RADIATION RESEARCH **145**, 501–507 (1996)
0033-7587/96 $5.00

COMMENTARY

Direct Biological Evidence for a Significant Neutron Dose to Survivors of the Hiroshima Atomic Bomb

David J. Brenner

Center for Radiological Research, Columbia University, 630 West 168th Street, New York, New York 10032

Brenner, D. J., Direct Biological Evidence for a Significant Neutron Dose to Survivors of the Hiroshima Atomic Bomb. *Radiat. Res.* 145, 501–507 (1996).

In the past few years much physical evidence has accumulated that the A-bomb survivors at Hiroshima were exposed to significant doses of neutrons, in contrast to the predictions of the current DS86 dosimetry. We discuss some biological measurements of exchange-type chromosomal aberrations in survivors at Hiroshima, which also strongly imply that the survivors received a significant neutron dose. Specifically, the ratio of translocations (an interchromosomal aberration) to pericentric inversions (intrachromosomal interarm aberration), the *F* value, was significantly smaller than would be expected from a γ-ray exposure, and was consistent with the majority of the effective dose coming from neutrons. If this biological evidence and the previous physical evidence are correct, the effective neutron dose at relevant locations at Hiroshima dominated the total effective dose, from which it may be concluded that (1) the risk coefficient for γ rays may have been considerably overestimated, and (2) there is a possibility of deriving from the A-bomb data, with reasonable confidence limits, the relative biological effectiveness (RBE) for carcinogenesis by neutrons. © 1996 by Radiation Research Society

INTRODUCTION

Because of the pivotal role of the A-bomb survivor cohorts in radiation risk estimation, dosimetry for the survivors at Hiroshima and Nagasaki continues to be of central importance.

The area of dosimetry in which there is still most uncertainty involves the magnitude of the neutron dose to the survivors at Hiroshima. Historically, the earlier "T65D" dose estimates suggested that the majority of the effective dose to the survivors at Hiroshima was due to neutrons (*1, 2*). However, when the doses were reassessed in 1986 (*3*), the revised "DS86" dosimetry suggested that neutron doses at relevant locations at Hiroshima were about an order of magnitude less than estimated previously. This decrease in the estimated neutron dose had two main consequences (*4*):

1. The estimated risk coefficient for γ rays increased, as a consequence in part of the lack of neutron-induced damage.[1]
2. It was no longer possible to estimate (with useful confidence limits) the relative biological effectiveness (RBE) of the neutrons for carcinogenesis—eliminating the only direct epidemiologically based estimate of the RBE for cancer induction by densely ionizing radiations.

However, since 1987, a series of reports (e.g. *5–19*) have documented the conclusion that the results of measurements of neutron activation at Hiroshima are not consistent with DS86 predictions. In particular, at the ground range of most interest for risk estimation for low-dose radiation (~900–1,450 m), predictions significantly underestimate the measured neutron-induced activation. For example, at a ground range of 1,450 m, the ratio of measured to DS86-calculated neutron-induced chlorine activation is 15 ± 2 (*5*). Figure 1 shows a compilation of comparisons between neutron-induced activation measurements and the corresponding DS86-based predictions.

Much research has been devoted to resolving this problem (see ref. *19*), focusing on uncertainties in either (1) the neutron energy spectrum emerging from the bomb, (2) calculated transport of the neutrons to relevant locations or (3) activation measurement uncertainties. At present the issue has not been resolved satisfactorily, though an explanation based on a reassessment of the neutron energy spectrum emitted from the Hiroshima bomb is now considered the most likely possibility (*20, 21*).

In this Commentary we suggest that there is direct *biological* evidence that the neutron component at Hiroshima not only is significant, but dominates the total effective dose at the ground distances of most relevance for risk estimation (~900–1450 m); this conclusion would suggest that the activation measurements at Hiroshima are valid and perti-

[1]The risk coefficient also increased for other reasons, such as the increased observation time of the A-bomb survivors (*4*).

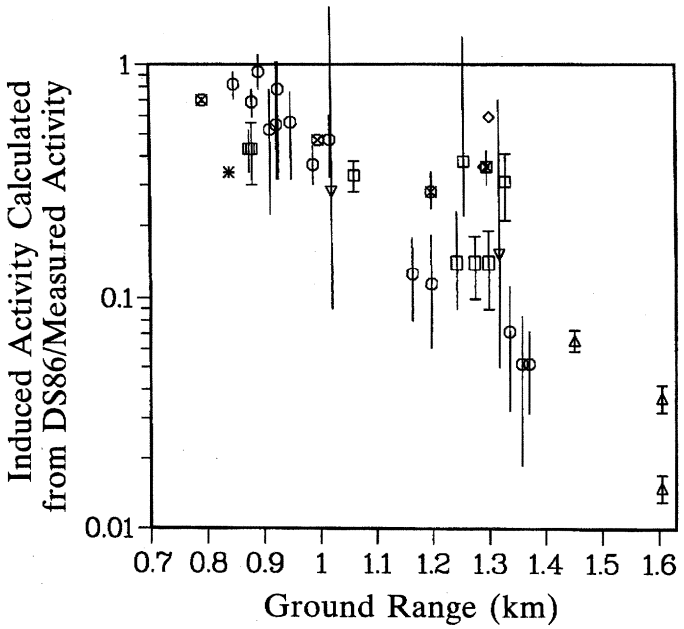

FIG. 1. Ratio of A-bomb neutron-induced activation as predicted with the DS86 dosimetry, to the measured neutron activity, as a function of ground distance from the epicenter of the explosion at Hiroshima. Only data beyond 750 m ground distance are shown, which includes the ground range of most importance for risk estimation (900–1,450 m), where the measured neutron-induced activity is significantly underpredicted by the DS86 dosimetry. The different symbols refer to measurements by different investigators using neutron activation of chlorine, europium, cobalt and sulfur. Corresponding calculations are those reported (*5–7*) by the group at SAIC (Science Applications International Corporation, San Diego). (△) Chlorine activation, Straume *et al.* (*5*); (○) europium activation, Shizuma *et al.* (*9*); (□) europium activation, Nakanishi *et al.* (*10–12*); (✳) europium activation, Sakanoue *et al.* (*13*); (◇) cobalt activation, Kerr *et al.* (*14*); (⊗) cobalt activation, Hashizume (*15*); (⊠) cobalt activation, Kimura *et al.* (*16*); (▽) sulfur activation, Hamada (*17, 18*).

nent, and that the DS86 dosimetry at Hiroshima requires further reassessment, with attendant consequences for radiation risk estimation, for both neutrons and γ rays.

BIOLOGICAL EVIDENCE FOR NEUTRONS AT HIROSHIMA

As well as the physical "fingerprint" of activation, neutrons also produce a stable and measurable characteristic biological fingerprint or biomarker (*22*). Briefly, when they interact with matter, neutrons give rise to secondary charged particles that deposit energy, say within a cell, over very short distances, in contrast to X or γ rays, which deposit energy fairly randomly across a cell (Fig. 2). This difference turns out to result in the induction of different proportions of various types of chromosomal aberrations (Fig. 3), which can still be measured in the survivors to this day.

Specifically, exchange-type chromosomal aberrations are caused by misrepair of pairs of breaks in one or two chromosomes (i.e., the wrong ends join together) (Fig. 3). If the breaks are in different chromosomes, *inter*chromosomal aberrations can result, whereas if both breaks are in one chromosome, an *intra*chromosomal aberration can be formed. It is the ratio of the yields of these two types of chromosomal aberrations (the F value) that is the biomarker for neutron exposure (*22*). If breaks were produced at random in the cell, and they were all equally likely to interact with one another, the ratio (F) of interchromosomal to intrachromosomal interarm aberrations, simply based on the number and length of chromosomal arms, would be approximately 90 (*23*). In fact pairs of breaks that are close to one another within a cell nucleus are more likely to interact than pairs that are comparatively far apart

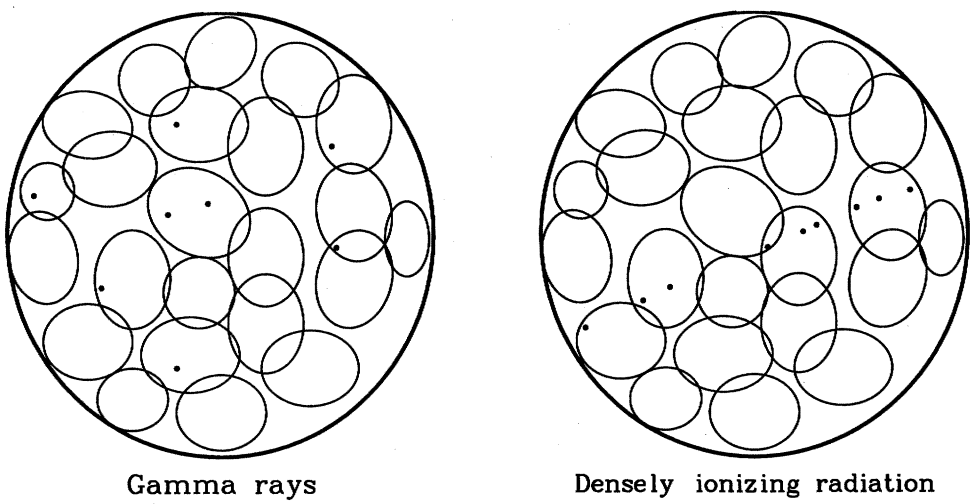

FIG. 2. The points represent typical relative locations of DSBs produced by equal low doses of γ rays (left panel, in this case 100 keV photons), and a densely ionizing radiation (right panel, in this case α particles); they were produced by Monte Carlo simulation. The locations have been superimposed on a cell nucleus (diameter 8 μm) on which schematic chromosomal "domains" have been drawn. The γ-ray-induced DSBs are essentially random in space, and thus multiple breaks within a single chromosome are comparatively rare. Densely ionizing radiations such as neutrons produce chromosomal breaks that are closer together, making multiple breaks within a single chromosome comparatively more frequent.

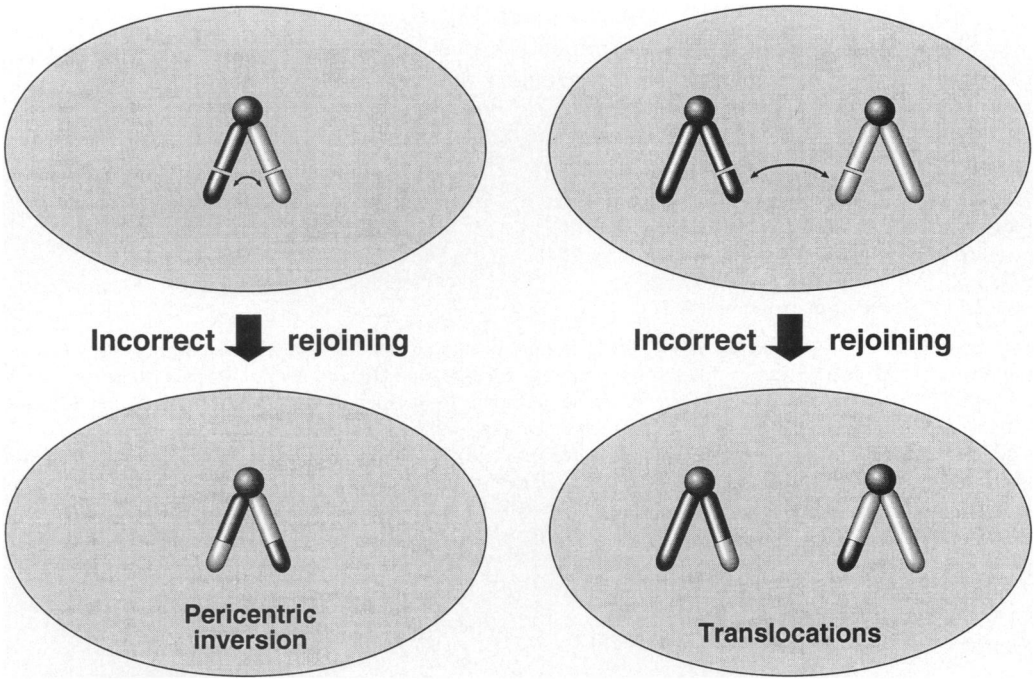

FIG. 3. Schematic illustration of the production of stable interchromosomal (left panel) and intrachromosomal interarm aberrations as a result of radiation-induced breaks (right panel). The *F* value is the ratio of the number of induced interchromosomal aberrations (translocations) to intrachromosomal interarm aberrations (pericentric inversions). Simply based on the number of chromosome arms and their lengths, the *F* value would be expected to be 90 in human cells. Because individual chromosomes are located in relatively small domains within the nucleus, intrachromosomal aberrations are, on average, produced by shorter-range, more probable interactions, which reduces actual *F* values for X or γ rays to about 15 or 20. Neutrons, which preferentially produce breaks that are very close together (see Fig. 2), give added weight to intrachromosomal aberrations, and reduce the *F* value to around 6.

(*24*). If, as is now known, individual chromosomes are localized in domains that are smaller than the cell nucleus (e.g. *25*), this increased interaction probability of nearby breaks will produce a bias toward intrachromosomal compared with interchromosomal aberrations. So, for γ rays, the *F* value is actually closer to 15, a literature survey of available data giving a value of 16 ± 5 (*23*).

However, densely ionizing radiations such as neutrons produce energy depositions, and thus chromosome breaks, that are, on average, much closer together than those produced by X or γ rays. Thus, at equal low doses, as illustrated schematically in Fig. 2, densely ionizing radiations are much more likely than sparsely ionizing radiations to produce multiple breaks *within* a given chromosome. Consequently, yields of intrachromosomal aberrations after exposure to low doses of densely ionizing radiations are increased even further relative to interchromosomal aberrations, and the resulting smaller *F* value is then a "fingerprint" of a past exposure to a densely ionizing radiation such as neutrons. *F* values in stable aberrations (Fig. 3) can often be measured in the cells (and their progeny) of an irradiated individual many years after exposure (*26*).

Are the differences in *F* values generally large enough to act as a genuine fingerprint of neutron exposure? Table I summarizes recent data from the literature, and it seems clear that densely ionizing radiations such as neutrons do produce a significantly smaller *F* value of ~6, compared with *F* values that are larger than ~15 for X or γ rays.

Experimental Results from Survivors at Hiroshima

There have been three independent measurements of yields of translocations and pericentric inversions in samples of peripheral lymphocytes taken from a total of over 400 exposed survivors of the Hiroshima explosion,[2] as well as controls (*34–36*). Each of the studies used the G-banding technique (*37*). In the first study, reported by Awa and colleagues (*34*), ~35,000 peripheral blood lymphocyte cells were examined from blood samples taken in 1968–1969 from 386 exposed individuals who received a mean T65D total dose of ~2.3 Gy (and 263 controls). Over 2,000 translocations and over 300 pericentric inversions were scored. In the second study, reported by Ohtaki (*35*), ~8,000 metaphase cells were assayed from 1977–1992 from individuals with a mean DS86 dose of ~1.5 Gy (and 11 controls), yielding a total of more than 1,000 translocations and more than 200 pericentric inversions. In the third study by Sachs *et al.* (*36*), 3,800 cells were assayed from blood sam-

[2]No corresponding data have been published for survivors at Nagasaki.

TABLE I
Survey of Experimentally Determined F Values[a] for Densely Ionizing Radiations (Neutrons or α Particles) and for X or γ Rays[b]

Human cells exposed to neutrons or α particles[c]		Human cells exposed to X or γ rays	
5.6 ± 0.5	*in vitro* exposure to neutrons (*27*)[d]	16.7 ± 0.5	*in vitro* exposure to X rays (*32*)[d]
5.0 ± 0.3	Thorotrast (α-particle exposure, *28*)[d]	22 ± 3	radiotherapy exposure (*33*)[d]
5.6 ± 0.3	plutonium (α-particle exposure, *29*)[e]	16 ± 5	literature survey (*23*)[d,f]
4.5 ± 2.0	plutonium (α-particle exposure, *29*)[d]		
5.7 ± 3.5	neutron exposure (*30, 31*)[e]		
5.0 ± 2.4	neutron exposure (*30, 31*)[d]		

Notes. For comparison, the measured value from survivors at Hiroshima is about 6 (see text). Further details are in ref. (*22*).

[a]Although it is the F value in stable aberrations that has the potential to act as a practical biomarker of past exposure to high-LET radiation, it is to be expected that F values for unstable aberrations follow the same pattern as those for stable aberrations. Thus, in investigating the validity of this biomarker, it is reasonable to use data for unstable aberrations to augment the results for stable aberrations.

[b]In assessing the data in this table, it is important to recognize that none represent the results of direct "head-to-head" experiments in which measurements are taken for both sparsely and densely ionizing radiations within a single experiment.

[c]The data for densely ionizing radiations are restricted to low doses, where the mean number of tracks passing through a cell is small. At higher doses of densely ionizing radiations, where multiple cellular traversals are common, the F value would be expected to increase, as intertrack interactions become more common.

[d]Unstable aberrations (dicentrics/centric rings).

[e]Stable aberration (translocations/pericentric inversions).

[f]This figure is based on values from 7 reports referenced in (*23*).

ples drawn during 1989–1990 from 31 individuals with a mean DS86 dose of ~1.3 Gy (and 7 controls), yielding over 600 translocations and over 100 pericentric inversions. The F values from the results of the three studies were 6.8 ± 0.4 (*34*), 5.7 ± 0.4 (*35*) and 6.2 ± 0.7 (*36*). The consistency of these values over a period of 20 years suggests that the F value does not change significantly over very long periods. These values are clearly significantly smaller than the estimated value of ≥15 for X or γ rays (Table I), and are consistent with the value of ~6 for densely ionizing radiations such as neutrons.

In a mixed neutron and photon field, it would be expected that the F value would be intermediate between those of "pure" neutrons and "pure" photons. The measured F value of about 6, being close to that expected for a pure neutron field, suggests that most of the measured exchange-type chromosomal aberrations were produced by neutrons, rather than X rays; thus we may conclude conservatively that

$$D_n \, \mathrm{RBE}_n > D_x, \qquad (1)$$

where D_n is the neutron dose, D_x is the photon dose, and RBE_n is the relative biological effectiveness at dose D_n for production of exchange-type chromosomal aberrations by neutrons.

For the end point of formation of an exchange-type chromosomal aberration, and for the doses of relevance here, a reasonable value of RBE_n is ~10 (*38, 39*), and thus

$$D_n/D_x > 0.1. \qquad (2)$$

Of course these considerations refer to an average over the ground ranges corresponding to the individuals examined in the three studies (*34–36*); based on the reported distribution of doses to the individuals, the mean ground range was between 1,000 and 1,100 m.

Comparison with DS86 Predictions

In fact, in the DS86 dosimetry system the estimated value of D_n/D_x varies from ~0.07 to ~0.02 in the ground range from 900 to 1450 m, which is the most relevant region for risk estimation. Thus the measured F values do not confirm the DS86 dosimetry, but rather imply that the D_n/D_x ratio is significantly larger than the DS86 estimate.

This conclusion is also in quantitative agreement with that derived from the results of the neutron activation discussed above, which also imply a larger D_n/D_x ratio than predicted by DS86. In some recent calculations, Rhoades *et al.* (*21*) made various adjustments to the Hiroshima bomb neutron source spectrum until the predicted activation results were reconciled with the actual measurements. In configurations where calculation and measurement were in agreement, the resulting predicted D_n/D_x ratio varied from 0.33 to 0.14 from 900 to 1,450 m, i.e. the ground range of interest. These values are consistent with the inequality, Eq. (2), derived from the biological data.

This result can also be derived from the quantitative model for F values described by Brenner and Sachs (*22*). According to that model, exchange-type aberrations are due to pairwise interactions of DNA double-strand breaks (DSBs) and the key determinant of the F value is whether the two DSBs involved in an interaction come from the same radiation track or from two different radiation tracks. The former case tends to produce a lower F value (approximately 6) than the latter (approximately 15 or more). Thus the measured values of 6.8 ± 0.4 (*34*), 5.7 ± 0.4 (*35*) and 6.2 ± 0.7 (*36*) in the lymphocytes of survivors at Hiroshima pro-

vide evidence that most of the exchange-type chromosome aberrations were made by DSB pairs originating from single radiation tracks; i.e., both DSBs of the pair were induced by one neutron (rather than by two different neutrons, a neutron and a photon, or two different photons, the probability of one photon inducing two DSBs which subsequently undergo an exchange-type aberration being treated as negligible). The calculation can be quantified if an RBE for neutron-induced DSBs (as opposed to exchanges) is assumed. Taking this RBE for DSB induction to be less than 2 (*40*), numerical calculations show that the inequality of Eq. (2) is a conservative conclusion from the observed F value of ~6.

DISCUSSION

From the biological data on F values of stable chromosomal aberrations in survivors in Hiroshima, we have concluded that $D_n > 0.1D_x$ at relevant ground distances, in significant disagreement with the DS86 prediction, but consistent with physical activation measurements in Hiroshima. Assuming that an appropriate radiation weighting factor for the neutrons in Hiroshima is 10–20 (*39*, *41*), we conclude the majority of the effective dose received by individuals in Hiroshima, in the ground range of significance for risk estimation, came from neutrons. In other words, the majority of the biological damage at Hiroshima was probably caused by neutrons, not photons.

These conclusions are also consistent with the analysis of yields of stable chromosomal aberrations from survivors in Hiroshima and Nagasaki reported by Stram *et al.* (*42*): They reported a curvilinear dose–yield relationship from survivors at Nagasaki, characteristic of low-LET radiation, in contrast to a linear dose–yield relationship for aberrations from survivors at Hiroshima, characteristic of high-LET radiation. The initial slope of the dose–yield relationship was ~6 times larger for survivors in Hiroshima compared to Nagasaki. Stram *et al.* (*42*) attempted to explain the higher yields of aberrations in Hiroshima compared to Nagasaki on the basis of the DS86 estimated neutron doses in Hiroshima. Using this dosimetry, a maximal neutron RBE of ~700 (95% confidence limits 200–∞) is required to reconcile the yields in the two cities. Even the lower RBE bound (200) is unrealistically large (*38*, *39*), and an increase in the estimated neutron dose in Hiroshima would lead to a corresponding decrease in the estimates for the neutron RBE, down to more plausible values.

More speculatively, several situations have recently attracted comment, where risk estimates based on A-bomb survivors are significantly larger than corresponding risk estimates based on other exposed cohorts. One example is lung cancer mortality in Canadian tuberculosis patients (*43*), which yields far lower risk estimates than those based on the data for A-bomb survivors. Another example is risk estimates for domestic exposure to radon, where risk estimates based on data for miners are significantly lower than appropriately adjusted risk estimates based on data for the A-bomb survivors (*44*). While such discrepancies are subject to several possible explanations, a significant exposure to neutrons in Hiroshima could, at least in part, reconcile these observations.

CONCLUSIONS

If the neutron doses at Hiroshima in the ground range from 900 to 1,450 m were indeed significantly larger than those predicted by DS86 dosimetry, there would be at least two important consequences:

1. The risk coefficient for γ rays would be decreased because the neutrons would account for more of the effect than currently assumed. For example, based on results in the report of the BEIR V Committee (*45*), and assuming no change in their assumed radiation weighting factor for neutrons, if the neutron doses at the ground ranges of interest were increased by a factor of 5 compared with DS86 predictions, the linear risk coefficient for γ rays for cancers other than leukemia would decrease by about 40%, per unit dose.
2. It might now be possible, for example using calculations analogous to those reported previously by Rossi and Mays (*2*) or Preston and Pierce (*46*, *47*), to extract from the A-bomb data, with reasonable confidence limits, an RBE for carcinogenesis by neutrons. A preliminary calculation[3] suggests that, if the neutron dose at Hiroshima is increased over the DS86 estimates in a manner suggested by the neutron activation data, it will be possible to derive a much better-defined likelihood profile for this RBE than was the case using DS86, where the likelihood profile for the RBE varied very little between values of 1 and 100 (*46*).

In summary, we have presented biologically based evidence to support the mounting physical evidence suggesting that the DS86 dosimetry system significantly underestimates neutron doses for relevant ground locations at Hiroshima. It appears that the underestimation of the neutron dose in Hiroshima is sufficiently large that risk coefficients for photons based on the data for the A-bomb cohort may well be significantly affected.

ACKNOWLEDGMENTS

I am indebted to Drs. Ray Sachs and Charles Geard and several reviewers for their helpful advice. This work was supported by Grants CA-12536 and DE-FG02-88ER60631.

Received: July 25, 1995; accepted: November 29, 1995

REFERENCES

1. R. C. Milton and T. Shohoji, *Tentative 1965 Radiation Dose Estimates for Atomic Bomb Survivors, Hiroshima and Nagasaki.* TR 1-68, Atomic Bomb Casualty Commission, Hiroshima, 1968.

[3]D. L. Preston, private communication, March 1988.

2. H. H. Rossi and C. W. Mays, Leukemia risk from neutrons. *Health Phys.* **34**, 353–360 (1978).
3. W. C. Roesch, Ed., *U.S.–Japan Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki*. Radiation Effects Research Foundation, Hiroshima, 1987.
4. W. H. Ellett, Neutrons at Hiroshima: How their disappearance affected risk estimates. *Radiat. Res.* **128**, S147–S152 (1991).
5. T. Straume, S. D. Egbert, W. A. Woolson, R. C. Findel, P. W. Kubik, H. E. Gove, P. Sharma and M. Hoshi, Neutron discrepancies in the DS86 Hiroshima dosimetry system. *Health Phys.* **63**, 421–426 (1992).
6. D. C. Kaul, W. A. Woolson, S. D. Egbert and T. Straume, A brief summary of comparisons between the DS86 A-bomb survivor dosimetry system and *in-situ* measurements in light of new measurements, revised nuclear data and improved calculational methods. In *Proceedings of the Eighth International Conference on Radiation Shielding*, pp. 232–237. American Nuclear Society, New York, 1994.
7. M. L. Gritzner and W. A. Woolson, Sulfur activation at Hiroshima. In *U.S.–Japan Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki, Final Report* (W. C. Roesch, Ed.), Vol. 2, pp. 283–292. Radiation Effects Research Foundation, Hiroshima, 1987.
8. M. Hoshi, K. Yokoru, S. Sawada, K. Shizuma, K. Iwatani, H. Hasai, T. Oka, H. Morishima and D. J. Brenner, Europium-152 activity induced by Hiroshima atomic-bomb neutrons. Comparison with the ^{32}P, ^{60}Co and ^{152}Eu activities in Dosimetry System 1986 (DS86). *Health Phys.* **57**, 831–837 (1989).
9. K. Shizuma, K. Iwatani, H. Hasai, M. Hoshi, T. Oka and H. Morishima, Residual ^{152}Eu and ^{60}Co activities induced by neutrons from the Hiroshima atomic bomb. *Health Phys.* **65**, 272–282 (1993).
10. T. Nakanishi, T. Imura, K. Komura and M. Sakanoue, Europium-152 in samples exposed to the nuclear explosions in Hiroshima and Nagasaki. *Nature* **302**, 132–134 (1983).
11. T. Nakanishi, K. Kobayashi, T. Yamamoto and K. Miyaji, Residual neutron-induced radioactivities in samples exposed in Hiroshima. In *U.S.–Japan Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki, Final Report* (W. C. Roesch, Ed.), Vol. 2, pp. 310–319. Radiation Effects Research Foundation, Hiroshima, 1987.
12. T. Nakanishi, T. Ohtani, R. Mizuochi, K. Miyaji, T. Yamamoto, K. Kobayashi and T. Imanaka, Residual neutron-induced radionuclides in samples exposed to the nuclear explosion over Hiroshima: comparison of the measured values with the calculated values. *J. Radiat. Res.* **32** (Suppl.), 69–82 (1991).
13. M. Sakanoue, K. L. Tan and K. Komura, *In situ* measurement and depth profile of residual ^{152}Eu activity induced by neutrons from the atomic bomb in Hiroshima. In *U.S.–Japan Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki, Final Report* (W. C. Roesch, Ed.), Vol. 2, pp. 261–265. Radiation Effects Research Foundation, Hiroshima, 1987.
14. G. D. Kerr, F. F. Dyer, J. V. Pace, III, R. L. Brodzinski and J. Marcum, *Activation of Cobalt by Neutrons from the Hiroshima Bomb*. Report ORNL-6590, Oak Ridge National Laboratory, Oak Ridge, TN, 1990.
15. T. Hashizume, Present plans for dose reassessment experiments by the Japanese. In *U.S.–Japan Workshop for Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki* (D. J. Thompson, Ed.), pp. 7–12. Radiation Effects Research Foundation, Hiroshima, 1983.
16. T. Kimura, N. Takano, T. Iba, S. Fujita, T. Watanabe, T. Maruyama and T. Hamada, Determination of specific activity of cobalt ($^{60}Co/Co$) in steel samples exposed to the atomic bomb in Hiroshima. *J. Radiat. Res.* **31**, 207–213 (1990).
17. T. Hamada, Measurement of ^{32}P activity induced in sulfur in Hiroshima. In *U.S.–Japan Joint Workshop for Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki* (D. J. Thompson, Ed.), pp. 45–54. Radiation Effects Research Foundation, Hiroshima, 1983.
18. T. Hamada, Measurements of ^{32}P in sulfur. In *U.S.–Japan Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki, Final Report* (W. C. Roesch, Ed.), Vol. 2, pp. 272–279. Radiation Effects Research Foundation, Hiroshima, 1987.
19. R. A. Kehlet and R. W. Young, The DNA program to resolve the Hiroshima discrepancy, an overview. In *Proceedings of the Eighth International Conference on Radiation Shielding*, pp. 209–211. American Nuclear Society, New York, 1994.
20. T. Straume, L. J. Harris, A. A. Marchetti and S. D. Egbert, Neutrons confirmed in Nagasaki and at the Army Pulsed Reactor Facility: Implications for Hiroshima. *Radiat. Res.* **138**, 193–200 (1994).
21. W. A. Rhoades, J. M. Barnes and R. T. Santoro, An explanation of the Hiroshima activation dilemma. In *Proceedings of the Eighth International Conference on Radiation Shielding*, pp. 238–244. American Nuclear Society, New York, 1994.
22. D. J. Brenner and R. K. Sachs, Chromosomal "fingerprints" of prior exposure to densely ionizing radiation. *Radiat. Res.* **140**, 134–142 (1994). [Commentary]
23. L. Hlatky, R. K. Sachs and P. Hahnfeldt, The ratio of dicentrics to centric rings produced in human lymphocytes by acute low-LET radiation. *Radiat. Res.* **129**, 304–308 (1992).
24. S. Wolff, Interpretation of induced chromosome breakage and rejoining. *Radiat. Res.* Suppl. **1**, 453–462 (1959).
25. H. Van Dekken, D. Pinkel, J. Mulliken, B. Trask, G. Van den Engh and J. Gray, Three-dimensional analysis of the organization of human chromosome domains in human and hamster hybrid cells. *J. Cell Sci.* **94**, 299–306 (1989).
26. J. N. Lucas, A. Awa, T. Straume, M. Poggensee, Y. Kodama, M. Nakano, K. Ohtaki, H. U. Weier, D. Pinkel, J. Gray and G. Littlefield, Rapid translocation frequency analysis in humans decades after exposure to ionizing radiation. *Int. J. Radiat. Biol.* **62**, 53–63 (1992).
27. J. Pohl-Ruling, P. Fisher, D. C. Lloyd, A. A. Edwards, A. T. Natarajan, G. Obe, K. E. Buckton, N. O. Bianchi, P. P. W. Buul, B. C. Das, F. Dashil, L. Fabry, M. Kucerova, A. Léonard, R. N. Mukherjee, U. Mukherjee, R. Nowotny, P. Palitti, Z. Polivkova, T. Sharma and W. Schmidt, Chromosomal damage induced in human lymphocytes by low doses of D-T neutrons. *Mutat. Res.* **173**, 267–272 (1986).
28. M. S. Sasaki, T. Takatsuji, Y. Ejima, S. Kodama and C. Kido, Chromosome aberration frequency and radiation dose to lymphocytes by alpha-particles from internal deposit of Thorotrast. *Radiat. Environ. Biophys.* **26**, 227–238 (1987).
29. E. J. Tawn, J. W. Hall and G. B. Schofield, Chromosome studies in plutonium workers. *Int. J. Radiat. Biol.* **47**, 599–610 (1985).
30. M. A. Bender and P. C. Gooch, Persistent chromosome aberrations in irradiated human subjects. *Radiat Res.* **16**, 44–53 (1962).
31. M. A. Bender and P. C. Gooch, Persistent chromosome aberrations in irradiated human subjects. II. Three and one-half year investigation. *Radiat Res.* **18**, 389–396 (1963).
32. D. C. Lloyd, A. A. Edwards and J. S. Prosser, Chromosome aberrations induced in human lymphocytes by *in vitro* acute x and gamma radiation. *Radiat. Prot. Dosim.* **15**, 83–88 (1986).
33. A. Léonard, I. Baltus, E. D. Léonard, G. B. Gerber, F. Richard and A. Wambersie, Dose–effect relationship for *in vivo* and *in vitro* induction of dicentric aberrations in blood lymphocytes of children. *Radiat. Res.* **141**, 95–98 (1995).
34. A. A. Awa, T. Sofuni, T. Honda, M. Itoh, S. Neriishi and M. Otake, Relationship between the radiation dose and chromosome aberrations in atomic bomb survivors of Hiroshima and Nagasaki. *J. Radiat. Res.* **19**, 126–140 (1978).
35. K. Ohtaki, G-banding analysis of radiation-induced chromosome damage in lymphocytes of Hiroshima A-bomb survivors. *Jpn. J. Human Genet.* **37**, 245–262 (1992).
36. R. K. Sachs, A. Awa, Y. Kodama, M. Nakano, K. Ohtaki and J. N. Lucas, Ratios of radiation-produced chromosome aberrations as indicators of large-scale DNA geometry during interphase. *Radiat. Res.* **133**, 345–350 (1993).

37. M. Seabright, A rapid banding technique for human chromosomes. *Lancet* **2**, 971–972 (1971).

38. D. C. Lloyd, R. J. Purrott, G. W. Dolphin and A. A. Edwards, Chromosome aberrations induced in human lymphocytes by neutron irradiation. *Int. J. Radiat. Biol.* **29**, 169–182 (1976).

39. D. J. Brenner, Significance of neutrons from the atomic bomb at Hiroshima for revised radiation risk estimates. *Health Phys.* **60**, 439–442 (1991).

40. D. J. Brenner and J. F. Ward, Constraints on energy deposition and target size of multiply-damaged sites associated with DNA double-strand breaks. *Int. J. Radiat. Biol.* **61**, 737–748 (1992).

41. ICRP, *1990 Recommendations of the International Commission on Radiological Protection*. Publication 60, *Annals of the ICRP* **21**, Pergamon Press, Oxford, 1991.

42. D. O. Stram, R. Sposto, D. Preston, S. Abrahamson, T. Honda and A. A. Awa, Stable chromosome aberrations among A-bomb survivors: An update. *Radiat. Res.* **136**, 29–36 (1993).

43. G. R. Howe, Lung cancer mortality between 1950 and 1987 after exposure to fractionated moderate-dose-rate ionizing radiation in the Canadian fluoroscopy cohort study and a comparison with lung cancer mortality in the atomic bomb survivors study. *Radiat. Res.* **142**, 295–304 (1995).

44. A. Birchall and A. C. James, Uncertainty analysis of the effective dose per unit exposure from radon progeny and implications for ICRP risk-weighting factors *Radiat. Prot. Dosim.* **53**, 133–140 (1994).

45. National Research Council, Committee on the Biological Effects of Ionizing Radiations, *Health Effects of Exposure to Low Levels of Ionizing Radiation (BEIR V)*. National Academy Press, Washington, DC, 1990.

46. D. L. Preston and D. A. Pierce, *The Effect of Changes in Dosimetry on Cancer Mortality Risk Estimates on the Atomic Bomb Survivors*. TR 9-87, Radiation Effects Research Foundation, Hiroshima, 1987.

47. D. L. Preston and D. A. Pierce, The effect of changes in dosimetry on cancer mortality risk estimates in the atomic bomb survivors. *Radiat. Res.* **114**, 437–466 (1988).