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Relative Biological Effectiveness of 144 keV Neutrons in Producing Dicentric Chromosomes in Human Lymphocytes Compared with ^{60}Co Gamma Rays under Head-to-Head Conditions

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The RBE for neutrons was assessed in a head-to-head experiment in which cultures of lymphocytes from the same male donor were irradiated simultaneously with 144 keV neutrons and with ^{60}Co γ rays as the reference radiation and evaluated using matched time, culture conditions, and the end point of chromosomal aberrations to avoid potential confounding factors that would influence the outcome of the experiment. In addition, the irradiation time was held constant at 2 h for the high-dose groups for both radiation types, which resulted in rather low dose rates. For the induction of dicentric chromosomes, the exposure to the 144 keV neutrons was found to be almost equally as effective (yield coefficient $\alpha_{dic} = 0.786 \pm 0.066$ dicentrics per cell per gray) as that found previously for irradiation with monoenergetic neutrons at 565 keV ($\alpha_{dic} = 0.813 \pm 0.052$ dicentrics per cell per gray) under comparable exposure and culture conditions (*Radiat. Res.* 154, 307–312, 2000). However, the values of the maximum low-dose RBE (RBE_m) relative to ^{60}Co γ rays that were determined in the present and previous studies show an insignificant but conspicuous difference: 57.0 ± 18.8 and 76.0 ± 29.5, respectively. This difference is mainly due to the difference in the α_{dic} value of the ^{60}Co γ rays, the reference radiation, which was 0.0138 ± 0.0044 Gy^{-1} in the present study and 0.0107 ± 0.0041 Gy^{-1} in the previous study. In the present experiment, irradiations with 144 keV neutrons and ^{60}Co γ rays were both performed at 21°C, while in the earlier experiment irradiations with 565 keV neutrons were performed at 21°C and the corresponding reference irradiation with γ rays was performed at 37°C. However, the temperature difference between 21°C and 37°C has a minor influence on the yield of chromosomal alterations and hence RBE values. The large cubic PMMA phantom that was used for the γ irradiations in the present study results in a larger dose contribution from Compton-scattered photons compared to the mini-phantom used in the earlier experiments. The contribution of these scattered photons may explain the large value of α_{dic} for γ irradiation in the present study. These results indicate that the yield coefficient α_{dic} for 144 keV neutrons is similar to the one for 565 keV neutrons, and that modification of the α_{dic} value of the low-LET reference radiation, due to changes in the experimental conditions, can influence the RBE_m. Consequently, α_{dic} values cannot be shared between cytogenetic laboratories for the purpose of assessment of RBM_m without verification of the comparability of the experimental conditions.

INTRODUCTION

A considerable part of our knowledge about the biological effectiveness of neutrons has been derived from experimental studies of the dose–response relationship for the induction of dicentric chromosomes, summarized e.g. in NCRP Report No. 104 (*1*) and ICRP Publication 60 (*2*). Provision of additional data is particularly important at energies below 1 MeV to improve the biological dosimetry. Such data will have some bearing on the general question of radiation risk from medium-energy neutrons. The primary purpose of the present study therefore was to investigate the value of the yield coefficient α_{dic} and the RBE relative to ^{60}Co γ rays for monoenergetic neutrons at 144 keV, and to compare the results with the α_{dic} value and the RBE determined previously for 565 keV neutrons (*3*). In that paper, the choice of the reference radiation was found to be crucial for determining the magnitude of the neutron RBE.

Therefore, the present experiment was aimed at performing both the neutron and the corresponding ^{60}Co reference irradiations under head-to-head conditions, i.e. using matched time, culture and evaluation conditions, with blood from the same donor. The exposure conditions included identical exposure durations and irradiation temperatures. The geometrical conditions for the reference irradiation with ^{60}Co γ rays were designed to simulate the influence of the human body, using a large polymethylmethacrylate (PMMA) phantom.

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TABLE 1
Neutron Fluence and Adult Blood Kerma due to Nominal 144 keV Neutrons at a Source–Sample Distance of 50 cm, Normalized to the Proton Charge Collected by the Target

Spectral fraction	Neutron fluence in free air (cm^{-2} μC^{-1})	Neutron fluence in adult blood (cm^{-2} μC^{-1})	Neutron kerma in adult blood (Gy μC^{-1})
Uncollided neutrons	$(6.38 \pm 0.14) \times 10^4$	$(5.78 \pm 0.23) \times 10^4$	$(4.61 \pm 0.26) \times 10^{-7}$
Scattered neutrons	$(0.12 \pm 0.01) \times 10^4$	$(1.70 \pm 0.07) \times 10^4$	$(0.73 \pm 0.04) \times 10^{-7}$
All neutrons	$(6.50 \pm 0.14) \times 10^4$	$(7.48 \pm 0.30) \times 10^4$	$(5.34 \pm 0.30) \times 10^{-7}$
Scattered/unscattered	1.8%	29.5%	15.9%

MATERIALS AND METHODS

For the present experiment, peripheral blood was taken from the same healthy male donor used in our previous experiments for irradiation with neutrons at 565 keV (*3*) with X or γ rays as reference radiations (*4–6*). Informed consent was obtained from the donor. All photon and neutron irradiations were performed at the Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, and the biological evaluation was carried out at the GSF National Research Center for Environment and Health, Neuherberg.

All studies were carried out on the same sample, which was heparinized to prevent coagulation during the experiments. The whole blood was kept at room temperature of 21°C during exposure to either neutrons of 144 keV or ^{60}Co γ rays. This irradiation temperature had to be used because of the experimental conditions in the PTB laboratories. Blood samples of 1 ml each were placed in flat ring-shaped plastic (polyvinylcarbazol) chambers which were sealed by two stretched 20-μm-thick Mylar foils (polyethylenterephthalate) and were irradiated with five doses of neutrons between 0.0219 Gy and 0.0924 Gy at a dose rate of 0.00077 Gy min^{-1}. For reference, blood samples of 2 ml each were placed in cylindrical polypropylene chambers that were tightly embedded in a large PMMA phantom and were irradiated with six doses of ^{60}Co γ rays between 0.25 Gy and 4 Gy at a dose rate of 0.033 Gy min^{-1}. The irradiation conditions were chosen to ensure delivery of the desired absorbed doses to the blood samples within 2 h for both radiation qualities (head-to-head conditions). For controls, the blood was kept unirradiated at a room temperature of 21°C for the same period of 2 h.

Neutron Source and Neutron Dosimetry

The neutron irradiations were performed in the low-scattering experimental hall of the PTB accelerator facility (*7*). Dose measurements for monitor calibration and irradiations of blood samples were done in a neutron field with a nominal energy of 144 keV. The neutrons were produced by the ^{7}Li(p,n)^{7}Be reaction using a beam of 24.9 μA van de Graaff accelerated 1.96 MeV protons. The blood probe (24 mm in diameter, 2.2 mm thick) was positioned in the 144 keV neutron field at a distance of 50 mm from the target surface at 0° with respect to the direction of the proton beam. The temperature of the blood probe, 21°C, was determined by the controlled room temperature.

The neutron fluence was measured with a hydrogen-filled, cylindrical recoil proton proportional counter (*8*) with the center of its sensitive volume positioned 1152 mm from the lithium hydroxide target. Since the solid angle spanned by the blood probe is much larger than the one spanned by the proportional counter, the procedure described previously (*3*) was used. A Monte Carlo simulation with MCNP-4B (*9*) was used to simulate the neutron transport in the contributing parts of the target and in the blood sample. The spectral neutron fluences free in air and in the blood sample were calculated. All calculated results were related to the fluence measurement free in air.

Table 1 presents the results of the calculation of the neutron fluence and the values of neutron kerma in adult blood derived from the calculation. An overall uncertainty of 4% was estimated for the kerma factor taken from ICRU Report 46 (*10*) to convert neutron fluence to adult blood kerma. The tabulated expanded uncertainties of neutron kerma correspond to a confidence level of 68%. Adult blood kerma was regarded as the appropriate measure of absorbed dose in the blood samples. The mean neutron energy both in free air and in the blood sample was 138 keV (32 keV full-width half-maximum) weighted according to the (uncollided) neutron fluence.

Figure 1 shows the spectral distribution of the neutron adult blood kerma for the uncollided and scattered neutrons in the present experiment (left scale). The broad kerma distribution from uncollided neutrons, ranging from 70 keV to 175 keV, has a mean neutron energy of 139.5 keV (31 keV full-width half-maximum). Scattered neutrons in this range contribute 72% to the kerma from scattered neutrons and amount to 15.9% of the uncollided neutron kerma. The photon contamination of the neutron field, measured with a Geiger-Müller counter, contributed about 1% to the total kerma.

^{60}Co γ -Ray Source and γ -Ray Dosimetry

The experiments were performed in the reference ^{60}Co γ-radiation field of the PTB normally used to measure the quantity absorbed dose to water with high accuracy under specified conditions. A ferrous sulfate solution calibrated by total absorption of high-energy electrons (*11*) was used for dosimetry of the γ-ray beam of the ^{60}Co source (*12*). The conversion from the absorbed dose rate measured under the standard conditions specified for the reference radiation field (water phantom, source-to-surface distance 83 cm, field diameter at the phantom surface 10 cm, reference point at a depth of 5 cm) to the conditions of the blood irradiation in a PMMA phantom was accomplished using a transfer standard ionization chamber of the type PTW Roos M34001 according to the rules given in the German Standard DIN 6800-2 (*13*). The absorbed dose to water was converted to the absorbed dose to adult blood using the respective mass energy absorption coefficients listed in ICRU Report 46 (*9*), resulting in the conversion factor $D_{blood}/D_{H2O} = 0.99$.

The blood to be irradiated was placed in a cylindrical polypropylene vessel 5.9 cm long and 1.2 cm in diameter with a wall thickness of 1 mm. This vessel was embedded tightly in a PMMA phantom 30 cm long, 30 cm wide, and 30 cm high. This large phantom was chosen because it was in routine use at PTB for dosimetry comparisons under conditions similar to those for ^{60}Co radiotherapy, so that very accurate dosimetry was available. The center of the vessel was placed at a depth of 4.42 cm on the beam axis. The axis of the vessel was upright, perpendicular to the beam axis. The source-to-phantom surface distance was 172.3 cm, and the diameter (of the 50% isodose) of the circular field at the phantom surface was about 23 cm. These irradiation conditions were chosen to obtain the desired mean absorbed dose rate of 0.0033 Gy min^{-1} in the vessel. The irradiation temperature was 21.0°C.

In addition to the dose rate at the center of the vessel, the dose distribution across the vessel was also measured. As a result of the absorption of the radiation, an almost constant dose gradient along the direction of the beam axis was observed, amounting to a relative variation in the dose rate of 0.5% per millimeter of depth. This causes a maximum deviation of the dose inside the vessel of ±2.5% from the mean value on the axis. The effect caused by the inhomogeneity of the radiation field perpendic-

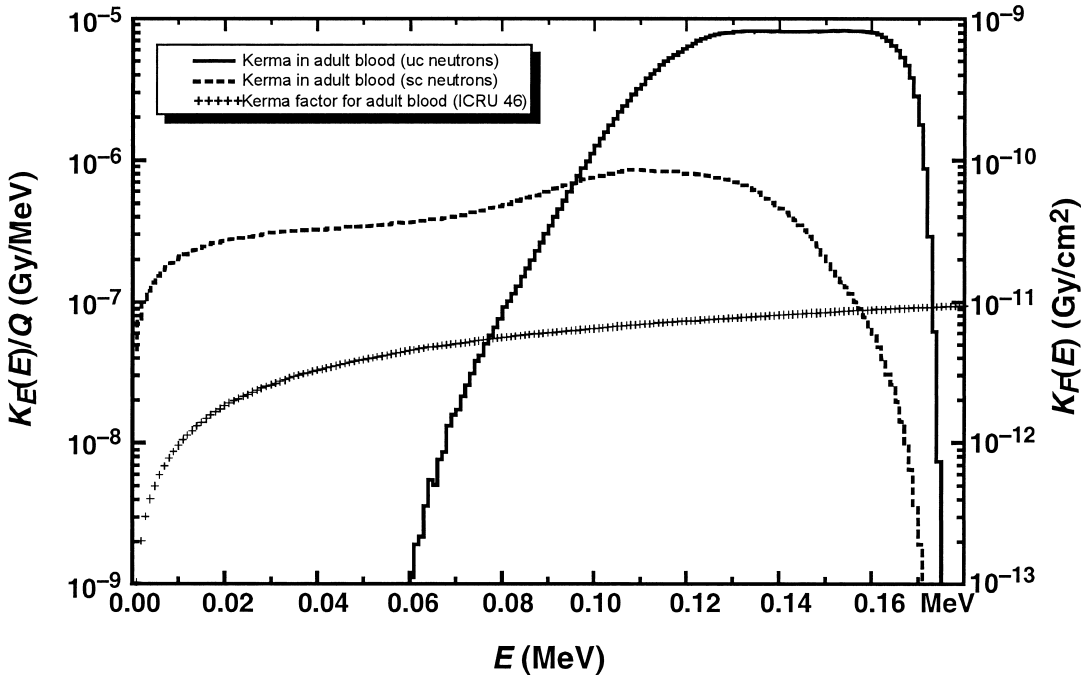

FIG. 1. Energy distribution of neutron kerma in the irradiated blood samples, normalized to proton charge collected by the target, contributed by uncollided neutrons (uc) and scattered neutrons (sc), left scale, and neutron energy dependence of the adult blood kerma factor, right scale.

ular to the beam axis was less than 0.2%. Before and after blood irradiation, the dose rate was measured using the transfer standard. In addition, the dose rate during the irradiations was monitored by a second transfer standard.

The combined standard uncertainty for the mean value of the absorbed dose in adult blood in the vessel was calculated according to the ''Guide to the Expression of Uncertainty in Measurement'' (*10*). Its relative value is $\delta = 1.7\%$, resulting in a relative expanded uncertainty of $\varepsilon = 3.4\%$ ($k = 2$). The dominant contributions to the uncertainty are the combined standard uncertainty of the calibration factor of the transfer standard $\delta = 0.93\%$, including the uncertainty in the national standard of water absorbed dose, and the combined standard uncertainty $\delta = 1.4\%$ for the quotient of the mass energy absorption coefficients of adult blood and water from ICRU Report 46 (*9*).

Culture Conditions and Chromosome Analysis

Immediately after irradiation of a blood chamber with a particular dose, cultures were established. The cultures contained 0.5 ml whole blood, 4.5 ml RPMI 1640 medium supplemented with 15% fetal calf serum, 1% glutamine, 2.5% phytohemagglutinin, 2.9 μg/ml bromodeoxyuridine (BrdU), and antibiotics. During a 6-h transport from PTB to the Cytogenetics Laboratory at GSF, the cultures were maintained at 37°C in a portable temperature-controlled incubator. After arrival, the cultures were incubated for a further 41 h at 37°C. For the final 3 h, 0.1 μg/ml Colcemid was present.

The culture conditions ensured that the chromosome analysis was performed exclusively in metaphases of the first cell cycle *in vitro*. Chromosome preparation and staining were carried out according to standard GSF procedures (*14*). After fluorescence-plus-Giemsa (FPG) staining, chromosome analysis was carried out exclusively in complete first-division metaphases identified by uniformly stained sister chromatids. In the dose range considered, for both radiation types, there was no recognizable influence found on the mitotic index.

Although the frequencies of the different chromosome aberration types were determined, in the present study only the data for dicentrics were used in the quantitative analysis. The background frequency of 3.26×10^{-4} dicentric chromosomes per cell from the present donor is not significantly different from the mean value of 4.1×10^{-4} dicentric chromosomes per cell obtained for samples from 141 control individuals (total number of cells 92,550) examined in our laboratory (*16*).

RESULTS

The results of the chromosome analysis for blood exposures to 144 keV neutrons are presented in Table 2. At two doses, 0.0228 and 0.0481 Gy, the intercellular distribution of dicentrics is slightly overdispersed compared to Poisson, whereas at the other doses there is no deviation from regular dispersion, as seen from the dispersion coefficients, σ^2/y, which are close to the value 1, corresponding to the Poisson distribution. A value of the test quantity u in excess of 1.96 indicates overdispersion at the two-sided 95% confidence level. There is no recognizable trend of overdispersion with dose.

Weighted least-squares approximation was applied to fit a linear function $y = c + \alpha D$ to the data for dicentrics, with $c = (3.26 \pm 1.89) \times 10^{-4}$ given by the controls. Reciprocals of the estimated variances were used as weighting factors. Stated uncertainties are standard deviations of the mean. From the linear curve parameter, the value $\alpha_{dic} = 0.786 \pm 0.066$ Gy^{-1} has been determined. The resulting dose–response curve for dicentrics is shown in Fig. 2, together with our previous curve obtained for exposure to monoenergetic neutrons at 565 keV with $\alpha_{dic} = (0.813 \pm 0.052)$ Gy^{-1} (*3*). The difference between the two dose–response curves is not statistically significant.

The results of the analysis of dicentrics after exposure to ^{60}Co γ rays are presented in Table 3. For all doses, the frequencies of dicentrics show no deviation from Poisson.

TABLE 2
Intercellular Distribution of Dicentrics Induced in Human Lymphocytes by Monoenergetic Neutrons at 144 keV

Dose (Gy)	Cells scored	Dicentrics per cell	Distribution				σ^2/y	*u* value
			0	1	2	3		
0	9200	0.0003	9197	3			1.00	−0.01
0.0219	1000	0.014	986	14			0.99	−0.30
0.0228	1000	0.021	981	17	2		1.17	3.92
0.0481	1200	0.038	1159	37	4		1.14	3.47
0.0706	800	0.053	760	38	2		1.04	0.89
0.0924	400	0.085	368	31	0	1	1.09	1.35

Weighted least-squares approximation was applied to fit the data for dicentrics to the linear-quadratic model, $y = c + \alpha D + \beta D^2$ with $c = (3.26 \pm 1.89) \times 10^{-4}$ given by the background frequency in unirradiated samples. The coefficients of the dose–response relationships for dicentrics are shown in Table 4, together with the corresponding values from our earlier experiments with ^{60}Co γ rays determined at different dose rates and at a temperature of 37°C for purposes of biological dosimetry (*4*). The stated uncertainties are standard deviations of the means. The value $\alpha_{dic} = 0.0138 \pm 0.0044$ Gy^{-1} was determined from the linear curve parameter. Figure 3 shows the data from the recent study and the dose–response curve for dicentrics determined in the present study, along with the dose–response curves fitted to our previous data. At the higher doses, the irradiation used in the present study was significantly less effective than the irradiation used in the previous experiments (*4*).

The RBE_m (equivalent to the ratio of the yield coefficients α_{dic} of the dose–response curves) for the production of dicentrics by monoenergetic neutrons at 144 keV was determined with respect to ^{60}Co γ rays as the reference radiation examined in the present study under the same exposure and culture conditions (head-to-head) (Fig. 4). From the respective α_{dic} values, an RBE_m of 57.0 ± 18.8 was obtained.

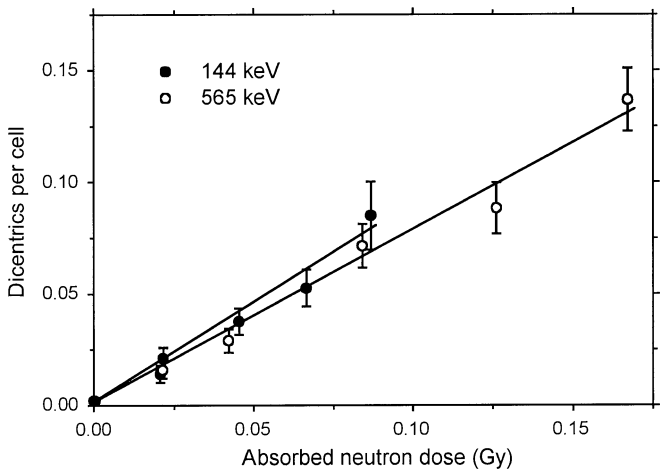

FIG. 2. Dose dependence of the yield of dicentrics induced by 144 keV neutrons in the present study together with the corresponding curve for 565 keV neutrons published earlier (*3*). Standard deviations of the means are indicated by vertical bars.

DISCUSSION

Yield Coefficient α_{dic} as a Function of Neutron Energy

In the present experiment with 144 keV neutrons, a linear dose–response relationship for the induction of dicentrics was found, resulting in an α_{dic} value of 0.786 ± 0.066 Gy^{-1} over the dose range of 0.0219 Gy to 0.0924 Gy. In the previous study with monoenergetic neutrons at 565 keV, a linear dose–response relationship for the induction of dicentrics in human lymphocytes over the dose range of 0.0213 Gy to 0.167 Gy was obtained (*3*). The resulting value of α_{dic} of 0.813 ± 0.052 Gy^{-1} was consistent with most published results obtained for irradiation with neutrons from different sources and with different spectra, at energies lower than 1 MeV (*3, 16*).

Therefore, the present result does not indicate a significant alteration of the α_{dic} values of monoenergetic neutrons at energies between 565 keV and 144 keV. This finding is consistent with the results of Sasaki *et al.* (*17*), who also used a cell cycle-controlled culture technique and scored dicentrics and centric rings. For exposure of human lymphocytes to uranium fission neutrons, the α components of the dose–response curves were very similar for neutron sources with mean neutron energies varying from 27 keV to 2 MeV. However, α_{dic} values in the literature are scattered over a broad range between 0.342 ± 0.027 and 1.365 ± 0.047 for exposure to monoenergetic neutrons or between 0.227 ± 0.010 and 1.18 ± 0.017 for fission neutrons, which can be explained either by differences in the neutron sources and spectra or by differences in the culture techniques, some of which were not controlled for cell cycle progression, e.g. due to the use of culture times of 52 h or even 58 h (*3*).

However, the findings of Sasaki *et al.* (*17*) for neutrons with energies below 1 MeV as well as our results for 144 keV neutrons in the present study and 565 keV neutrons in the previous study (*3*) are inconsistent with the results of Pandita and Geard (*18*) for the neutron-induced yield of

TABLE 3
Intercellular Distribution of Dicentrics Induced in Human Lymphocytes by ^{60}Co γ Rays

Dose (Gy)	Cells scored	Dicentrics per cell	Distribution 0	1	2	3	4	σ^2/y	*u* value
0	9200	0.0003	9197	3				1.00	0.01
0.25	2000	0.007	1986	14				0.99	0.23
0.50	2000	0.014	1963	27				0.99	0.42
1.0	1200	0.047	1147	50	3			1.05	1.23
2.0	700	0.146	607	85	7	1		1.05	0.94
3.0	600	0.282	455	125	17	2	1	1.06	1.08
4.0	300	0.613	170	84	38	8		1.06	1.06

dicentrics and centric rings in normal human fibroblasts at the first mitosis postirradiation. Their α_{dic} value was highest at a neutron energy of 0.43 MeV and gradually declined with a decrease in the neutron energy to 0.34 and 0.22 MeV. However, for neutrons at 1 MeV, they observed a lower effectiveness in producing dicentrics than for the three lower neutron energies. This energy dependence with a peak effectiveness at about 0.4 MeV has been noted for a variety of biological end points (see e.g. ref. *19*) and has been discussed in ICRU Report 40 (*20*). Therefore, the question may arise of whether the very similar biological effectiveness of 144 keV neutrons in the present experiment and of 565 keV neutrons in the previous experiment (*3*) is in contrast to the findings of Pandita and Geard (*18*), which indicate a significant dependence on neutron energy in the same energy range.

Influence of the Reference Radiation on Neutron RBE

Whereas the present investigation with 144 keV neutrons showed little change in the α_{dic} values for neutrons compared to the previous one with 565 keV neutrons (*3*), the reference α_{dic} values obtained with ^{60}Co γ rays changed to 0.0138 ± 0.0044 Gy^{-1} in the present study from 0.0107 ± 0.0041 Gy^{-1} in the previous study (*3*). Consequently the RBE_m changed to 57.0 ± 18.8 for 144 keV neutrons from 76.0 ± 29.5 for 565 keV neutrons. It should be pointed out that, based on the previous α_{dic} value of 0.0107 ± 0.0041 Gy^{-1} for ^{60}Co γ rays, the present RBE for 144 keV neutrons would result in a value of 73.5 ± 28.8. Although these RBE_m values are compatible within the estimates of uncertainty, there is a tendency in the RBE_m value which may be the result of some effect that has influenced the α_{dic} reference value. The possible reasons for this variation are discussed below.

Irradiation Temperature

In our previous study (*3*), we concluded that the neutron RBE may depend on the choice of the low-LET reference radiation. In the present study, we saw a need to perform an experiment with low doses of monoenergetic neutrons at 144 keV simultaneously with an experiment using ^{60}Co γ rays as the reference radiation under the same exposure and culture conditions (head-to-head). For each experiment, the irradiation temperature was 21°C. At this temperature, the value of the linear coefficient of the linear-quadratic dose–response relationship for dicentrics determined for irradiation with ^{60}Co γ rays was 0.0138 ± 0.0044, whereas in our earlier experiment a linear coefficient of 0.0107 ± 0.0041 was obtained in lymphocytes from the same blood donor at a temperature of 37°C (*4*).

It is known that changing the irradiation temperature between 37°C and room temperature may be a dose-modifying factor for the yield of dicentrics. Bajerska and Liniecki (*21*) found that lowering the temperature from 37°C to 20°C during irradiation with X rays led to a pronounced reduction in the yield of dicentrics. Moreover, the decreased temperature abolished the dependence of the dose–response curve for dicentrics on the dose rate at which the X rays were delivered. Though only a limited amount of data were reported in their study, a general trend can be recognized, which is that changes in the α coefficient of the linear-quadratic dose–response curve dominated the reduction of the yield of dicentrics with decreasing temperature, whereas the β coefficient remained virtually constant. This obser-

TABLE 4
Estimated Parameters for the Linear-Quadratic Model, $y = c + \alpha D + \beta D^2$, for Dicentrics Induced in Human Lymphocytes by ^{60}Co γ Rays

Dose rate (Gy min^{-1})	Temperature (°C)	Linear coefficient $\alpha_{dic} \pm$ SE	Quadratic coefficient $\beta_{dic} \pm$ SE	Reference
0.5	37	0.0107 ± 0.0041	0.055 ± 0.003	(*4*)
0.017	37	0.0090 ± 0.0040	0.042 ± 0.003	(*4*)
0.033	21	0.0138 ± 0.0044	0.030 ± 0.002	present study

Note. Control value $c = (3.26 \pm 1.9) \times 10^{-4}$.

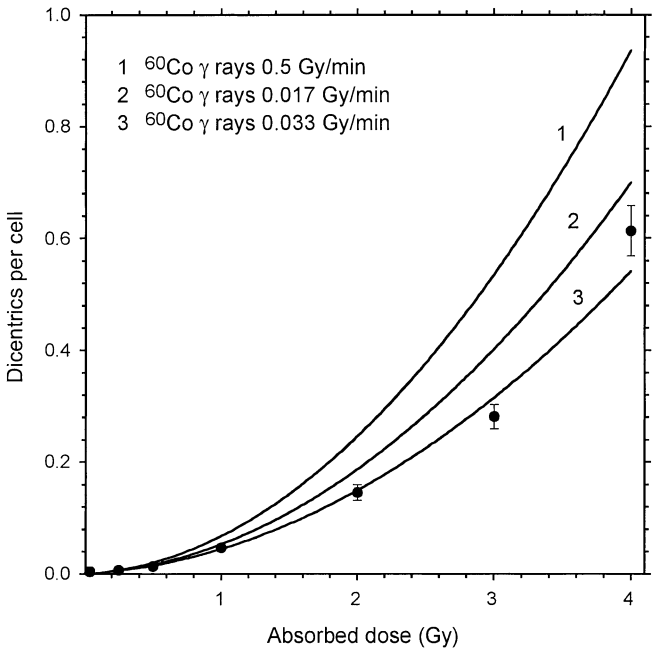

FIG. 3. Dose dependence of the yield of dicentrics in human lymphocytes induced by irradiation with ^{60}Co γ rays at different dose rates and temperatures. Points are from the present study. Vertical bars indicate standard deviations of the means; the lines represent linear-quadratic dose–response relationships. Curves 1 and 2 were obtained earlier (*4*).

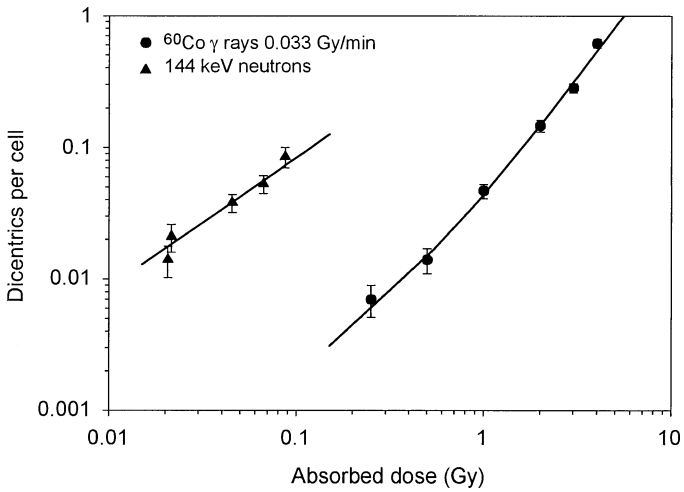

FIG. 4. Dose dependence of the yields of dicentrics in human lymphocytes obtained by irradiation with 144 keV neutrons and ^{60}Co γ rays under the same exposure and culture conditions (head-to-head). Standard deviations of the means are indicated by vertical bars.

vation is consistent with the results published by Lloyd *et al.* (*22*) indicating that lowering the irradiation temperature from 37°C to 20°C led to a reduction of the dicentric yields especially at low doses where the α coefficient of the dose response predominates. Gumrich *et al.* (*23*) observed a characteristic S-shaped temperature dependence of the yield of dicentrics resulting from irradiation at a constant dose of X rays at temperatures varying from 4°C to 37°C, with a steep increase in the aberration yield between 10°C and 20°C. They showed that both coefficients of the linear-quadratic dose–response relationship depend on the irradiation temperature and concluded that the temperature influences the formation of chromatin lesions, rather than their interaction. However, Gumrich *et al.* (*23*) did not find a further substantial variation in the yield of dicentrics at temperatures higher than 20°C; this was confirmed in a study by Blenn.[2] Our own current investigations show no evidence for an influence of temperature on the yield of aberrations between 21°C and 37°C, which results will be published separately.

Dose Rate

The dose rates used in our studies were chosen to keep an equal time of 2 h for the exposure at the highest dose. It is known from numerous studies using a number of end points in a variety of organisms that for X and γ rays there is a reduction in the biological effect of a given dose when the dose rate is lowered (*1, 24*). However, as noted in Table 4, changing from a dose rate of 0.5 Gy min^{-1} to 0.017 Gy min^{-1} produced an insignificant change in the value of α_{dic}, so that irradiation at a low dose rate of 0.033 Gy min^{-1} is not expected to change α_{dic} significantly. Therefore, the increased α_{dic} for ^{60}Co γ rays in the present experiment cannot be the result of a dose-rate effect. The observed decrease of β_{dic} for ^{60}Co γ rays (Table 4) also cannot be attributed to a dose-rate effect, because the present dose rate was higher than the previous one of 0.017 Gy min^{-1} (see Fig. 3).

Spectral Distribution of ^{60}Co γ Rays in a Large PMMA Phantom

The PMMA phantom used in the present study was 30 cm long, 30 cm wide and 30 cm high. In the earlier experiments, a mini-phantom was used with dimensions of 7 cm wide, 11.5 cm high and 2.3 cm thick, irradiated perpendicular to the two large planes; the wall thickness in the beam direction was 5.5 mm. As a result of Compton scattering in the large PMMA phantom used in the present study, the spectral distribution of ^{60}Co γ radiation may be expected to be partly shifted toward lower energies, which should result in a change in the value of α_{dic} (*25*). Using Monte Carlo simulation of the histories of photons from a ^{60}Co source (mean primary photon energy 1.25 MeV) in a semi-infinite water phantom, Miljanic *et al.* (*26*) calculated that the mean energy of the scattered photons is only 581 keV at a depth of 5 cm, while the mean energy of all photons at this depth is 820 keV. Using the knowledge from ref. (*27*) that the α_{dic} value of 0.015 ± 0.05 Gy^{-1} for ^{137}Cs γ rays (662 keV) appears to be larger than that of 0.0107 ± 0.0041 Gy^{-1} found for ^{60}Co γ rays (*3*), as determined in two experiments done with a mini-phantom and with blood from the same donor, we conclude that, in the present ex-

[2] A. Blenn, Temperature Dependence of the Induction of Chromosomal Aberrations in Human Lymphocytes by High-Energy Electron Radiation. Ph.D. thesis, University of Göttingen, Germany, 1985.

periment with a large phantom, the spectral contribution by scattered photons may explain the relatively high α_{dic} value of 0.0138 ± 0.044 Gy^{-1}. The preliminary results of our ongoing experiments, carried out with different phantom sizes at the same temperature of 21°C, appear to confirm this hypothesis. Those results will be published separately.

CONCLUSIONS

The production of dicentrics in human lymphocytes by approximately monoenergetic neutrons at 144 keV, achieved under head-to-head conditions, resulted in an α coefficient of 0.786 ± 0.066 dicentrics per cell per gray. This biological effectiveness is very consistent with the corresponding value of α_{dic} of 0.813 ± 0.052 dicentrics per cell per gray induced by approximately monoenergetic neutrons at 565 keV published earlier (*3*). However, an RBE_m value of 57.0 ± 18.8 was determined using the initial slope of the linear-quadratic dose–response relationship for dicentrics of 0.0138 ± 0.0044 per cell per gray, determined for ^{60}Co γ rays as the reference radiation. This RBE_m value is lower than the corresponding RBE_m of 76.0 ± 29.5 obtained in the previous experiment with 565 keV neutrons, using an α_{dic} value of 0.0107 ± 0.0041 dicentrics per cell per gray for the reference ^{60}Co γ radiation. This tendency is explained by the differences in the experimental conditions in the two experiments, particularly in the phantom size. Scattered photons with energies degraded by the Compton effect are thought to be responsible for the increase in α_{dic} and the decrease in β_{dic} for the reference ^{60}Co γ radiation. The effect of the phantom size on the spectrum of the secondary radiation generated in this phantom is a phenomenon to be considered generally in radiation protection (*25*).

The data presented here for head-to-head conditions confirm our previous results (*3*) that the choice of the reference radiation is very important for estimating the RBE_m of neutron-induced dicentrics in human lymphocytes. They clearly show the need for a precise specification of the experimental conditions which may influence the values of RBE_m. The results of the present experiment indicate that the dependence of α_{dic} on the scattered radiation in a ^{60}Co γ-ray field may be responsible for differences in neutron RBE.

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