INVITED EDITORIAL

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In this issue of the journal, J D Harrison and P Day provide a review of methodology used in the estimation of doses and risks from internal emitters—that is, from radionuclides taken into the body. Their review is based on material prepared for the UK government Committee Examining Radiation Risks from Internal Emitters (CERRIE 2004), but also takes account of the new ICRP (2007) recommendations and other recent developments. Among the recommendations made by the Committee on Medical Aspects of Radiation in the Environment (COMARE 2004), in its response to the CERRIE (2004) report, was that: "… the NRPB be asked to carry out a review, with the widest possible consultation, of internal tritium dosimetry, paying particular attention to tritiated water and organic compounds containing tritium". The NRPB (now the Radiation Protection Division of the HPA) asked its independent advisory group on ionising radiation (AGIR) to consider this issue. Accordingly, an AGIR sub-group was set up under the chairmanship of Professor Bryn Bridges. The AGIR report (HPA 2007) includes the recommendation that an RBE value of 2 should be used for tritium in epidemiological studies and in individual retrospective risk assessments. The advisory group also suggested that consideration be given by ICRP to the use of a radiation weighting factor (w_R) of 2 for routine radiation protection. This issue was also discussed in an editorial by Bridges (2008) in the March issue of the journal, accompanying a paper on tritium epidemiology (Little and Wakeford 2008). Here, we take the opportunity to explain on behalf of ICRP why a w_R of 1 will continue to be applied to all low LET radiations, supported by the broader context provided by the review of Harrison and Day and by ICRP (2007). We also comment on the intended applications of the ICRP protection quantities and approaches to the assessment of doses and risks in situations where the use of the ICRP quantities is inappropriate.

The ICRP quantities, equivalent and effective dose, were devised for the purposes of practical radiation protection, to enable the summation of exposures from different internal emitters and external radiation for comparison with limits, constraints and optimised levels that relate to whole body exposure. Individuals may be exposed externally and internally to radiation of different qualities (e.g. photons, neutrons, alpha particles) and the spatial and temporal distribution of dose delivered from internal emitters may differ widely. Radionuclides in the body may concentrate in and irradiate a single organ or tissue (e.g. ^{131}I in the thyroid), a number of organs (e.g. ^{239}Pu mainly in lungs, liver and skeleton) or be distributed throughout all body tissues (e.g. ^{3}H as tritiated water, ^{137}Cs) and dose may be delivered over weeks (^{3}H as tritiated water) or throughout a person's lifetime (e.g. ^{239}Pu). The ICRP scheme provides a highly convenient method for the summation of all such exposures in terms of the quantity effective dose for protection purposes, but it is important to recognise that simplifying assumptions are made in these calculations and that effective dose is not intended to provide a measure of risks to individuals; it can only be regarded as an approximation for assessing individual risks.

Tritium is one of many radionucIides for which ICRP provides dose coefficients (Sv per Bq intake) for ingestion or inhalation by workers or members of the public, including children (ICRP 1994, 1996). Dose coefficients have also been published for *in utero* exposures following maternal intakes of radionuclides (ICRP 2001) and ingestion of radionuclides in

breast-milk (ICRP 2004). In each case, defined biokinetic and dosimetric models are used in dose calculations, including reference anatomical data for the organs and tissues of the human body. Because the intended use of effective dose is limited to protection purposes, the radiation weighting factors are chosen as a simple representation of the different effectiveness of different radiations in causing stochastic effects at low doses and dose rates. They do not take account, for example, of observed differences between low LET radiations (e.g. photons of different energies), and of different alpha particle RBE values for different cancer types. A single set of tissue weighting factors is used to take account of the contribution of individual organs and tissues to overall detriment from cancer and hereditary effects. These factors are based on age- and sex-averaged values of relative detriment. While ICRP will in future calculate doses to reference male and female adults separately using recently developed anatomical models, equivalent doses to males and females will be averaged before calculation of effective dose (ICRP 2007).

It is clear from the approaches taken to the calculation of equivalent and effective dose that these quantities are not individual-specific but relate to reference persons, to reference workers and reference members of the public of different ages. They are intended for use within the ICRP system of protection and are used in this way for regulatory purposes worldwide. Practical protection would not be improved by calculating effective dose separately for males and females, and to do so might imply a degree of precision in the calculations that may be misleading. Similarly, a more complex treatment of radiation or tissue weighting would be inconsistent with the intended purpose of the protection quantities and may again imply greater precision than is justified. Constrained optimisation of planned exposures should ensure appropriate levels of protection, using the protection quantities as defined by ICRP, including a w_R of 1 for all low LET radiations including tritium beta particles.

Bridges (2008) considers a hypothetical and unlikely case of a worker whose effective dose from tritium is assessed as 18 mSv; this would clearly be 36 mSv if the w_R for tritium beta particles was 2. However, Bridges (2008) recognises that in practice constraints would be set on such workplace exposures at some fraction of the 20 mSv dose limit. For nuclear workers for whom tritium exposure is a dominant contributor to dose, a constraint might be set at 5 mSv per year, for example. A routine monitoring programme would then be set up to measure the urinary excretion of tritium periodically throughout normal operations with an investigation level corresponding to a dose of about 1–2 mSv. For members of the public, a constraint of 300 μSv per year is usually set for doses received from a single source of exposure, assessed on the basis of the behaviour of an identified critical group or representative person, together with measurements of tritium and other radionuclides in air and foodstuffs (ICRP 1991, 2006, 2007). Doses of a fraction of the constraint (approaching 100 μSv) should raise concern and lead to further analysis and review. Thus, constrained optimisation is regarded as central to the protection system and the principal means of keeping doses as low as reasonably achievable.

In the control of radiation exposures, therefore, the use of a single w_R value of 1 for all low LET radiations has to be seen as one of the many simplifying assumptions made in the calculation of the ICRP protection quantities that do not compromise their intended use. Although equivalent and effective dose are risk-related, as already stated they can only be taken as approximate correlates of risks to individuals. Thus, in the estimation of risks to individuals, for calculations of probability of cancer causation, for example, all available information must be used to provide best estimates of organ doses and associated risks for the age, sex and population group of the specific individuals. It is in this context that it would be appropriate to consider RBE data for tritium in more detail.

Straume and Carsten (1993) provided a thorough review of experimental data on the carcinogenic, genetic, developmental and reproductive effects of exposure to HTO and

OBT in animals and *in vitro* cell systems. The AGIR report (HPA 2007) provided further review, updating and, in some cases, reanalysing data. The spectrum of observed effects is indistinguishable from the effects of whole body external irradiation with x-rays or gamma rays. Based mainly on *in vitro* studies, there is evidence for RBE values of greater than 1 for tritium beta particles compared to gamma irradiation and x-irradiation. Considering all observed effects of HTO exposure, RBE values are in the range of 1–3.5. For comparisons with gamma rays, most values were from 1–3 while for x-rays most were from 1–2, with values of 1–1.5 predominating. These measured RBE values for tritium beta irradiation are reasonably consistent with estimates based on microdosimetric considerations (e.g. Bigildeev *et al* 1992, Morstin *et al* 1993, Moiseenko *et al* 1997). For the purposes of assessing risk at low chronic doses, studies of carcinogenesis are the most appropriate. These include studies of the acceleration of the appearance of mammary tumours in rats (Gragtmans *et al* 1984) and the induction of acute myeloid leukaemia in mice (Johnson *et al* 1995). Both these studies compared chronic exposure to HTO and x-rays (250 kVp) and gave RBE values of about 1. However, the AGIR report (HPA 2007) drew attention to the limitations of these studies and questioned their applicability to RBE at low doses. On the basis of a rigorous analysis of a restricted number of studies considered to provide the best data, the advisory group obtained aggregated RBE estimates of 2.2 (95% CI of 2.0–2.3) and 1.2 (95% CI of 1.0–1.4), compared to chronic exposures to gamma rays and x-rays, respectively. These estimates necessarily rely on *in vitro* data.

An issue addressed by the HPA advisory group (HPA 2007) in general terms is the relationship between RBE values and DDREF—dose and dose rate effectiveness factor. DDREF is a recognition of the curvilinear dose–response of low LET radiations such that the slope of the dose–response is less at low doses and dose rates than at higher doses and dose rates (ICRP 1991, 2003, 2007). Largely on the basis of animal data, ICRP use a DDREF of 2 in the calculation of risk factors for solid cancers at low doses and dose rates, based on the Japanese survivor data. Different experimental systems exhibit different DDREF values, and higher observed values of tritium RBE are likely to correlate with higher values of DDREF for the reference radiation (x-rays or gamma rays). Since RBE values for different low LET radiations will be smaller and tend to a value of 1 at high dose and dose rate, and given that there is also evidence for a small DDREF for tritium, the use of a DDREF of 2 for cancer induction in humans might be taken to suggest maximum RBE values for tritium-induced solid cancers of between 1 and 2. On this basis, a best estimate of cancer risk from tritium in humans would be between the high dose rate and DDREF-corrected estimates for gamma rays. All such estimates are, of course, subject to uncertainties.

In the new recommendations, ICRP (2007) emphasise that dose coefficients for internal emitters and dose conversion coefficients for external exposures are calculated using defined models and weighting factors and published as point values without consideration of uncertainty. Harrison and Day (2008) discuss uncertainties in the calculation of dose coefficients and conclude that an understanding of the various contributions to uncertainty should help inform judgements on the optimisation of protection. Uncertainties relating to the calculation of dose coefficients have been assessed to be smaller for tritium, as tritiated water or in organically-bound forms, than for many other radionuclides (Leggett *et al* 1998, Harrison *et al* 2002, Apostoaei and Miller 2004).

In conclusion, the main points that we would wish to convey are:

(1) The ICRP protection system is scientifically based but makes a number of simplifying assumptions so that doses from different radiation types can be summed and compared with limits, constraints and reference levels that relate to whole body radiation exposure. Effective dose is defined for reference persons and evaluated using reference phantoms.

The underlying simplifications include the use of a w_R value of 1 for all low LET radiation, including tritium beta particles. For planned exposures, appropriate levels of protection are determined by constrained optimisation, resulting in doses that will be typically a small fraction of the relevant dose limit. Increased complexity in the calculation of equivalent and effective dose would not improve protection and might suggest a degree of precision in the calculations that is unwarranted.

(2) For risk assessments, the available data on RBE values of tritium irradiations compared to gamma ray irradiations suggest that an RBE value of 2 might be appropriate for cancer induction at low doses. However, this conclusion relies on the results of *in vitro* cellular studies, with little direct information on *in vivo* carcinogenesis. Considerations of the relationship between RBE and DDREF can be interpreted to suggest a low value of tritium RBE for cancer induction in humans at low doses and dose rates.

While ICRP has concentrated on the development of a system of protection that can be applied simply to reference workers and reference members of the public, it is clear that in particular situations of protection consideration of dose and risk to individuals is required. Such situations include, for example, the assessment of doses received by astronauts and the assessment of risks to individual patients from medical imaging procedures. Furthermore, as discussed in ICRP recommendations (1991, 2007), assessments of exposures received by individual workers, as might be required if dose limits are exceeded, will always need to take account of all available information, including RBE values, to provide best estimates of risk. Similarly, estimates of risk to population groups should properly be based on best available data. It may be that ICRP should consider providing further guidance for such individual assessments, for use in situations for which the system of protection using equivalent and effective dose was not designed. On the specific issue of tritium, we agree with the conclusion of the HPA advisory group (HPA 2007) concerning the importance of pursuing epidemiological studies on workers exposed to tritium. While it may be that these studies will lack the power to provide unequivocal conclusions, it is important that the most is made of opportunities to obtain human data. There is also a need for further *in vivo* carcinogenesis data and it may be that genetically modified mice will provide suitable radiation-sensitive models for such studies.

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