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Relative Biological Effectiveness (RBE), Quality Factor (Q), and Radiation Weighting Factor (w_R)

Editor
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Guest Editorial

A CURRENT VIEW ON RADIATION WEIGHTING FACTORS AND EFFECTIVE DOSE

The International Commission on Radiological Protection (ICRP) developed radiation weighting factors (w_R) for use in radiological protection in *Publication 60* (ICRP, 1991), and Table 1 includes the w_R values that were recommended. Since 1990, there have been substantial developments in biological and dosimetric knowledge that justify a re-appraisal of w_R values and how they may be derived. This re-appraisal is the principal objective of the present report (*Publication 92*), which was a joint venture between ICRP Committees 1 and 2.

This report is one of a set of documents being developed by ICRP Committees in order to advise the ICRP on the formulation of its next Recommendations for Radiological Protection. Here, we summarise our personal views on the principal implications of the report and how the ICRP might proceed with the derivation of w_R values ahead of its forthcoming recommendations. Table 1 provides a comparison of w_R values from *Publication 60* with values proposed in the present report.

In *Publication 60*, the ICRP defined effective dose as the doubly weighted sum of absorbed dose in all the organs and tissues of the body. Dose limits are set in terms

Table 1. A comparison of existing w_R values and those proposed to the ICRP

Type and energy range of incident radiation	Radiation weighting factor (w_R)	
	<i>Publication 60</i>	Proposed ^c
Photons, all energies	1	1
Electrons and muons (all energies) ^a	1	1
Protons (incident)	5	2
Neutrons, energy	5	Use the proposed w_R function in Fig. 1 below
< 10 keV	5	
10 keV–100 keV	10	
> 100 keV–2 MeV	20	
> 2 MeV–20 MeV	10	
> 20 MeV	5	
Alpha particles, fission fragments, and heavy ions ^b	20	20 ^d

^a Exclude Auger electrons from emitters localising to cell nucleus/DNA- special treatment needed.

^b Use Q-LET relationships of *Publication 60* for unspecified particles.

^c Changes for neutron energies < 1 MeV are required to account for gamma contribution to internal organs (see text).

^d ICRP Committee 4 Task Group on Radiological Protection in Space Flight to consider w_R for high energy neutrons and heavy ions of LET > 200 keV/μm.

of effective dose and apply to the individual for radiological protection purposes, including the assessment of risk in general terms.

The values of both radiation and tissue weighting factors depend on current knowledge of biophysics and radiobiology and, accordingly, the ICRP acknowledges that judgements on these factors may change from time to time. When such changes are made, the ICRP does not recommend that any attempt is made to correct individual historical estimates of effective dose or of equivalent dose (in a single tissue or organ) that have been incurred.

We believe that the ICRP should continue the use of w_R values that relate, for external radiation, to the incident field. For radionuclide intakes, w_R values should relate to the internal fields that cause the doses to specific organs and tissues. These w_R values are intended to take account of the radiation quality component of effective dose.

For calculating effective dose, we suggest the use of the same set of w_R values for all organs/tissues. This is a judgement of practicability not based on firm radiobiological knowledge.

For photons and beta particles, there are cellular and biophysical data that indicate energy-dependent variations of up to a few-fold in relative biological effectiveness (RBE) at low doses; the extent to which this variation applies to cancer risk is not clear, and available epidemiological data suggest little variation. Also, given the UNSCEAR 2000 judgement of several-fold uncertainty on the judgement of the nominal risk coefficient for cancer, including that for the dose and dose-rate effectiveness factor (DDREF), we do not see the need to ascribe different values of w_R to different low-linear-energy-transfer (LET) radiations. A w_R of 1 may therefore be retained for all low-LET radiations.

Publication 60 had ascribed a w_R of 5 to all protons of energy > 2 MeV. We suggest that this is a significant overestimate of the biological effectiveness of these protons and, for incident protons of practical importance (> 10 MeV), we propose a w_R of 2, i.e. a value which is somewhat in excess of the w_R for other low LET radiations in order to account for the densely ionising secondaries released by high energy protons in the human body. A joint ICRU–ICRP Task Group on Doses from Cosmic Ray Exposure to Aircrew is expected to provide additional information in this respect.

Auger emitters, which have the potential to localise to the cell nucleus and bind to DNA, were recognised in *Publication 60* as a special case for low-LET radiation. We believe that such Auger emitters will need continued special attention in radiological protection. It would, however, be necessary to obtain specific physiological and biophysical data on the uptake, cellular localisation, and turnover of candidate Auger-emitting compounds in order to ascribe meaningful w_R values. This would involve considerable effort.

For neutrons, we suggest that the ICRP continues the use of w_R values that depend upon the energy of the incident neutrons. However, a continuous function (see Fig. 1) should be used, rather than the step function given in *Publication 60*. This procedure will reduce problems of computation of effective dose but should not be taken to imply precise knowledge of the underlying biological effectiveness. The

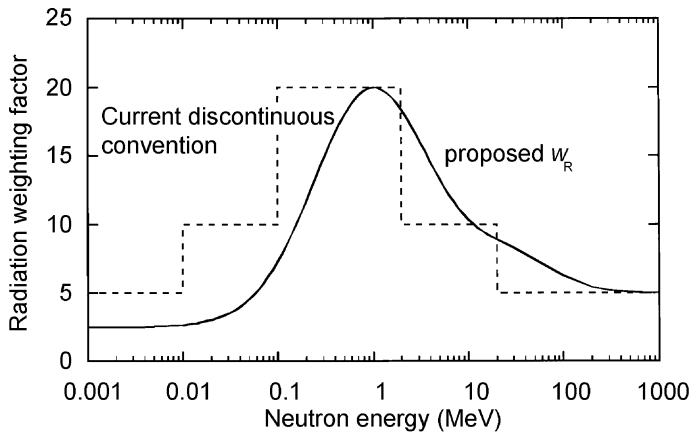


Fig. 1. The radiation weighting factor w_R for neutrons introduced in *Publication 60* (ICRP, 1991) as a discontinuous function of the neutron energy (---) and the proposed modification (—).

neutron w_R should be decreased for neutron energies below around 1 MeV to take account of the absorbed dose contribution by low-LET γ rays ($w_R = 1$) that are induced in the body by neutron capture. This γ component is considerably greater than implied in *Publication 60*, and the relative contribution of the densely ionising dose component is correspondingly smaller. The modified values of w_R , including those at high neutron energies, are—unlike the earlier values—consistent with an internal weighting factor that depends on LET, which facilitates the comparison of measurements with computed values of effective dose.

We recognise that there are uncertainties in ascribing appropriate w_R values for neutrons of high energy (> 20 MeV). This is a significant issue primarily for exposures at high altitude. We anticipate that the current ICRP Committee 4 Task Group on Radiological Protection in Space Flight will advise on these matters.

For alpha particles and for all heavy ions, we suggest that a w_R of 20 continues to be appropriate, but recognise considerable remaining uncertainty with respect to heavy ions of LET greater than around 200–300 keV/ μm . We anticipate that the uncertainty will be considered in depth by the Task Group on Space Flight. For specific circumstances involving heavy charged particles, we suggest that the quality factor and the numerical $Q(L)$ values introduced in *Publication 60* be used for deriving w_R .

Measurements are an essential element of radiological protection, e.g. determinations of radionuclide intakes, ambient dose equivalent, and personal dose equivalent in a defined phantom. The reference quantities and the measurement procedures are generally chosen to provide conservative estimates of effective dose. The intention is to ensure that compliance with measured quantities may be used to demonstrate compliance with legal limits. Estimates of effective dose that are close to or above these limits should prompt follow-up computations specific to the individual. Dosimetric anomalies, as may occur in highly non-uniform external fields or with the

intake of radionuclides, may require assessments that take individual characteristics of the exposed person and specifics of the exposure situation into account.

Finally, it is important to remember that effective dose is a quantity intended for use in radiological protection and was not developed for use in epidemiological studies or other specific investigations of human exposure. For these other studies, absorbed dose in the organs of interest and specific data relating to the RBE of the radiation type in question are the most relevant quantities to use.

ROGER COX
ALBRECHT M. KELLERER

PREFACE

In 1998, on the proposal of its Committee 1 on Radiation Effects, the International Commission on Radiological Protection (ICRP) established a Task Group on Radiation Quality Effects in Radiological Protection.

The Terms of Reference of the Task Group were to collate and evaluate data for alpha particles, neutrons, and protons; to consider deterministic and stochastic effects; and to provide comments on effects after both acute and prolonged exposure.

The Terms of Reference also requested the Task Group to examine the methods of handling differences and uncertainties in radiation quality effects for the purposes of radiological protection.

The Task Group had the following full members:

R.J.M. Fry	A.M. Kellerer	G. Dietze
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The Task Group was chaired by Dr Fry from 1998 to April 2001, and by Professor Kellerer from May 2001 until completion of the report in the spring of 2003.

The corresponding members of this Task Group were:

D. Goodhead	W.K. Sinclair	H.R. Withers
A.A. Edwards	M. Harms-Ringdahl	P. Pihet

The extensive contribution of Dr Sinclair was particularly important for this project.

During the period of preparation of this report, the membership of ICRP Committee 1 was:

(1997–2001)

R. Cox (Chairman)	A.V. Akleyev	R.J.M. Fry
J.H. Hendry	A.M. Kellerer	C.E. Land
J.B. Little	K. Mabuchi	R. Masse
C.R. Muirhead	R.J. Preston	K. Sankaranarayanan
(Secretary)		
R.E. Shore	C. Streffer	R. Ullrich
K. Wei	H.R. Withers	(1998–; Vice-Chairman)

(2001–2005)

R. Cox (Chairman)	A.V. Akleyev	M. Blettner
J.H. Hendry	A.M. Kellerer	C.E. Land
J.B. Little	C.R. Muirhead (Secretary)	O. Niwa
D. Preston	R.J. Preston	E. Ron
K. Sankaranarayanan	R.E. Shore	F.A. Stewart
M. Tirmarche	R. Ullrich (Vice-Chairman)	P.-K. Zhou

The report was approved by the Commission in October 2002. The Commission approved of the guest editorial and the executive summary in January 2003.



PERGAMON

ICRP Publication 92



Relative biological effectiveness (RBE), quality factor (Q), and radiation weighting factor (w_R)

ICRP Publication 92

Approved by the Commission in January 2003

Abstract—The effect of ionising radiation is influenced by the dose, the dose rate, and the quality of the radiation. Before 1990, dose-equivalent quantities were defined in terms of a quality factor, $Q(L)$, that was applied to the absorbed dose at a point in order to take into account the differences in the effects of different types of radiation. In its 1990 recommendations, the ICRP introduced a modified concept. For radiological protection purposes, the absorbed dose is averaged over an organ or tissue, T , and this absorbed dose average is weighted for the radiation quality in terms of the radiation weighting factor, w_R , for the type and energy of radiation incident on the body. The resulting weighted dose is designated as the organ- or tissue-equivalent dose, H_T . The sum of the organ-equivalent doses weighted by the ICRP organ-weighting factors, w_T , is termed the effective dose, E . Measurements can be performed in terms of the operational quantities, ambient dose equivalent, and personal dose equivalent. These quantities continue to be defined in terms of the absorbed dose at the reference point weighted by $Q(L)$.

The values for w_R and $Q(L)$ in the 1990 recommendations were based on a review of the biological and other information available, but the underlying relative biological effectiveness (RBE) values and the choice of w_R values were not elaborated in detail. Since 1990, there have been substantial developments in biological and dosimetric knowledge that justify a re-appraisal of w_R values and how they may be derived.

This re-appraisal is the principal objective of the present report. The report discusses in some detail the values of RBE with regard to stochastic effects, which are central to the selection of w_R and $Q(L)$. Those factors and the dose-equivalent quantities are restricted to the dose range of interest to radiation protection, i.e. to the general magnitude of the dose limits. In special circumstances where one deals with higher doses that can cause deterministic effects, the relevant RBE values are applied to obtain a weighted dose. The question of RBE values for deterministic effects and how they should be used is also treated in the report, but it is an issue that will demand further investigations.

This report is one of a set of documents being developed by ICRP Committees in order to advise the ICRP on the formulation of its next Recommendations for Radiological Protection.

Thus, while the report suggests some future modifications, the w_R values given in the 1990 recommendations are still valid at this time. The report provides a scientific background and suggests how the ICRP might proceed with the derivation of w_R values ahead of its forthcoming recommendations.

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Keywords: Equivalent dose; Effective dose; Radiation protection; Stochastic; Deterministic.

1. INTRODUCTION

(1) Unambiguous definition of the basic quantities is the precondition of a sound system of radiation dosimetry and radiation protection. Before the 1990 recommendations of the International Commission on Radiological Protection (ICRP, 1991), all dose-equivalent quantities were defined in terms of a weighting factor, the quality factor, $Q(L)$, that was applied to the absorbed dose at a point. The weighted absorbed dose was called the dose equivalent, H . Averaging over an organ or a tissue, T , provided the mean organ or tissue dose equivalents, H_T , and their organ weighted average was the effective dose equivalent, H_E :

$$H_T = \int_m \int_L Q(L) D_L \, dL dm/m \text{ and } H_E = \sum_T w_T H_T \quad (1.1)$$

where D_L is the distribution of absorbed dose in unrestricted linear energy transfer (LET), and the integral ranges over LET and the mass, m , of the organ.

(2) $Q(L)$ is a function of unrestricted LET specified by the International Commission on Radiation Units and Measurements (ICRU, 1980) as:

$$L_\infty = dE/dx \quad (1.2)$$

where dE is the energy lost by a charged particle in traversing a distance dx . The unrestricted LET, L_∞ , is commonly denoted by L (ICRU, 1980, 1993b).

(3) The unit of absorbed dose and of all dose-equivalent quantities is the joule per kilogramme. To avoid confusion between the quantities, the term ‘gray (Gy)’ is used for this unit when reference is made to absorbed dose, while the term ‘sievert (Sv)’ is used with the dose-equivalent quantities.

(4) The 1990 recommendations (ICRP, 1991) introduced a modified concept to take into account the differences in the effects of different types of radiation. For radiation protection purposes, the absorbed dose is averaged over an organ or tissue, T , and this absorbed dose average is weighted for the radiation quality in terms of the radiation weighting factor, w_R , for the type and energy of radiation incident on the body. The resulting weighted dose was designated as the organ- or tissue-equivalent dose:

$$H_T = \sum_R w_R D_{T,R} \quad (1.3)$$

where $D_{T,R}$ is the absorbed dose averaged over the tissue or organ, T , due to the incident radiation, R .

(5) The sum of the organ-equivalent doses weighted by the ICRP organ weighting factors, w_T , is termed the effective dose, E :

$$E = \sum_T w_T H_T \quad (1.4)$$

(6) The reason for replacing the quality factor, i.e. the Q – L relationship, with w_R values in the definition of the organ-equivalent doses and the effective dose was that the Commission believed:

‘that the detail and precision inherent in using a formal Q – L relationship to modify absorbed dose to reflect the higher probability of detriment resulting from exposure to radiation components with high LET is not justified because of the uncertainties in the radiological information’.

(7) Measurements are performed in terms of the operational quantities, ambient dose equivalent, and personal dose equivalent. These quantities are still defined in terms of the absorbed dose at the reference point weighted by $Q(L)$.

(8) In the same recommendations (ICRP, 1991) that introduced w_R and E , the Commission modified the earlier relationship (ICRP, 1977) between $Q(L)$ and L (see Fig.1.1). The change reflected higher relative biological effectiveness (RBE) values for intermediate-energy neutrons, and the reduced effectiveness of heavy ions with L greater than 100 keV/ μ m, as suggested by the Joint ICRU and ICRP Task Group on ‘The Quality Factor in Radiation Protection’ (ICRU, 1986). The current Q – L relationship is compared with the earlier convention in Fig. 1.1 and it is specified in Table 1.1.

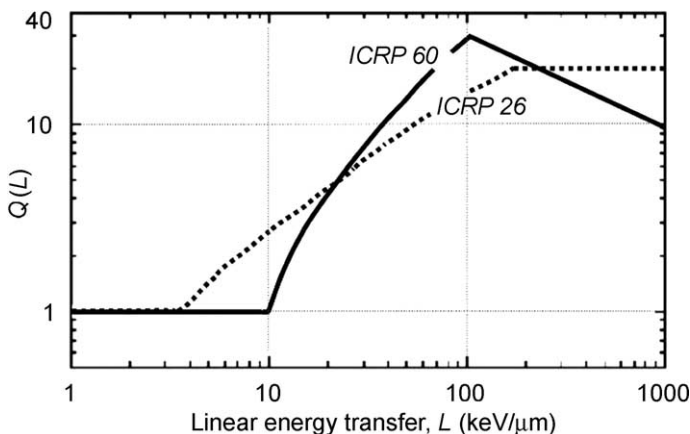


Fig. 1.1. The earlier convention for the quality factor, $Q(L)$, as a function of linear energy transfer according to Publication 26 (-----: ICRP, 1977) and the current convention according to Publication 60 (——: ICRP, 1991).

Table 1.1. Quality factor relationship

Unrestricted linear energy transfer, L (keV/ μ m)	Quality factor, $Q(L)$
< 10	1
10–100	$0.32 L^{-2.2}$
> 100	$300/\sqrt{L}$

(9) The Q - L relationship, the Commission contended:

‘was originally intended to do no more than provide a rough indication of the variation of the values of Q with changes of radiation, but it was often interpreted to imply a spurious precision which the Commission hopes will not be inferred from the new radiation weighting factors’.

(10) The Commission selected the values for w_R shown in Table 1.2 ‘based on a review of the biological information, a variety of exposure circumstances and inspection of the traditional calculations of the ambient dose equivalent’. The 1991 report did not elaborate which RBE values had been considered nor how a single value of w_R for each radiation category had been chosen. However, as has been stated above, the modified convention for $Q(L)$ reflected the advice of the ICRU-ICRP Liaison Committee (ICRU, 1986), and the selected values of w_R (Table 1.1) were chosen to be broadly compatible with $Q(L)$. The numerical inter-relationship between w_R and $Q(L)$ is assessed in detail in Chapter 4.

(11) ICRU (1986) called the quality factor Q and stated

‘The dimensionless factor Q , is termed the quality factor. The selection of its numerical values depends not only on appropriate biological data, but also on judgement. Judgement may include deciding which biological endpoints are of importance and how their RBE values should be weighted in order to establish Q . It should also include an assumption about the shape of the dose-effect relationship for human risk at low doses. Linearity is usually assumed in this range, but conditions such as dose rate may have to be taken into account in determining the slope. The importance of Q derives from the fact that it establishes the values of the absorbed dose of any radiation that engenders the same risk as a given absorbed dose of a reference radiation’.

(12) As shown in Table 1.2, a w_R of 1 was selected for all low-LET radiations, i.e. x and γ rays of all energies as well as electrons and muons.

A smooth curve, considered an approximation, was fitted to the w_R values as a function of incident neutron energy in terms of the relationship:

Table 1.2. Radiation weighting factors (ICRP, 1991)

Radiation type and energy range	Radiation weighting factor, w_R
Photons, all energies	1
Electrons and muons, all energies	1
Neutrons, energy < 10 keV	5
10–100 keV	10
> 100 keV–2 MeV	20
> 2–20 MeV	10
> 20 MeV	5
Protons, other than recoil protons, energy > 2 MeV	5
α particles, fission fragments, heavy nuclei	20

$$w_R = 5 + 17\exp(-(\ln(2E_n))^2/6) \quad (1.5)$$

where E_n is the neutron energy in MeV. This relationship is purely calculational.

(13) No specifications were given to derive the equivalent dose or the effective dose from Auger electrons. The assessment of their relative effectiveness will have to be based on microdosimetry; no attempt to do so was made in *Publication 60* (ICRP, 1991).

(14) For types of radiation and energy not included in [Table 1.1](#), the ICRP suggests that w_R be obtained by calculation of the ambient quality factor, i.e. the mean $Q(L)$ at a depth of 10 mm in the ICRU sphere exposed to the aligned radiation field (ICRU, 1985):

$$q^* = \int Q(L) D_L dL / D \quad (1.6)$$

where $D_L dL$ is the absorbed dose at 10 mm depth between L and $L+dL$. The quality of radiation can also be defined in terms of lineal energy, y (ICRU, 1986).

(15) This report is concerned with the current use of w_R and $Q(L)$ for the derivation of equivalent doses for radiation protection related to stochastic effects. As explained in [Chapter 4](#), w_R is a simplified concept to replace $Q(L)$ in practice. RBE values with regard to stochastic effects are central to the selection of w_R and $Q(L)$, and these factors and the dose-equivalent quantities are restricted to the dose range of interest to radiation protection, i.e. to the general magnitude of the dose limits. In special circumstances where one deals with higher doses that can cause deterministic effects, the relevant RBE values are applied to obtain a weighted dose that takes the relative effectiveness of different types of radiation into account. The question of RBE values for deterministic effects and how they should be used is treated separately in [Chapter 5](#).

2. THE CONCEPT OF RBE, RELATIVE BIOLOGICAL EFFECTIVENESS

2.1. Background

(16) The effect of ionising radiation is influenced by the dose, dose rate, and quality of the radiation. In 1931, Failla and Henshaw reported on determination of the relative biological effectiveness (RBE) of x rays and γ rays. This appears to be the first use of the term 'RBE'. The authors noted that RBE was dependent on the experimental system being studied. Somewhat later, it was pointed out by Zirkle et al. (1952) that the biological effectiveness depends on the spatial distribution of the energy imparted and the density of ionisations per unit path length of the ionising particles. Zirkle et al. coined the term 'linear energy transfer (LET)' to be used in radiobiology for the stopping power, i.e. the energy loss per unit path length of a charged particle.

(17) RBE has been used in somewhat different ways in radiobiology and radiation protection. In the former, it equals the ratio of the absorbed doses of two types of radiation that produce the same specified effect. In radiation protection, a more general parameter is required as a weighting factor for absorbed doses of radiation of different qualities to enable comparison and addition. Initially, the ICRP employed the term 'relative biological efficiency' for this purpose, when it based its recommendations (ICRP, 1951) 'on considerations of the equivalent energy absorbed in tissue coupled with the appropriate relative biological efficiency'.

(18) However, it was soon realised that the use of RBE as a weighting factor is complicated by the fact that it is dependent on dose, dose rate, fractionation, and the cells or tissues in which the effect is being assessed. Consequently, in 1959, the ICRU recommended that the term:

'RBE be used in radiobiology only and that another name be used for the linear-energy-transfer dependent factor by which absorbed doses are to be multiplied to obtain for purposes of radiation protection a quantity that expresses on a common scale for all ionising radiations the irradiation incurred by exposed persons'.

The name chosen for this factor was quality factor (QF) and the dose equivalent (DE) was defined as the product of absorbed dose D and QF. These recommendations were taken up and were endorsed by the RBE Committee (ICRU-ICRP, 1963). Currently, RBE is only used in radiation protection in terms of the derived quantities, quality factor, $Q(L)$, and radiation weighting factor, w_R .

(19) RBE has been criticised in some cases because it was thought to have been inappropriately employed to explore the biological mechanisms of radiation action. However, until the biological effectiveness of different types of ionising radiations can be accounted for in terms of individual contributing factors, the summary concept of RBE will continue to be used (see Sinclair, 1996).

(20) In the case of radiation protection in which RBE values for different types of radiation for the induction of stochastic effects are used to generate values of w_R and Q , there are a number of concerns:

- for the ratio of doses to be meaningful for interpretation of the relative effectiveness of the radiation, it is necessary to know the characteristics of the radiations at the target cells or tissues. Usually, however, RBE values are related to the characteristics of the incident radiation that is appropriate if the quality of radiation under study is not substantially altered in the passage to tissues deep in the body. In cell studies and animal experiments, this condition is usually met. In the exposure of the human body to neutrons, the external and internal field characteristics differ markedly; this issue is discussed in detail with regard to w_R values for neutrons in [Chapter 4](#).
- there is an important assumption in the use of RBE, namely that the effects of various types of radiation differ quantitatively and not qualitatively. Recent studies on the nature of DNA damage, including mutations, especially in the case of heavy charged particles, have shown differences from the changes induced by low-LET radiation. The question is whether differences such as in the induction of complex DNA lesions that are recalcitrant to repair make the assumption untenable. If the endpoint under study that is induced by the different types of radiation is precisely the same, e.g. the severity (degree of malignancy) of radiogenic cancers is not influenced by radiation quality, the assumption that any differences due to radiation quality are only quantitative should be valid.
- for control purposes in radiation protection, a single and maximum value is required, defined by the ICRP–ICRU RBE Committee ([ICRU–ICRP, 1963](#)) as the RBE at minimal doses. This value, RBE_M , is determined as the ratio of the initial slopes of the dose–effect curves for the radiation under study and the reference radiation. Determination of the initial linear slopes of the dose–response curves for the induction of specific cancers by different radiations is not a trivial task. Based on the assumption that the linear-quadratic model is applicable to the dose–response relationship of the low-LET reference radiation, the initial slope can be determined from the response at a low dose rate. The RBE values quoted in ‘The Quality Factor in Radiation Protection’ ([ICRU, 1986](#)) are based on ‘different types of exposure, for example single, fractionated, and low-dose-rate γ radiation and x rays’.

(21) The use of RBE_M was introduced to avoid the problems with RBE values which were determined at a single dose level not on the initial linear component of the dose–response curve for the reference radiation. However, the RBE_M approach is obviously not applicable if—as may be the case for certain types of bone tumours and for some skin tumours—there is a threshold, or if the response is best described by a dose-squared model. Such dose responses present a problem in how the effectiveness of high-LET radiations should be estimated and underline the need to develop a method of assessing the effect directly *without comparison to a reference radiation*. This would entail the development of an acceptable method of extrapolation across species.

2.2. Reference radiation

(22) The original reference radiation for the weighting factor in radiation protection was stated to be γ rays from radium ([ICRP, 1951](#); [Taylor, 1984](#)):

‘The relative biological efficiency of any given radiation has been defined by comparison with the γ radiation from radium filtered by 0.5 mm of platinum. It has been expressed numerically as the inverse of the ratio of the doses of the two radiations required to produce the same biological effect under the same conditions. It has been assumed, for purposes of calculations, that the relative biological efficiency of a given radiation is the same for all effects mentioned in the Introduction with the single exception of gene mutations. The following values have been adopted:

Radiation	Relative biological efficiency
γ rays from radium x rays of energy 0.1–3 MeV β rays Protons Fast neutrons <20 MeV α rays	1 10 10 20

The effective figure for slow neutrons should be derived in any given case from an evaluation of the separate contributions to the biological effect by protons arising from the disintegration of the nitrogen nuclei and by γ rays arising from capture of neutrons by hydrogen nuclei’.

(23) Apart from the notable fact that hereditary effects, the ‘gene mutations’ were excluded, the weighting factor was understood to be of a very general nature, as the list of ‘effects mentioned in the Introduction’ indicates:

- superficial injuries;
- general effects on the body, particularly the blood and blood-forming organs, e.g. production of anaemia and leukaemias;
- the induction of malignant tumours;
- other deleterious effects including cataract, obesity, impaired fertility, and reduction of life span;
- genetic effects.

(24) While γ rays were declared to be the reference radiation, the above table shows that a value of 1 was, in fact, assigned to a broad range of photon and electron radiations. It was, thus, no major reversal when [ICRP changed its position in 1955](#) and stated:

‘RBE should be expressed in terms of the pertinent biological effectiveness of ordinary x rays taken as 1 (average specific ionisation of 100 ion pairs per μm of water or linear energy transfer of 3.5 keV per μm of water)’.

(25) Subsequently, there have been different conventions, but the issue became less critical after the concept of RBE was clearly separated from the adopted weighting factors, $Q(L)$ and later w_R .

(26) With regard to the weighting factors, there is no specific reference radiation. Instead, a value of 1 is assigned to a range of low-LET radiations. In *Publication 60* (ICRP, 1991), w_R was set at 1 for all photons and electrons, which suggests that the differences of effectiveness between different photon radiations are not considered to be of sufficient consequence to require explicit accounting in radiation protection regulations. The current convention for $Q(L)$ is in line with the recommendation for w_R , because it attributes a value of 1 to $Q(L)$ for unrestricted LET, $L < 10 \text{ keV}/\mu\text{m}$. Since LET values in excess of $10 \text{ keV}/\mu\text{m}$ are reached only by electrons below 1.5 keV, it is clear that the convention for $Q(L)$ is largely consistent with $w_R = 1$ for x rays and electron radiations.

(27) For RBE—which serves as important input into the selection of the weighting factor—the situation is different. It is essential that any statement of RBE must be accompanied by a specification of the reference radiation. The significant difference (see Fig. 2.3) between the (dose-average) LET of ^{60}Co (about $0.4 \text{ keV}/\mu\text{m}$) or ^{137}Cs γ rays (about $0.8 \text{ keV}/\mu\text{m}$), and that of 200 kV x rays (about $3.5 \text{ keV}/\mu\text{m}$) makes it clear that RBE values can differ substantially depending on which photon radiation is taken as reference.

(28) While there is no need for an exclusive convention, it is nevertheless convenient to adopt a reference radiation that is understood to apply whenever there is no explicit statement to the contrary. There are practical arguments to favour γ rays for this purpose. It is difficult and expensive to determine the initial slope of dose responses of the induction of cancer in animals, especially with low-dose-rate x rays rather than low-dose-rate γ rays. For this and a number of other reasons, hard γ rays are preferable as the reference radiation because:

- most experimental animal studies of cancer induction and life shortening (and deterministic effects) have been carried out with γ rays, and, importantly, some with exposures at low dose rates;
- the most important body of data for estimating radiogenic cancers in humans are from the atomic bomb survivors who were exposed to γ rays;
- hard γ rays have the lowest LET (dose average LET, L_D , $0.4 \text{ keV}/\mu\text{m}$ or less) among photon radiations;
- the distribution of the deposition of energy from γ rays in large fields is more uniform than with x rays.

(29) The convention to assign the same w_R to photons and electrons of all energies is advantageous for the purposes of radiation protection, since it facilitates measurements as well as calculations. It is, of course, restricted to the w_R as part of the definition of effective dose and equivalent doses, and it does not imply that all low-LET radiations are assumed to be equally effective. For risk assessment, for example in a comparison of γ rays and x rays or conventional x rays and soft x rays, the w_R value is not applicable, LET or microdosimetric parameters must be invoked, and radiobiological or radio-epidemiological data need to be used. The general magnitude of RBE values that are expected and have been observed with photons or electrons will, therefore, be reviewed briefly.

2.2.1. In-vitro studies

(30) It has long been recognised that, especially at low doses, low-LET radiations do not all have the same effectiveness. Conventional 200 kV x rays are considered to be about twice as effective at low doses as high-energy γ rays based upon studies of mutations in *Tradescantia*, aberrations in human lymphocytes, and killing of mouse oocytes (Bond et al., 1978). Fast electrons may be even less effective than γ rays. These differences are of interest in themselves, but must also be taken into account when different photon radiations are used as reference radiation (Sinclair, 1985; ICRU, 1986).

(31) The most reliable and detailed data on photon RBE exist for chromosome aberrations in human lymphocytes. In choosing the $Q(L)$ values, the report of the Joint ICRP and ICRU Task Group (ICRU, 1986) has given special consideration to observations on chromosome aberrations in human lymphocytes (Edwards et al., 1982) for 15 MeV electrons, ^{60}Co γ rays, and 250 kV x rays. These authors obtained the data for dicentrics in human lymphocytes listed in Table 2.1, i.e. they have shown substantial differences of effectiveness for different types of penetrating low-LET radiations. New data have since confirmed and extended these findings.

(32) Sasaki et al. determined the yields of dicentrics over a broad range of photon energies. Figure 2.1 gives the linear coefficients (and standard errors) from linear-quadratic fits to the dose dependencies. The upper panel refers to peripheral human lymphocytes (Sasaki et al., 1989; Sasaki, 1991), and the lower panel gives data for the cultured cell line m5S from embryonic mouse cells (Sasaki, 2003, private communication); these cells are immortalised but not malignantly transformed and they retain near-diploid chromosome constitution. The circles relate to γ rays and broad x-ray spectra, and the squares relate to characteristic x rays and mono-energetic photons from synchrotron radiation.

(33) Figure 2.1 demonstrates that there is a substantial decrease of the yield of dicentrics from conventional x rays to γ rays for both human lymphocytes and mouse cells. Photon energies below 20 keV are of particular interest with regard to biophysical considerations, but are less relevant to exposure situations in radiation protection. They are included here to show the full trend of energy dependence.

(34) Figure 2.2 represents analogous data obtained by Schmid et al. (2002b) for chromosome aberrations in human lymphocytes from blood samples of one and the same donor. The upper and lower panels give the initial slope for dicentric and acentric fragments, respectively. For dicentrics, it is seen that the RBE_M of moderately filtered 200 kV x rays is about 2–3 relative to γ rays, while the RBE_M of

Table 2.1. Low dose coefficient (and standard error) for the induction of dicentrics in human lymphocytes by low-linear-energy-transfer penetrating radiation (Edwards et al., 1982)

Radiation type	Dicentrics per cell/Gy
15 MeV electrons	0.0055 (± 0.0112)
^{60}Co γ rays	0.0157 (± 0.0029)
250 kV x rays	0.0476 (± 0.0054)

mammography x rays (29 kV) relative to the moderately filtered 200 kV x rays is somewhat in excess of 1.5. The corresponding values for acentrics are about 2 for comparison of 200 kV x rays and γ rays, and less than 1.5 for comparison of mammography x rays and moderately filtered 200 kV x rays.

(35) For the RBE_M of mammography x rays relative to γ rays, a value of about 5 is obtained with regard to dicentrics, and a value of about 3 with regard to acentrics.

(36) The difference by a factor of 2–3 in the low dose effectiveness of conventional x rays and γ rays is known and, even if this should apply equally to radiation-induced late effects, this would not necessarily require a departure from the current convention which assigns $w_R = 1$ to all photon radiations. However, the difference needs to be noted whenever risk estimates are derived from exposures to γ rays and are then applied to x rays. As stated, the difference is also important when RBE_M values are derived for densely ionising radiation, and different low-LET reference radiations are chosen.

(37) Apart from these considerations, it is uncertain whether the marked dependence of RBE_M on photon energy for chromosome aberrations is also representative for late radiation effects in man. The dependence of RBE_M on photon energy for dicentric chromosomes reflects the fact that the dose dependencies have a large

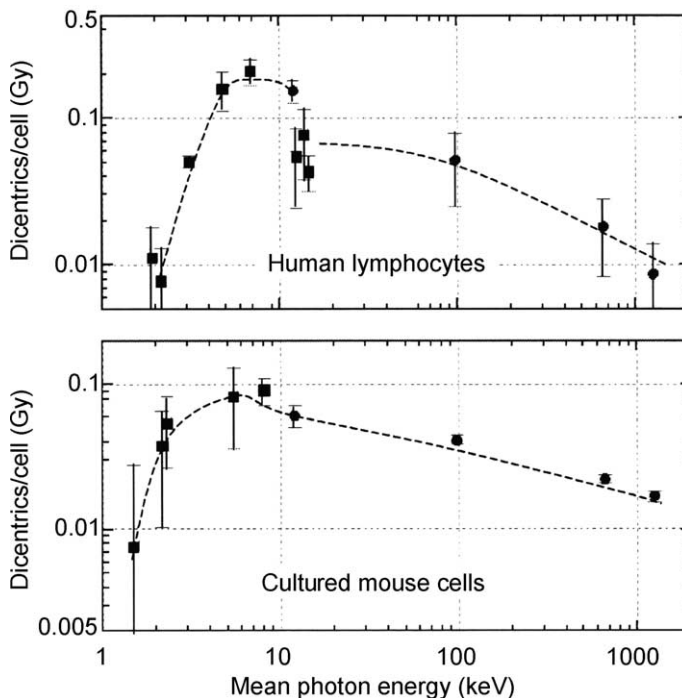


Fig. 2.1. Photon energy and linear coefficients (and standard errors) of the dose dependence for dicentric chromosomes in human peripheral blood lymphocytes (upper panel) (Sasaki et al., 1989; Sasaki, 1991) and in mouse m5S cells (lower panel) (Sasaki, 2003, private communication). Squares, mono-energetic photons; circles, broad x-ray spectra and high energy γ rays. The broken curves are inserted for visual guidance.

curvature for ^{60}Co γ rays [$\alpha/\beta = 0.2$ Gy in the data reported by Schmid et al. (2002b)] but little curvature for 29 kV x rays ($\alpha/\beta = 1.9$ Gy). If there were no curvature below 1 Gy in the dose relationships for chromosome aberrations, the RBE_M of the 29 kV x rays would be only 1.65 against the ^{60}Co γ rays. Since the dose dependence for solid tumours among the atomic bomb survivors indicates no substantial curvature, a similarly weak dependence on photon energy cannot be excluded for tumour induction in man.

(38) The increased effectiveness of low-energy x rays has found particular attention with regard to risk–benefit considerations for mammography. The relatively large RBE_M for mammography x rays relative to ^{60}Co γ rays is, therefore, notable. Added interest has been focused on this issue because of a recent claim of an RBE_M in excess of 3 for mammography x rays relative to conventional x rays, based on an experiment on cell transformations in a human hybrid cell line and on re-interpretation of various earlier RBE data (Frankenberg et al., 2002). However, there have been strong objections (Schmid, 2002) against the experimental investigation as well as the survey of RBE data.

(39) The data for dicentrics appear to provide the largest reliable set of RBE_M values for conventional and soft x rays against γ rays. It is, thus, evidently of interest

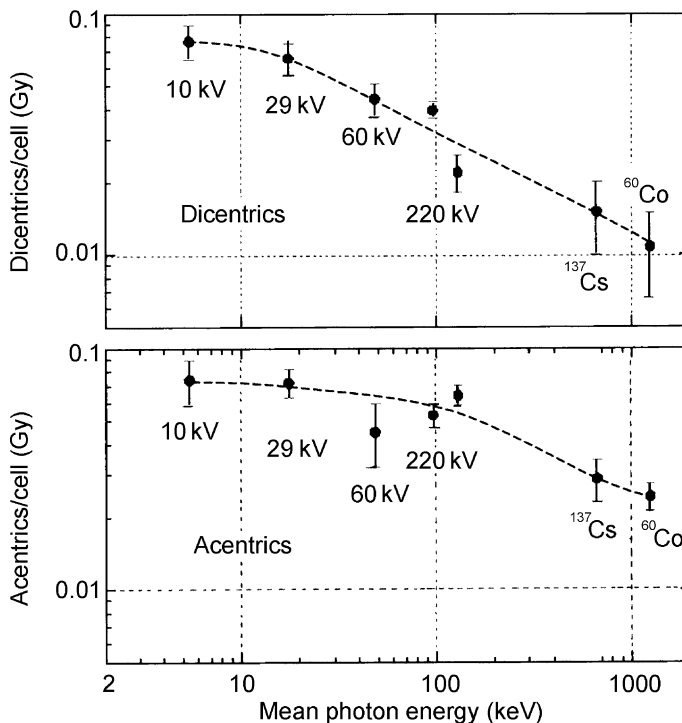


Fig. 2.2. The α coefficients with standard errors for induction of dicentrics and of acentrics in human lymphocytes from the same donor by different x and γ rays in vitro (Schmid et al., 2002b). The broken curves are inserted for visual guidance.

to assess these findings in terms of LET and microdosimetric data, and to compare them with the radio-epidemiological evidence for health effects, such as breast cancer.

2.2.2. Biophysical considerations

(40) Radiobiological determinations of RBE have frequently been related to LET. For protons and heavy ions, this is fairly straightforward because cell studies can be performed with mono-energetic particles in so-called track-segment experiments with comparatively well-defined LET values. In experiments with x rays or electrons, the situation is different because there is always a broad spectrum of LET values (ICRU, 1970) and reference is usually made to the dose-average LET or to the related microdosimetric parameter, dose-averaged lineal energy, y_D .

(41) Figure 2.3 gives computed values for the dose-average LET for the electrons released by mono-energetic photons (solid curves) and also the values for mammography x rays and 200 kV x rays (solid circles and squares, respectively) (Kellerer, 2002). In addition to the dose average, L_D , of the unrestricted LET, the diagram contains the dose averages, $L_{D,\Delta}$, of the restricted LET, L_Δ . L_Δ treats δ rays beyond the specified cut-off energy, Δ , as separate tracks. This accounts in an approximate way for the increased local energies due to δ rays, and therefore provides larger values that are more meaningful than those of unrestricted LET.

(42) The local maximum LET at about 60 keV reflects an important aspect with regard to the effectiveness of x rays. High-energy photons, e.g. ^{60}Co γ rays, release Compton electrons of comparatively high energy and correspondingly low LET. Photons of less energy, e.g. conventional 200 kV x rays, produce less energetic Compton electrons with higher LET. However, as the photon energy is further reduced, the photoelectric effect—i.e. the total transfer of photon energy to electrons—begins

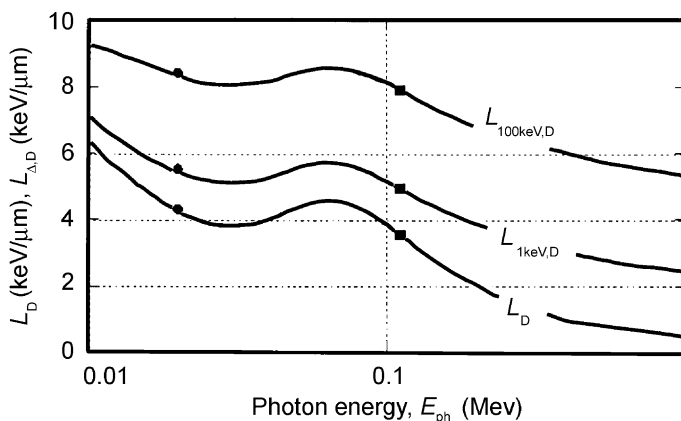


Fig. 2.3. The dose mean restricted and unrestricted linear energy transfer for electrons liberated by mono-energetic photons of energy E_{ph} . The circles and squares give values for 30 and 200 kVp x rays, respectively. They are plotted at the weighted photon energies of the x-ray spectra (Kellerer, 2002).

to dominate, and accordingly the average energy of the electrons begins to increase again. This explains the local minimum of the LET at a photon energy of about 30 keV. Below this energy, the LET increases anew as the photo-electrons have less and less energy. This complexity accounts for the notable fact that, overall, LET does not differ greatly for x rays between 200 and 30 keV.

(43) $L_{D,\Delta}$ is a parameter that correlates with the low dose effectiveness of photon or electron radiation. With a cut-off value $\Delta = 1$ keV, the numerical values of $L_{D,\Delta}$ are consistent with a low-dose RBE of about 2 of conventional x rays vs γ rays. A similar dependence on photon energy is seen in the related microdosimetric parameter dose, lineal energy, y , which has been used as a reference parameter by the ICRP-ICRU Liaison Committee on 'The Quality Factor in Radiation Protection' (ICRU, 1983). Figure 2.4 gives values of y_D as measured by Dvorak and Kliauga (1976) for various photon radiations and for different simulated site diameters, d .

(44) The γ rays from the atomic bomb explosions had a mean energy in the range of 2–5 MeV at the distances relevant for survivors (Straume, 1996). This energy range is not covered in Figs 2.3 and 2.4. However, it is apparent from Fig. 2.3 that the mean L_Δ values do not decrease substantially beyond the photon energy 1 MeV. In the microdosimetric parameters, too, there is little change with photon energy above 1 MeV; Lindborg (1976) obtained the value $y_D = 2.1$ keV/ μm for 42 MeV photons, which is very close to his value $y_D = 2.4$ keV/ μm for ^{60}Co γ rays (see also ICRU, 1983). There is, thus, little evidence that the hard γ rays from the atomic bombs should have an RBE substantially less than 1 compared with ^{60}Co γ rays.

(45) The RBE_M value of about 6 in Fig. 2.2 for 29 kV x rays vs ^{60}Co γ rays indicates—in terms of Fig. 2.3—a correlation with $L_{D,\Delta}$ for a cut-off value in excess of 1 keV. But the essential conclusion from Fig. 2.3 is that the LET values are reasonably consistent with the low-dose RBE values obtained with various photon radiations for chromosome aberrations.

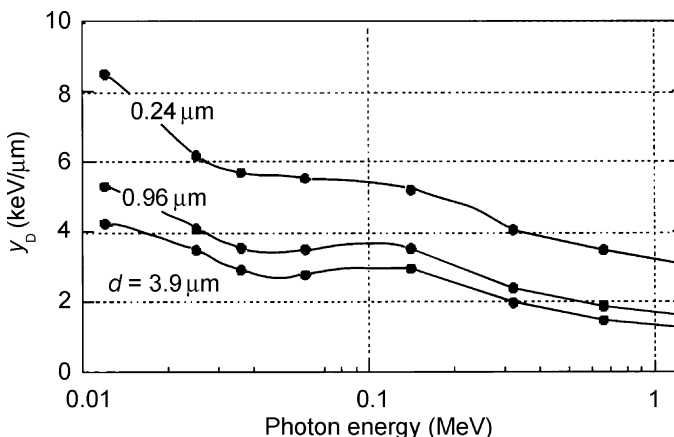


Fig. 2.4. Measured dose-average lineal energy, y_D , for mono-energetic photons and for different simulated site diameters, d (Dvorak and Kliauga, 1978).

(46) Figures 2.3 and 2.4 confirm that it would be difficult to explain the recently claimed RBE_M larger than 3 for mammography x rays against conventional x rays. Instead, they suggest a value between 1 and 2, and this is in agreement with an analysis by Brenner et al. (2002) in terms of the microdosimetric data which is supported by new transformation data suggesting an RBE_M of about 1.3.

(47) The analysis (Kellerer, 2002) in terms of the explicit electron spectra at different photon energies leads to the conclusion that the RBE_M of mammography x rays compared with conventional x rays will, regardless of the underlying mechanisms, not exceed 2; this includes a consideration of the potential effect contribution of the 0.5 keV Auger electrons from oxygen that accompany all photo-electrons in water, but only a minority of the Compton electrons which predominate at the higher photon energies.

2.2.3. Information from radio-epidemiology

(48) The follow-up of the atomic bomb survivors has become the major basis of risk estimates for γ rays. Numerous epidemiological studies on medical cohorts have provided risk estimates that exhibit considerable variations. Many of these studies on patients relate to x-ray exposures, but there is no consistent epidemiological evidence for larger risk factors from x rays than γ rays. In fact, while the risk estimates from medical studies are not inconsistent with those for the atomic bomb survivors, they tend to be, as a whole, somewhat lower (UNSCEAR, 2000). The radiation-related increase of breast cancer incidence can serve as an example because it has been studied most thoroughly, and also because it is central to the recent discussions on mammography screening.

(49) Figure 2.5 gives the risk estimates obtained in the major studies on radiation-induced breast cancer. The estimated risk coefficients (and 90% confidence ranges) are expressed in terms of the excess relative risk (ERR) per Gy and the excess absolute risk (EAR) per Gy and 10,000 person years.

(50) The uncertainties are large and the risk estimates vary widely. This is not surprising given that in studies on patients, the patient treatment regimes differ not just in terms of the type of radiation but also in terms of the various exposure modalities, such as acute, fractionated, or protracted exposure, whole or partial body exposure, exposure rate, and magnitude of exposure. Equally important are ethnic differences, including lifestyle-related differences, that are associated with greatly different background breast cancer rates. Thus, there is, even now, a factor of about 6 between the low rates in Japan and the high rates in most Western populations. Populations with low spontaneous rates tend to exhibit comparatively large ERR while their EAR tends to be low. This complicates the comparison of risk estimates, since it remains uncertain whether relative or absolute excess incidence is the more appropriate measure of risk.

(51) It also needs to be noted that the various exposed cohorts differ greatly with regard to the duration of follow-up and, especially, the age at exposure. The last two studies in Fig. 2.5 relate to exposures in childhood, while the other studies refer to exposures at intermediate or higher ages. The last factor is especially critical,

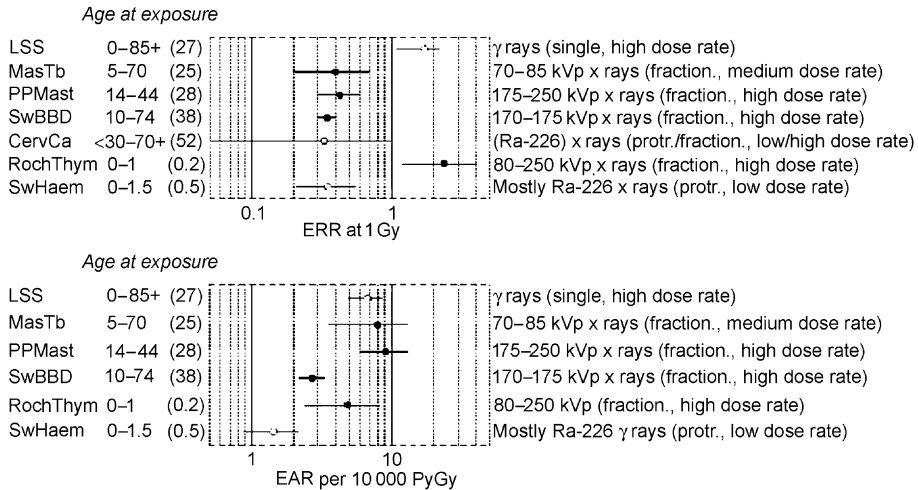


Fig. 2.5. The excess relative risk (and 90% confidence range) from various epidemiological studies on breast cancer. The upper panel gives the excess relative risk per Gy, and the lower panel gives the absolute risk per 10,000 person years and Gy [for description of the individual studies, see [UNSCEAR \(2000\)](#) and [Preston et al. \(2002\)](#)]. The confidence limit for the study on cervix carcinoma patients is recalculated. Cohorts: LSS, Life span study of atomic bomb survivors; MasTb, Massachusetts tuberculosis patients; PPMast, New York post-partum mastitis patients; SwBBD, Swedish benign breast disease patients; CervCa, cervical cancer patients (case control study); RochThym, Rochester infants with thymic enlargements; SwHaem, Swedish infants with skin haemangioma.

because both ERR and lifetime-integrated EAR decrease very substantially with increasing age at exposure.

(52) The dominant influence of the various modifying factors makes it impossible to confirm the difference in effectiveness between γ rays and x rays, or the difference between x rays of different energies on the basis of the epidemiological data. Studies related to other types of cancer are even further removed from providing an answer.

(53) The conclusion is, thus, that cell studies and biophysical considerations suggest an RBE of conventional x rays against hard γ rays of about 2–3, but that this difference has not been confirmed through epidemiological investigations. Therefore, the recommendation of the ICRP to attribute the same w_R (i.e. 1) for γ rays, x rays, and electrons remains a matter of practicability in the absence of definitive information.

2.2.4. The special case of Auger electron emitters

(54) Auger electrons emitted from nuclei bound to DNA are an exception from the *Publication 60* (ICRP, 1991) recommendation for electrons:

‘Auger electrons emitted from nuclei bound to DNA present a special problem because it is not realistic to average the absorbed dose over the whole mass of DNA as would be required by the present definition of equivalent dose. The effects of Auger electrons have to be assessed by the techniques of microdosimetry.’

The reference to averaging the ‘absorbed dose over the whole mass of DNA’ may not be entirely clear, but otherwise the argument is convincing. For Auger emitters incorporated into DNA, RBE values between 20 and 40 have been found in transformation studies (Chan and Little, 1986), and calculations of energy-deposition patterns have made the high values plausible (Baverstock and Charlton, 1988; Charlton, 1988). However, at present, there is no recommendation regarding how the microdosimetric assessment is to be performed. y_D can be a suitable substitute for LET (ICRU, 1986), but there is no convention on the size of the reference region in which y is to be measured. Therefore, the issue requires further study.

(55) For Auger emitters bound to DNA, high RBE values have been reported and a w_R of 20 or more appears to be appropriate. For those Auger electron emitters that enter the cell but are not bound to DNA, RBE values between 1.5 and 8 have been found for different endpoints in cell studies (Kassis et al., 1987; Makrigiorgios et al., 1990). Even the less critical case of more uniformly distributed Auger emitters should, therefore, be included in future considerations on a convention for w_R values for Auger electron emitters.

2.3. Different uses of the concept of RBE

2.3.1. RBE as a low-dose equivalence factor

(56) The concept of RBE is treated in this report because it guides the selection of weighting factors for radiation quality. The weighting factors are required to define effective dose, E , which serves as a common scale in radiation protection by attributing equal values to different exposure situations that are presumed to carry roughly the same risk with regard to stochastic effects. Accordingly, the RBE serves in this report strictly as an equivalence factor which is equally dependent on the two types of radiation that are being compared.

(57) The weighting factors relate to low doses, so the present report is—with regard to stochastic radiation effects, such as cancer—primarily concerned with the limit values which the RBE reaches at low doses. These limit values are denoted by RBE_M .

(58) With reference to low doses, it is particularly important to recognise the dependence of RBE on both types of radiation that are being compared. While a high neutron RBE at low doses tends to be seen as an indication of high absolute effectiveness of the neutrons per unit dose, the increase of neutron RBE at low doses is in fact primarily due to the reduced effectiveness per unit dose of γ rays. At low doses, low-LET radiation exhibits a much stronger dependence on modifying factors, such as dose rate or fractionation, than high-LET radiation.

(59) There are practical problems in the determination of RBE at low doses. The major difficulty is the determination of the initial slope of the dose–response curve for single doses of low-LET radiation. Assuming that the response to the reference radiation can be fitted to the linear-quadratic model, the use of low-dose-rate exposures to both the radiation under study and the reference radiation can obviate this problem. Different approaches have been proposed to overcome this problem. They are discussed in Section 3.1.

2.3.2. Dependence of RBE on dose

(60) All experimental and epidemiological information on RBE derives from observations at doses that are considerably larger than the doses of interest in routine radiation protection practice. Assessments of RBE_M must, therefore, combine observed values of RBE with inferences on the increase of RBE toward its limit, RBE_M , at low dose.

(61) Different dependencies of RBE on dose have been found in different systems, but there appears to be a fairly general pattern that can, at low to intermediate doses, be related to a linear dose dependence for densely ionising radiation, such as neutrons, and a linear-quadratic relationship for the low-LET reference radiation, such as γ rays:

$$E_n(D_n) = \alpha_n D_n \quad \text{and} \quad E_\gamma(D_\gamma) = \alpha_\gamma D_\gamma + \beta_\gamma D_\gamma^2 \quad (2.1)$$

where E_n is the effect due to the high-LET exposure with absorbed dose D_n and E_γ is the effect from the low-LET exposure with absorbed dose D_γ .

(62) The linear and linear-quadratic dose relationships for high- and low-LET radiations were first invoked and explained with regard to exchange chromosome aberrations (Sax, 1938; Lea, 1946). A later analysis of various radiobiological investigations with neutrons in terms of microdosimetry (Kellerer and Rossi, 1972) related the linear and linear-quadratic dependencies more generally to the primary lesions that determine the observed effect, including those cases where the observed effect need not be proportional to the underlying lesions and may even have to be expressed, as is the case with lens opacification (Bateman et al., 1972; Di Paola et al., 1980; Worgul et al., 1996), on an arbitrary scale. The essential point is that the dose–effect relationships for the observed endpoint, e.g. for late effects in man, can involve complexities at the cellular or tissue level which cancel in the comparison of two types of radiation. The RBE is, under this condition, still governed by the linear and linear-quadratic dose dependence of the primary lesions. The Joint ICRP–ICRU Task Group on ‘The Quality Factor in Radiation Protection’ (ICRU, 1986) emphasised the resulting dose dependence of RBE and the need to consider the low dose extrapolation of RBE in order to estimate RBE_M .

(63) Let D_n and D_γ , respectively, be the high- and low-LET absorbed doses that produce equal levels of effect. The RBE against the dose D_γ of the low-LET reference radiation is then:

$$R(D_\gamma) = D_\gamma / D_n \quad (2.2)$$

and Eq(2.1) provides the relationship:

$$\alpha_n D_n = \alpha_\gamma D_\gamma + \beta_\gamma D_\gamma^2 \quad (2.3)$$

With the substitution $RBE_M = \alpha_n / \alpha_\gamma$, one obtains RBE either as a function of the γ -ray dose or as a, somewhat more complicated, function of the neutron dose:¹

¹ In the earlier literature, the expression for $R(D_n)$ is of different analytical form because a quadratic term had been included in the dose dependence for the high-LET radiation. Such a term has not been established in experiments, and it is irrelevant except at very high neutron doses.

$$R(D_\gamma) = \text{RBE}_M / (1 + D_\gamma / (\alpha_\gamma / \beta_\gamma)) \quad (2.4)$$

$$R(D_n) = (\sqrt{(1 + 4D_n \text{RBE}_M / (\alpha_\gamma / \beta_\gamma))} - 1) / 2D_n (\alpha_\gamma / \beta_\gamma) \quad (2.5)$$

(64) It has been usual to specify or plot the RBE of neutrons as a function of the neutron dose (Kellerer and Rossi, 1972, 1982; ICRU, 1986; Rossi and Zaider, 1996). However, in applications to radiation protection, the quantity of interest is the weighted dose, which is numerically equal to the photon dose. It is, therefore, more informative to specify the RBE as a function of the photon dose. This convention is employed throughout this document.

(65) Figure 2.6 exemplifies the dependency of RBE on the photon and neutron doses for dicentric chromosomes in human lymphocytes and for mutations in *Tradescantia*. The upper curve in the two diagrams refers to the same chromosome data

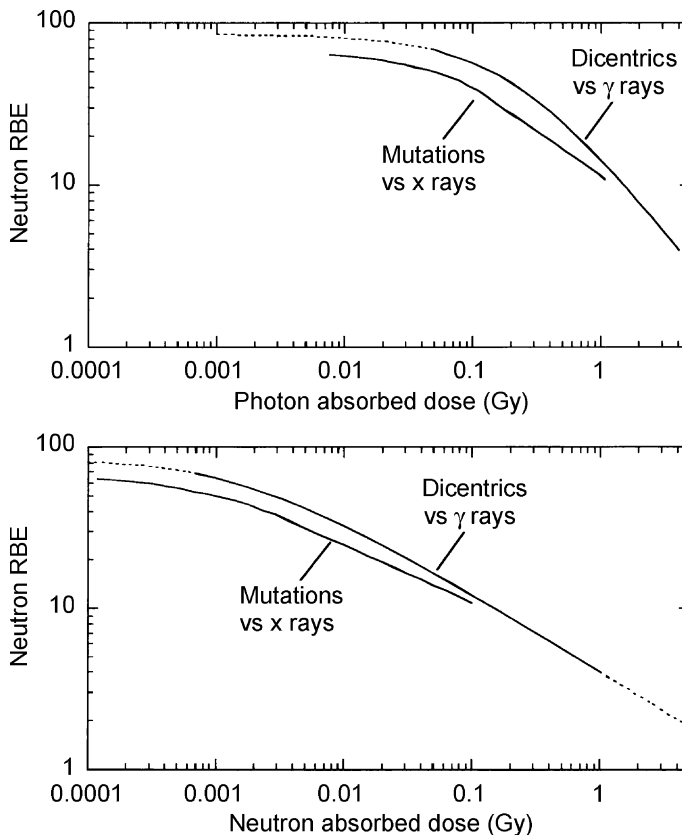


Fig. 2.6. The relative biological effectiveness (RBE) of neutrons for the induction of dicentric chromosomes (upper curves) (Schmid et al., 1998, 2000, 2002a, 2003) and for mutations in *Tradescantia* (lower curves) (Sparrow et al., 1972; see also Fig. 3.4) as a function either of the photon- (upper panel) or the neutron-absorbed dose (lower panel). Dotted sections of the curves are extrapolations beyond the actual data. The chromosome data refer to ^{60}Co γ rays and 0.39 MeV neutrons with the same parameters as in Fig. 3.3; the mutation data refer to 0.43 MeV neutrons and 250 kV x rays.

by Schmid et al. that are represented in Figs 2.2 and 3.3. The lower curve refers to the data by Sparrow et al. (1972) that are represented in Fig. 3.4.

(66) The study on *Tradescantia* is exceptional insofar as it actually shows the plateau of the RBE values at very low doses, and thus provides the RBE_M , which in this case is about 60. In the chromosome studies, there is strong but less direct evidence for an RBE_M value of about 80 for the 0.39 MeV neutrons against the ^{60}Co γ rays.

(67) In some animal experiments with single acute doses, it has not been possible to assess an excess tumour incidence below 1 Gy of the low-LET reference radiation. It is, therefore, difficult in such experiments to ascertain the low dose limit of the RBE. To estimate, nevertheless, the RBE_M from the observed RBE at higher dose, $R(D_\gamma)$, an assumed value of the ‘crossover dose’, $\alpha_\gamma/\beta_\gamma$, needs to be used in the relationship [see Eq(2.4)]:

$$RBE_M = (1 + D_\gamma/(\alpha_\gamma/\beta_\gamma)) \cdot R(D_\gamma) \quad (2.6)$$

(68) As noted earlier (ICRU, 1986; UNSCEAR, 1993), the term $(1 + D_\gamma/(\alpha_\gamma/\beta_\gamma))$ corresponds to the notion of the dose and dose-rate effectiveness factor (DDREF). This issue will be taken up in Sections 3.1 and 5.2.

(69) On the other hand, it is seen from Eq(2.4) that the observed RBE will approach RBE_M if low dose rates or the low doses in fractionated exposures reduce the coefficient β_γ , i.e. the quadratic term in the response to the low-LET radiation, sufficiently. This fact is used extensively in the studies of life shortening in mice (Section 3.2).

2.3.3. Derivation of the high-LET risk coefficient

(70) As pointed out in the preceding section, RBE values at higher dose and effect levels are employed in order to infer by extrapolation the low dose limit RBE_M . Apart from this indirect use of RBE at higher dose levels, there are also direct applications to risk quantification. While these other applications of RBE are not central to the subject of this report, they are nevertheless outlined here and in the subsequent section.

(71) Risk estimates for radiation protection purposes are obtained primarily from epidemiological observations on groups of people exposed to substantial doses of x rays or γ rays. The nominal risk coefficient for photon radiation is provided by an extrapolation to low doses or low dose rates that accounts, in terms of the DDREF, for an assumed degree of curvature in the dose relationship and for the related dose-rate dependence (ICRP, 1991). However, it needs to be noted that the risk estimates by extrapolation from higher doses are largely confirmed by the low dose data on cancer mortality and incidence in the A-bomb survivors (Pierce and Preston, 2000).

(72) The determination of risk coefficients on the basis of epidemiological data has also been possible for certain high-LET radiations, such as radon and its decay products (NAS, 1999), radium (see Machinami et al, 1999; Nekolla et al., 2000), or, more recently, plutonium (Kreishheimer et al., 2000; Koshurnikova et al., 2002). However, for other densely ionising radiations, such as fast neutrons, epidemiological information is lacking, and indirect procedures to determine the risk estimate,

C_n , for the high-LET radiation from experimental observations are employed. The common method is to derive, from animal experiments or other radiobiological studies, the RBE_M value for the high-LET radiation and then to multiply this value into the nominal risk coefficient, C_γ , for photons:²

$$C_n = \text{RBE}_M \cdot C_\gamma \quad (2.7)$$

(73) The two quantities RBE_M and C_γ need to be determined from low-dose or low-dose-rate data. With this low-dose procedure, the risk estimate $C_n = \text{RBE}_M \cdot C_\gamma$ is, thus, the product of two numerical values that are both based on extrapolation. The estimate, C_n , obtained by the low-dose procedure is, accordingly, subject to considerable uncertainty.

(74) A more direct high-dose method has been employed to derive the risk estimate for fission neutrons (Kellerer and Walsh, 2001). The approach requires the excess relative risk, ERR_{ref} , observed among the atomic bomb survivors at a high reference γ -ray dose, $D_{\gamma,\text{ref}}$. The observed effect-to-dose ratio is termed the reference slope (slope of the dotted line in Fig. 2.7):

$$c_{\gamma,\text{ref}} = \text{ERR}_{\text{ref}} / D_{\gamma,\text{ref}} \quad (2.8)$$

(75) The reference slope can be determined with considerably less uncertainty than the putative initial slope, C_γ , of the dose dependence for γ rays (i.e. the solid curve in Fig. 2.7). If an intermediate value of the reference dose is chosen, the reference slope is roughly equal to the slope of the linear fit to the γ -ray data.

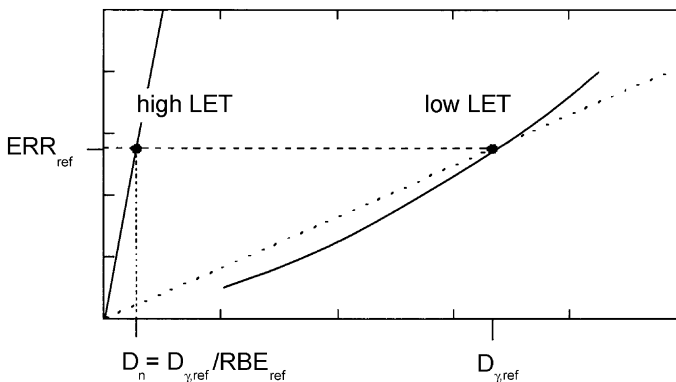


Fig. 2.7. Diagram of excess relative risk vs dose to explain the derivation of the high-linear-energy-transfer (LET) risk coefficient without recourse to the low-dose relative biological effectiveness (RBE). The low-dose part of the low-LET dose–effect relationship is omitted in order to emphasise the point that it is not reliably known and that it is not required for the specified approach.

² The notation C_γ rather than α_γ is used here for the initial slope of the dose dependence of risk (e.g. in terms of ERR) to make the distinction between epidemiological results and experimental radiobiological data.

(76) Furthermore, the method requires the RBE_{ref} of fission neutrons as observed in rodents against the same γ -ray reference dose. If the RBE for rodents also applies to man, the neutron dose $D_{\gamma,\text{ref}}/\text{RBE}_{\text{ref}}$ will cause the same ERR_{ref} as the γ -ray dose $D_{\gamma,\text{ref}}$. With the usual assumption of linearity for neutrons, the slope of the neutron dose-effect curve (straight solid line in Fig. 2.7), i.e. the risk estimate for the neutrons, is then:³

$$c_n = \text{ERR}_{\text{ref}} / (D_{\gamma,\text{ref}} / \text{RBE}_{\text{ref}}) = \text{RBE}_{\text{ref}} \cdot c_{\gamma,\text{ref}} \quad (2.9)$$

This estimate c_n is, unlike the familiar low-dose estimate, C_n , based on two observed, rather than two extrapolated, quantities.

(77) A suitable reference dose with regard to the data from the atomic bomb survivors happens to be $D_{\gamma,\text{ref}} = 1 \text{ Gy}$ (Kellerer and Walsh, 2001, 2002). Accordingly, in this high-dose procedure, one needs to refer to an estimate of the RBE from animal studies against the same γ -ray dose of 1 Gy, which tends to be in the lower range of γ -ray dose level for which neutron RBE values have been obtained (see Section 3.3).

(78) Both estimates, C_n and c_n , make sense, but the high-dose formulation in Eq(2.9) has the advantage that there is considerably less statistical uncertainty in the reference slope, c_γ , than in the estimated initial slope, C_γ . Furthermore, there is less uncertainty in RBE_{ref} than in RBE_M . The uncertainty of the neutron risk estimate c_n is, thus, considerably less than the uncertainty of the estimate C_n .

(79) In both the low- and the high-dose method, there is, of course, unavoidable uncertainty in the extrapolation of RBE from experiments in rodents to man, but this needs to be accepted in the absence of direct epidemiological information. There is also the assumption of a linear dose relationship for the high-LET radiation, but up to the neutron doses below 0.1 Gy that are involved in this analysis, it is well supported by radiobiological evidence.

(80) These considerations make it clear that the derivation of weighting factors for radiation quality and the quantification of the risk of high-LET radiation are two distinct issues. The uncertainty of the low dose effectiveness of low-LET radiation is inherent in RBE_M and w_R . It does not enter the high-LET risk estimates if derived in terms of the modified procedure.

(81) In Section 3.1, a low- and a high-dose approach to the derivation of RBE_M will be considered. This approach uses, in addition to an assumed DDREF, a high-dose RBE, RBE_H , which is roughly equivalent to RBE_{ref} .

2.3.4. Derivation of risk under specified conditions

(82) The nominal risk coefficient serves as a general guideline in the setting of dose limits, but it is not meant to be applied in the derivation of quantitative risk estimates under specific conditions. An example is the use of ionising radiation in medical diagnostics. One reason for the inapplicability of the nominal risk coefficient under these conditions is the fact that the age distributions of the exposed groups of people can differ substantially from the age distribution of the general population or

³ The accounting for the neutron component in the A-bomb radiation is disregarded in this summary explanation of the method.

of a working population, which can alter the risk substantially. Furthermore, in order to obtain a specific risk estimate, one may need to take specific characteristics of the exposed population, such as ethnic factors, into account. Finally, in the case of medical applications of ionising radiation, exposures are commonly organ specific. It is then necessary to base numerical evaluations of risk on organ doses, organ-specific risk estimates, and, where required, on specific estimates of the RBE.

(83) In view of these considerations, there is no conflict between the fact that all photon radiations are, with the current convention for effective dose, given the same weight, while risks from medical applications of soft x rays, conventional x rays, and hard γ rays are assessed differently. **w_R is designed for the practice of radiological protection, not for specific risk assessment.** Even the RBE values from experimental systems have limited applicability to risk assessment. For example, it would be inappropriate to base cost–benefit considerations for mammography screening primarily on risk estimates for γ rays and RBE values, rather than using the more relevant epidemiological data for x rays.

(84) The determination of probabilities of causation (PC) is another example of risk assessment under specified exposure conditions. (NIH, 1985; Kocher, 2001; Kocher et al., 2002; Land et al., 2002). PC values are computed for intermediate- or high-dose exposures that cause risks of a magnitude comparable to the background risk. This means that neither the values of RBE_M nor the weighting factor conventions w_R and $Q(L)$ are applicable; instead, high-dose information needs to be applied.

(85) Kocher et al. (2002) presented a synopsis of proposed w_R values for use in calculating probabilities of causation of cancers. Since this particular use of RBE data differs from the use for regulatory purposes, the authors state:

‘We have decided to abandon the term ‘relative biological effectiveness (RBE) factor’ to describe the biological effectiveness of different radiation types for the purpose of estimating cancer risks and probability of causation, basically to avoid misuse of the term ‘RBE’, which should be used only to describe the results of specific radiobiological studies. We also should not use the term ‘radiation weighting factor’ because this is an ICRP-defined point quantity used in radiation protection (i.e. to calculate equivalent doses). Therefore, we need a new term that is short and reasonably descriptive. We propose to describe the quantity of interest by the term ‘radiation effectiveness factor (REF).’

(86) A clear distinction of the various types of RBE and the quantities derived from RBE is essential. The term ‘radiation effectiveness factor (REF)’ was employed earlier (ICRP, 1984) with a different connotation to designate the ratio of the high-dose value of the RBE for deterministic effects to its maximum value, RBE_m , at low doses. In this earlier definition, REF was the analogue for deterministic effects to the DDREF for stochastic effects (see Section 5.2.2). However, the earlier definition was no longer used in *Publication 58* (ICRP, 1990). Accordingly, the proposal of Kocher et al. (2002) appears suitable, and it is recommended that the term REF be used for numbers that replace, by convention, RBE values in computations of the probability of causation.

3. QUANTIFICATION OF RBE

3.1. Two approaches to the determination of RBE_M

(87) *Publication 60* (ICRP, 1991, paragraph 32) stated:

‘Both equivalent dose and effective dose are quantities for use in radiological protection, including the assessment of risks in general terms. They provide a basis for estimating the probability of stochastic effects only for absorbed doses well below the thresholds for deterministic effects. For the estimation of the likely consequences of an exposure of a known population, it will sometimes be better to use absorbed dose and specific data relating to the relative biological effectiveness of the radiations concerned and the probability coefficients relating to the exposed population.’

Earlier in *Publication 60*, the ICRP (1991) stated that the radiation weighting factor (w_R) value for a specific type and energy of radiation was selected by the Commission to be representative of values of the relative biological effectiveness (RBE) of that radiation in inducing stochastic effects ‘at low doses’, and it went on to say ‘The RBE of one radiation compared with another is the inverse ratio of the absorbed doses producing the same effect’.

3.1.1. The low-dose method

(88) It was understood that for the purpose of defining an effective dose, E , and the organ-equivalent doses, H_T , values of the quality factor $Q(L)$ and w_R values were required that had to be related to the RBE of high-linear-energy-transfer (LET) radiations—such as neutrons—for low doses and/or low dose rates. Since the RBE is largest at low dose and low dose rate, the relevant values were termed RBE_M .

(89) The low-dose method used by the National Council on Radiation Protection (NCRP, 1990) was to determine RBE_M as the ratio of the initial slopes of the dose–response curves of the induction of tumours by fission neutrons and the reference radiation, γ rays.⁴ Values were reported for various types of tumour in two strains of mouse. Due to the difficulty in determining the initial linear slopes of the dose responses, especially of the reference radiation, the errors are large.

⁴ The value of the ratio was denoted RBE_M in the ICRU–ICRP report (1963) and NCRP Report 64 (NCRP, 1980). In 1980, the NCRP reviewed the experimental data from which a dose-rate effectiveness factor (DREF) could be derived:

DREF = effect per unit dose at high dose and dose rate / effect per unit dose at a low dose rate where the effect per unit dose represents the linear regression coefficients obtained for the high-dose-rate and low-dose-rate data for cancer induction. ICRP (1991) introduced the term ‘dose and dose-rate effectiveness factor (DDREF)’ which implied that the dose–response relationship was linear quadratic.

3.1.2. The high-dose method

(90) To remove the need to extrapolate the RBE in every single experimental system, the Committee on Interagency Radiation Research and Policy Co-ordination (CIRRPC) suggested a high-dose method which uses the observed high-dose RBE, RBE_H , and extrapolates it to low dose by the standard modifying factor (DDREF) (ICRP, 1991) which is inferred from the entirety of data relevant to late effects in man. As stated by the CIRRPC (1995):

‘... the RBE_M for humans is determined by the product of the appropriate neutron value determined under high-dose/dose-rate conditions and the DDREF selected for use with human low-LET acute exposure risk coefficients... Thus, the high-dose/dose-rate data (RBE_H) is modified for use in the case of low-dose/dose-rate exposure (RBE_M) by the DDREF selected for use with human low-LET acute-exposure risk coefficients, or:

$$RBE_M = RBE_H \cdot DDREF \dots' \quad (3.1)$$

(91) It was pointed out that, in principle, both methods should result in the same ‘value of RBE_M for human beings’. However, it was stated that the high-dose approach has the advantage of being based on high-dose and high-dose-rate data where the uncertainty of laboratory RBE values is smaller and less dependent on the choice of exposure conditions for the reference radiation.

(92) In response to a request by the British Committee on Radiation Units and Measurements (BCRU), the National Radiobiological Protection Board (NRPB) carried out a review of the RBE values and how they might be applied to the problem of deriving equivalent doses.

(93) The NRPB accepted the approach that had been proposed by the CIRRPC (1995) and made it more specific. It equated the RBE_H value of the high-dose RBE, in Eq(3.1), with the ratio of the initial slope (H) of the dose-response curve for the induction of cancer by high-LET radiation, and the slope (LL) of the linear fit to intermediate- and high-dose data for cancer induction by low-LET radiation.⁵ It selected—in line with the choice in *Publication 60* (ICRP, 1991) and with the subsequent recommendations by the NRPB (1997)—a value of 2 for the DDREF:

$$RBE_A = DDREF \cdot RBE_H = 2(H/LL) \quad (3.2)$$

(94) The NRPB chose the new notation RBE_A in order to indicate that this RBE_M value is derived through the specific approach represented by Eqs(3.1) and (3.2). As stated, the approach is an attempt to avoid the need to perform low-dose or low-

⁵ The unfamiliar notation LS , H , and LL for the slopes of the linear fit to the dose-effect relationship is retained solely for reference to the ‘high-dose method’ proposed by the CIRRPC panel and the NRPB in this section and in the following subsection.

dose-rate observations in each RBE assessment to determine the initial slope of the dose response of low-LET radiation. Instead, the approach uses an assumed standard value for DDREF.

(95) Values of DDREF based on experimental animal data were considered by the NCRP (1980) and by UNSCEAR (1988, 1993) to range between 2 and 10 with large associated errors. However, there are very few types of cancer for which adequate data have been obtained with low dose rates, and certainly such data are not available for a representative spectrum of relevant tumours for either mice or rats. In view of these limitations, it is not a priori clear which of the two methods to derive RBE_M is more reliable.

(96) In summary, obviously problems arise from not having epidemiological data for the effects of neutrons and having to rely on experimental data. However, despite the inherent uncertainties, the use of experimental data is unavoidable for both neutrons and heavy ions. The issue is considered in more detail in Chapter 4.

3.1.3. Relationship to risk estimation for high-LET radiation

(97) The preceding considerations were related to the derivation of the limiting RBE at low doses. But there is also a relationship between the high-dose method for the derivation of RBE_A and the high-dose method for the derivation of the high-LET risk coefficient (Section 2.3.3). As will be seen, the difference lies in the fact that the factor DDREF is not required for the high-dose risk estimate.

(98) Let LS be the slope of the linear fit to the data from the atomic bomb survivors and c_n the risk estimate for neutrons. Prior to the emergence of direct low-dose risk estimates from the follow-up of the A-bomb survivors (Pierce and Preston, 2000), the CIRRPC panel noted that the coefficient for human risk estimates for low-LET radiation is derived from the high-dose and high-dose-rate data (LS) from the atomic bomb survivors modified by the DDREF. To this corrected risk estimate, RBE_A values are applied to obtain c_n . The procedure is expressed by the relationship [see Eq(3.2)]:

$$c_n = (LS/DDREF)RBE_A = (LS/DDREF) \cdot DDREF \cdot (H/LL) \quad (3.3)$$

(99) If, as suggested by the CIRRPC panel and the NRPB, the same standard modifier DDREF is applied in the derivation of the corrected low-LET risk estimate ($= LS/DDREF$) and of the value $RBE_A [= DDREF(H/LL)]$, the factor DDREF cancels in Eq(3.3). With $RBE_H = H/LL$, one obtains from Eq(3.3):

$$c_n = RBE_H \cdot LS \quad (3.4)$$

This is equivalent to Eq(2.7) in Section 2.3.3 for the high-LET risk coefficient:

$$c_n = RBE_{ref} \cdot c_{\gamma,ref} \quad (3.5)$$