obtained from mouse experiments instead of human epidemiological studies (*21*).

In previous LSS data analyses, authors employed the DS02 system with stylized phantoms to calculate organ absorbed doses, while this study uses the DS02 system for source term evaluation but the J45 voxel phantom for radiation transport inside the human body. Owing to the introduction of the J45 phantom series, some organ doses significantly changed, particularly for the neutron contributions, although no trend was observed in the relationship between the old and new calculations (*20*). For example, the organ doses for colon differ by more than 10% and 60% for photon and neutron contributions, respectively. The update of colon dose using the stylized and J45 voxel phantoms can decrease the RBE estimated by the same methods (*7*). Different definitions of the shape and location of an organ will result in different estimates of

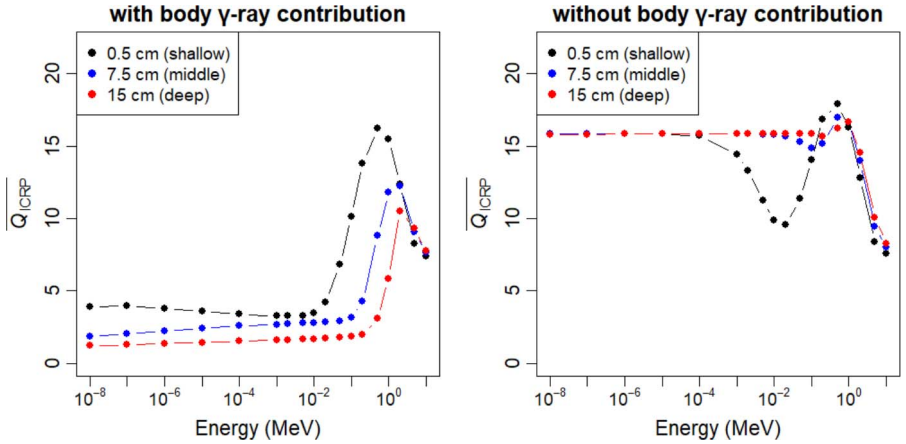

FIG. 6. $\overline{Q_{\mathrm{ICRP}}}$ at the depth of 0.5, 7.5, and 15 cm in the ICRU sphere irradiated with mono-energetic neutrons. This figure shows the data with and without considering the secondary γ-ray contributions, respectively.

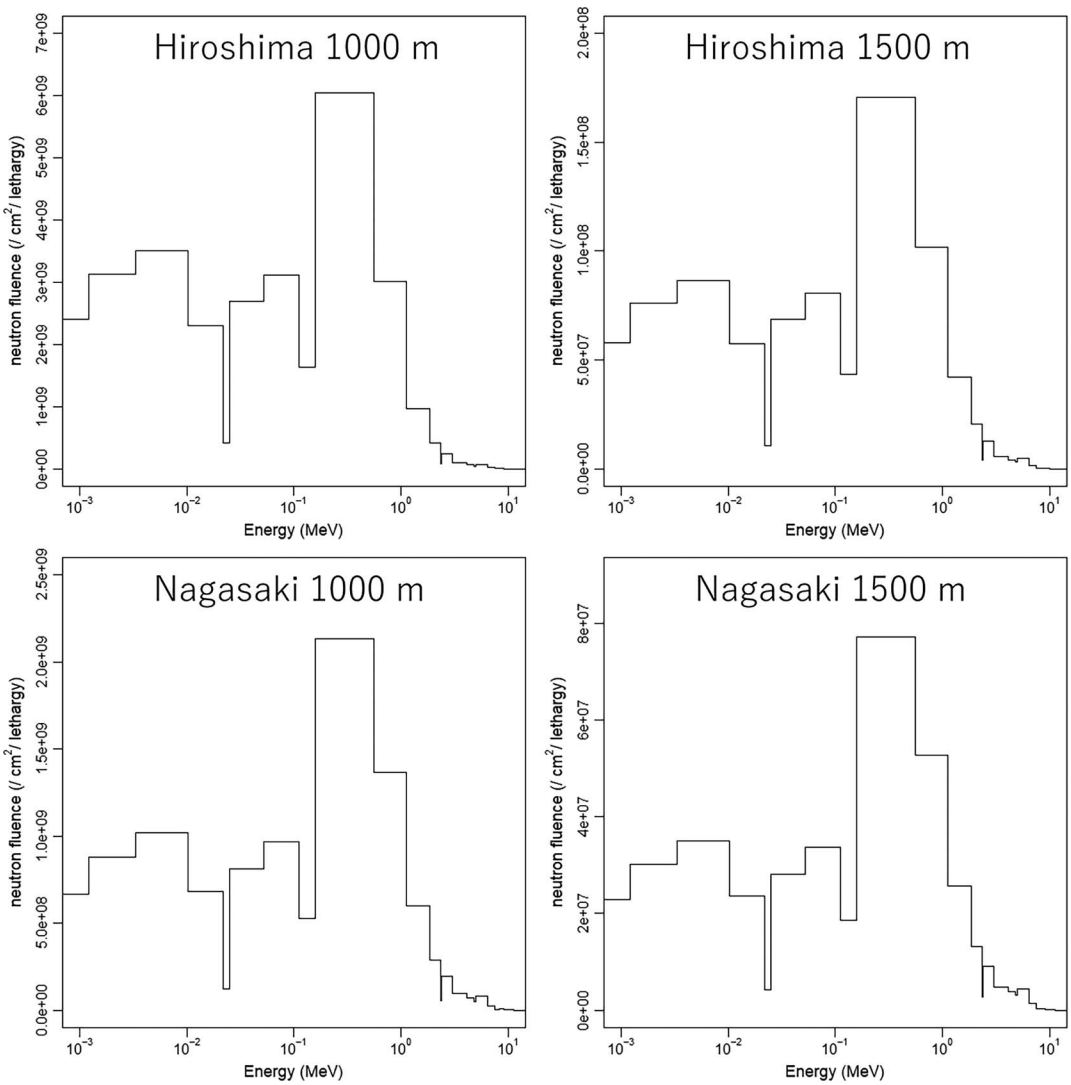

FIG. 7. Neutron fluences for four representative outdoor exposure scenarios adopted in this study.

neutron RBE due to the modification of neutron organ absorbed doses.

Also, it is worth noting the difference in the subjects used for RBE estimation. In this study, absorbed doses in several representative exposure situations were used, whereas in the LSS data analysis the RBE estimate was made using each set of organ doses to the entire A-bomb cohort in the LSS. In the neutron dose distribution in the LSS cohort, it should be noted that the majority of survivors received a neutron absorbed dose of less than 1 mGy, and that is a very small fraction of the total absorbed dose; this assumes a dose-independent Q among the 79,954 LSS cohort in the latest LSS statistical analysis (*7*, *9*). The total dose equivalent is likely to be affected by the uncertainty in the initial gamma-ray dosimetry at low doses, since the statistical analysis includes a large number of low-dose regions. This suggests the difficulty of statistical estimation of the neutron RBE from cancer incidence data from the LSS cohort. Indeed, the results on neutron RBE reported elsewhere (*6*, *7*, *9*) indicate this large statistical uncertainty.

Figure 3 also suggests that $\overline{Q_{\mathrm{NASA}}}$ is higher than the corresponding $\overline{Q_{\mathrm{ICRP}}}$ for all organs, which is consistent with the space dosimetry case (*28*, *30*). This is because $\mathrm{QF}_{\gamma\text{-Acute}}$ for protons, which predominantly contribute to the neutron dose for A-bomb survivors, are generally higher than the corresponding $Q(L)$ as shown in Fig. 1. However, the differences between the two estimates are limited up to about 20%. Such small differences confirm the adequacy of the use of $Q(L)$ for the RBE analysis of the neutron exposure, considering that $\mathrm{QF}_{\gamma\text{-Acute}}$ is designed for the risk estimate of solid cancers.

Figure 4 suggests that $\overline{Q_{\mathrm{ICRP}}}$ and $\overline{Q_{\mathrm{NASA}}}$ tend to be higher in Hiroshima and at 1,000 m in comparison to the corresponding data in Nagasaki and at 1,500 m, respectively. This is due to the harder neutron spectrum above 1 MeV in Nagasaki at 1,500 m, as shown in Fig. 7, results in lower quality factors due to higher recoil proton energies. The reason for lower and in marrow than those in other organs is the less atomic concentration of nitrogen

in marrow compared with other organs (see Supplementary Table S1; https://doi.org/10.1667/RADE-24-00199.1.S1); the quality factors due to secondary protons with an energy of 0.58 MeV produced by neutron capture reaction of nitrogen is very high – approximately 16 for $\overline{Q_{\mathrm{ICRP}}}$. These tendencies can be discussed in relation to the differences in chromosome aberrations between cities in the analysis using bone marrow doses. The analysis of chromosome aberrations due to the atomic bombs (*31*), where the neutron weighting was set to 10 and uniformly weighted for exposed persons, the frequency of stable chromosome aberrations in lymphocytes of indoor survivors was higher than that of outdoor survivors, indicating a discrepancy with the physical dose. In contrast, $\overline{Q_{\mathrm{ICRP}}}$ for bone marrow tend to be lower indoors than outdoors, as shown in Fig. 5. This opposite trend suggests that the difference between physical dose and the frequency of chromosome aberrations cannot be explained by the neutron quality factors. It should be noted that an increase of RBE is expected with decreasing neutron dose, considering the linear-quadratic (LQ) dose response of gamma radiation. However, the opposite trend was observed in Fig. 4, where the mean quality factors for deeper organs with lower doses are generally lower. This result is associated with the ignorance of the dose dependence in the concept of the quality factor. Thus, it does not imply that the mean quality factors of the A-bomb survivors is lower for organs with lower doses.

Figure 6 clearly indicates that $\overline{Q_{\mathrm{ICRP}}}$ significantly depends on whether the secondary γ rays, which are predominantly produced by $^{1}\mathrm{H}(\mathrm{n},\gamma)^{2}\mathrm{H}$ reaction, are considered in the dose calculation. It should be noted that, in general, there is no clear provision for the treatment of secondary γ rays in the definition of neutron RBE. When something as small as a cell is irradiated with neutrons, the absorbed dose is mostly due to recoil protons or heavier recoil particles from neutron collisions or neutron-induced nuclear reactions because any produced secondary gamma rays can leave the small sample. For larger volumes of biological material, such as the mouse and human, the situation is more complicated because of the mixed radiation field of secondary γ rays in the tissue (*14*, *32*). Thus, the neutron RBE is generally considered to be lower at deeper depths; this is the case when the contribution of secondary γ rays is considered. On the other hand, $\overline{Q_{\mathrm{ICRP}}}$ without considering the secondary γ rays, as is the definition of the DS02 system, is found to be almost constant at all depths except for the valley and peak observed around 10 keV and 1 MeV, respectively. The peak around 1 MeV is attributable to the fact that the LET of recoil protons reaches the maximum, while the valley around 10 keV observed only in the 0.5 cm data is due to the reduced stopping power of recoil protons with the decrease of neutron energy. The reason why $\overline{Q_{\mathrm{ICRP}}}$ is constant at low energies except for the 0.5 cm data is that most of the neutron doses are contributed from the neutron capture reaction of nitrogen. Since the neutron doses in the LSS data analysis do not include the secondary γ ray co-contributions, they should not depend much on depth, as shown in Fig. 6, right panel.

Although the LSS cohort is a neutron-exposed population, there might be a large uncertainty in the statistical estimation of the neutron RBE, considering the smaller contribution of neutrons to the total absorbed dose (approximately 0.5% in Hiroshima at 1,500 m from the hypocenter) (*20*). The latest study (*7*) analyzed all solid cancer mortality data (*33*) to estimate the best statistical-fitting neutron RBE. The results showed that the RBE for mortality was much higher than for incidence (*9*), and both RBEs were 50–190 using colon dose. It is likely that the neutron RBE estimate could have a large impact to significantly reduce the gamma risk estimate based on the A-bomb survivors study. Thus, further careful consideration is needed for estimating the neutron RBE from the LSS cohort, which affects estimation of cancer risk not only from neutrons but also γ rays.

Further studies are necessary for re-evaluating the neutron RBE from the LSS cohort using a new dosimetry system employing the J45 series phantoms. In analyzing neutron RBE, the shape of the dose-response curve must also be carefully taken into account in both epidemiological and computational studies because the photon and neutron dose responses are generally considered as the linear-quadratic and linear relationships, respectively. It should be noted that the RBE estimates of Cordova and Cullings (comparisons made in this paper) were derived using a model that was linear in both gamma ray and neutron dose response, and the result would be different from a linear-quadratic-linear (LQ-L) model in which gamma ray is linear quadratic and neutron is linear (*34*). Furthermore, the results of Cordova and Cullings had to use the sum of all solid cancers arising in all organs to obtain the best statistics, but the organs vary greatly in the neutron/gamma rays ratio that determines the results, leading to very different results depending on which organ dose was used. Future work could use some kind of a weighted average among organ doses, for example, but with the linear-linear (L-L) model this would apparently still give much higher values than those obtained here for the mean quality factors.

CONCLUSIONS

It would be useful to note what emerged from the comparison between the epidemiological estimates of RBE and the mean quality factors calculated for the adult male phantom of the J45 series using neutron source information from the output of the dosimetry system DS02, knowing the limitations of comparing QFs to epidemiological and biological RBEs.

The calculated mean quality factors based on ICRP and NASA definitions are lower than the neutron RBE obtained from the latest analysis on the LSS data. Our calculations indicate that the neutron RBE should not significantly depend on the organ depth from the body surface when the contributions from the secondary γ-rays are excluded from the neutron doses.

SUPPLEMENTARY MATERIALS

Supplementary Fig. S1. Comparison between the calculated $\overline{Q_{\mathrm{ICRP}}}$ and $\overline{Q_{\mathrm{NASA}}}$ for each organ in eight exposure scenarios.

Supplementary Table S1. Elemental compositions (percentage by mass), and their densities of organs.

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