Journal of Radiological Protection

Official journal of the Society for Radiological Protection

EDITORIAL

More on the risk of cancer among nuclear workers

To cite this article: Richard Wakeford 2009 *J. Radiol. Prot.* **29** 1

J. Radiol. Prot. **29** (2009) 1–4 doi:10.1088/0952-4746/29/1/E02

EDITORIAL

More on the risk of cancer among nuclear workers

In the September 2005 issue of this journal (Wakeford 2005) I commented upon the findings of an epidemiological study led by researchers from the International Agency for Research on Cancer (IARC) of cancer mortality among nuclear workers from 15 countries (Cardis *et al* 2005). This study resulted from an impressive effort to collect, collate and analyse large volumes of data, and it addressed an issue at the heart of radiological protection: how good are the assumptions that are made in applying the findings of studies of moderate and high doses of radiation received briefly to those exposed to low doses and/or low dose-rates? Direct studies of these latter exposure circumstances are difficult to conduct because they require the inclusion of large numbers of individuals to stand any realistic chance of detecting the level of excess cancer risk predicted by standard models, or any deviation from this prediction that is not large. Further, it is easy for systematic errors to creep into these studies, especially when large datasets are combined that originate from different countries with different recording practices, and dealing adequately with potential confounding factors (such as tobacco smoking) presents real difficulties because it is unlikely that adequate data on such factors will be comprehensively available for individual members of large cohorts, and somewhat crude surrogates (such as socioeconomic status) must be used instead.

I pointed to three issues that I considered to pose problems in the reliable interpretation of the findings of the 15-country study, and that these were especially important to take into account since the results had been portrayed in some quarters as suggesting an underestimation of risk by the models that underlie radiological protection. The first problem is the influence of lung cancer upon the risk estimate for cancers other than leukaemia, implying possible confounding by smoking, a possibility that had been recognised by the authors. Second, the influence of the Canadian data for cancer other than leukaemia is surprisingly large: the Canadian deaths represent 4% of the total number of deaths in this disease category, but when the Canadian workers are excluded from the analysis the risk coefficient reduces by 40%. This suggests that there may be problems with the Canadian data, a possibility that requires investigation before the result including the Canadian data can be relied upon. Third, the study was of the effect of the cumulative recorded dose received from external sources of penetrating radiation upon the risk of cancer mortality, and the authors excluded from the analysis of external dose those workers who had the potential of receiving material internal doses from deposited radionuclides or neutron doses. Although the desirability of removing the influence of these doses from a study of external photon doses is understandable, the practical effect was to remove from the study a large number of workers with high cumulative external photon doses, which substantially reduced the statistical power of the study. Consequently, although the 15-country study represents a laudable effort at addressing an important question—a study that should most certainly be continued—at present the results have to be treated with some caution.

Recently, the findings of the third analysis of data from the UK National Registry for Radiation Workers (NRRW) have been published (Muirhead *et al* 2009)—the results of the second analysis of the NRRW were published ten years ago in the March 1999 issue of this journal (Muirhead *et al* 1999). NRRW-3 also concentrated on cumulative recorded doses received from external sources of penetrating radiation, but unlike the IARC 15-country study, workers who had been monitored for exposure to internal emitters or who may have received significant doses of neutrons were not excluded from the analyses. This latest study of UK nuclear workers is particularly important because those workers who tend to have received the highest cumulative doses from working in the early years of the nuclear industry are now reaching an age when they have an increased chance of developing a serious illness and dying, and this will materially increase the statistical power of the study. Thus, the study now includes just over 8000 deaths from cancer, whereas only about 3500 cancer deaths were included in the second analysis—173 cancer deaths occurred among workers with cumulative external doses ⩾400 mSv, which compares with 74 deaths in this dose group in the second analysis. By way of comparison, 5233 cancer deaths were included in the 15-country study, but only 13 of these deaths occurred in the 400+ mSv dose group, a substantial reduction in the number of high external dose workers occurring because of the criterion of excluding workers with a potential for material internal and/or neutron doses, which was not done in NRRW-3. NRRW-3 was also able to analyse cancer registration data, allowing for the inclusion in the study of non-fatal cancers—just over 11 000 incident cancer cases were included in the study, of which 225 occurred among workers with cumulative doses ⩾400 mSv. It is of note that the power of studies such as NRRW-3 to detect any radiation-induced health effects relies heavily on workers who have accumulated reasonable doses of radiation during their working lives—it is not strictly accurate to refer to these studies as *low dose* studies, but rather *chronic low dose-rate* studies or studies of *protracted exposure* to multiple low doses.

The third analysis of the NRRW shows the usual strong ‘healthy worker effect’ in that rates of mortality from all causes and from all cancers are significantly lower than those expected from national mortality rates, which is undoubtedly the result of a lower level of important background risk factors (such as smoking) among the NRRW population than among the general population. What is of greatest interest is how the risks of various types of cancer vary with the cumulative dose of external radiation and the slopes of any trends with dose—the slope gives the risk coefficient (excess risk per unit dose) that may be compared with that assumed for the purposes of radiological protection. In NRRW-3 estimates of the excess relative risk (ERR) per unit dose were made, which is the proportional increase in the risk of cancer over the background risk (i.e. with no occupational dose) by increment of dose accumulated occupationally, where the cumulative dose was lagged by 2 years for leukaemia and 10 years for all other cancers to account for the minimum latent period between exposure and the clinical manifestation of a cancer.

For leukaemia (excluding chronic lymphatic leukaemia, CLL) mortality, the ERR/Sv (the slope of the trend) was 1.71 (90% confidence interval (CI): 0.06, 4.29), while for leukaemia incidence the slope was 1.78 (90% CI: 0.17, 4.36). For mortality from all cancers other than leukaemia, the ERR coefficient was 0.28 (90% CI: 0.02, 0.56), and for the incidence of all cancers other than leukaemia it was 0.27 (90% CI: 0.04, 0.51). These positive trends with dose are statistically significant at the 0.05 level if a one-sided test is assumed, i.e. it was assumed at the outset that the risk would increase with dose rather than decrease, which is a reasonable assumption. The positive trends with dose for mortality from, and incidence of, all cancers other than leukaemia did not, in contrast to the 15-country study, depend materially on lung cancer—the ERR/Sv for mortality from all cancers other than leukaemia and cancers of the lung and pleura was 0.32 (90% CI: 0.02, 0.67), and for the incidence of these cancers it was 0.31 (90% CI: 0.05, 0.58). This is reassuring evidence that smoking is not playing a major confounding role in the generation of these positive trends with dose.

This important study is the most powerful statistically of nuclear worker studies carried out to date, reflected in the comparatively narrow confidence intervals for the risk coefficients.

This permits the important conclusion that the cancer risk estimates that underlie radiological protection are not in error by a large margin. On the other hand the findings of NRRW-3 do imply that protracted exposure to low dose-rate radiation increases the risk of cancer, an inference supported by the findings of studies of workers at the Mayak facility in Russia (see, for example, Sokolnikov *et al* 2008), a worker cohort that was not included in the 15-country study. Although this is a fundamental assumption of radiological protection it is not universally accepted, and certain groups are vocal in their insistence that there is no dependable evidence of the harmful effect of low doses or low dose-rates of radiation and that the presumption of a 'no-threshold' dose–response relationship is unrealistic and leads to a waste of money implementing unnecessary protective measures. The findings of NRRW-3 add to the scientific evidence that low doses and/or low dose-rates of radiation do indeed increase the risk of cancer, albeit that the increased risk is small and at a level compatible with the predictions of standard risk models; but the study should give pause for thought among those who argue for a threshold dose (or even for a 'hormetic', i.e. beneficial, effect of low doses).

Where do we go from here? Well, the findings of NRRW-3 certainly warrant the continued follow-up of the NRRW cohort to include more deaths from, and incident cases of, cancer and consequent increased statistical power and more precise estimates of risks. Continuing the efforts to combine the NRRW with equivalent worker cohorts from other countries, as in the IARC 15-country study, would also be highly desirable; but it should be appreciated that the power of such international studies will mainly derive from the number of cancer deaths in high cumulative dose groups, and this will be predominantly due to workers in those countries that have had large nuclear power/weapons programmes over several decades, so it is important to include as many workers as possible from France, Canada and, of course, the USA. But where are the large multi-site worker cohort studies from the USA—where is the US equivalent of NRRW-3? Such studies were underway in the late 1980s and early 1990s (see, for example, Gilbert *et al* 1993) at much the same time as the first analysis of the NRRW data was being conducted (Kendall *et al* 1992), but the US multi-site cohort studies seem to have petered out. This is very disappointing because if an effect of occupational exposure among nuclear industry workforces in the West is to be found then one would expect the combined workforce of the US Department of Energy nuclear sites to be the prime candidate for its manifestation. One can only hope that the results of NRRW-3 will be the spur for an increased effort from the USA.

Finally, what about other doses received by nuclear workers, in particular doses from radioactive materials inadvertently taken into the body? These doses from internal emitters are of interest in their own right, especially the effect of doses received from radionuclides emitting short-range, densely ionising alpha-particles, such as plutonium, and there is increasing interest in the effects of tritium due to the possibility of nuclear fusion power, among other things. Accurate tissue-specific doses for these radionuclides are much more difficult to calculate than those from external sources of penetrating radiation, but efforts to generate such internal doses for plutonium workers, among others, have been underway for some time (see, for example, Riddell *et al* 2000) and it is important to derive relevant risk estimates from the direct study of such groups of exposed workers. It is also of interest to know how these additional internal doses affect the risk estimates for external doses, as produced by NRRW-3, since they have not been taken into account in the derivation of risk coefficients, although with the exception of the risk of lung cancer from inhaled radioactive material, internal doses may not have a major impact upon these external irradiation risk estimates. The incorporation of internal doses into nuclear worker studies is an important next step in radiation epidemiology.

So, the findings of the third analysis of the National Registry for Radiation Workers represent an important milestone in our understanding of the risks posed by low doses and low dose-rates of radiation. They offer reassurance that the cancer risk estimates used in radiological protection are not in error by a substantial degree and demonstrate that the investment in large worker cohort studies can produce scientifically valuable results, which has been doubted by some. It's been a long time coming (the NRRW was established in the mid-1970s), but perseverance has paid off. Carefully conducted international worker studies in the future can be expected to produce risk estimates to rival those generated by the Japanese atomic bomb survivors, which was a primary objective of those who originally established the large worker cohorts. It goes to show what can be done with sufficient effort and application, not to mention funding.

References

Cardis E *et al* 2005 Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries *Br. Med. J.* **331** 77–80

Gilbert E S, Cragle D L and Wiggs L D 1993 Updated analyses of combined mortality data for workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Weapons Plant *Radiat. Res.* **136** 408–21

Kendall G M *et al* 1992 Mortality and occupational exposure to radiation: first analysis of the National Registry for Radiation Workers *Br. Med. J.* **304** 220–5

Muirhead C R *et al* 1999 Occupational radiation exposure and mortality: second analysis of the National Registry for Radiation Workers *J. Radiol. Prot.* **19** 3–26

Muirhead C R *et al* 2009 Mortality and cancer incidence following occupational radiation exposure: third analysis of the National Registry for Radiation Workers *Br. J. Cancer* **100** 206–12

Riddell A E, Battersby W P, Peace M S and Strong R 2000 The assessment of organ doses from plutonium for an epidemiological study of the Sellafield workforce *J. Radiol. Prot.* **20** 275–86

Sokolnikov M E *et al* 2008 Lung, liver and bone cancer mortality in Mayak workers *Int. J. Cancer* **123** 905–11

Wakeford R 2005 Cancer risk among nuclear workers *J. Radiol. Prot.* **25** 225–8

Richard Wakeford
Editor-in-Chief