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EDITORIALS

Ionising radiation in the workplace

Low risk but not no risk

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Information on radiation risk for cancer has come from several sources,[1] in particular the Japanese atomic bomb survivors that comprise the Life Span Study cohort.[2] It remains a controversial question whether there is a risk at low doses and low dose rates; although some have suggested the existence of thresholds below which there is no excess radiation risk or even beneficial (hormetic) effects of radiation exposure,[3] this evidence has been disputed.[4] The International Commission on Radiological Protection[5] assumes, for regulatory purposes, that cancer risks can be linearly extrapolated from high radiation doses and high dose rates to low radiation doses and low dose rates by applying a dose and dose rate effectiveness factor (DDREF) of 2. However, the use of DDREF is controversial, and there is some evidence to suggest that excess cancer risks per unit dose do not fall in the lowest ranges of dose rate.[6]

In a linked article,[7] the International Nuclear Workers Study (INWORKS) suggests significant risks associated with low dose rate occupational exposure to radiation in a combined cohort of 308 297 radiation workers from France, the United Kingdom, and the United States. This important study extends the follow-up of parts of a previous pooled analysis of nuclear worker data, the so called 15-Country Study.[8] Overall, relative risks of solid cancer increased by an extra 47% per Gy of cumulative exposure (90% confidence interval 18% to 79%). Reassuringly, results were not driven by results from any particular country, by contrast with the troubling heterogeneity by country present in the 15-Country analysis.[8]

Strengths of the present study were the largely complete recruitment from the various component cohorts, use of national mortality registers, and a comprehensive dose reconstruction, incorporating adjustments to recorded film badge doses to estimate cumulative doses to the colon.[9] Weaknesses included the lack of information on other important socioeconomic and lifestyle factors (such as smoking) and occupational exposures (such as benzene and asbestos), which could conceivably confound the association between radiation dose and cancer risk.

Although exclusion of lung cancer—the cancer with strongest relative risk associated with smoking—had almost no effect, exclusion of a larger group of all cancer sites related to smoking (about 70% of all solid cancers) from analyses reduced the magnitude of the association, which also became non-significant. This suggests either heterogeneity of radiation risk by cancer site or some degree of confounding by smoking. The authors had limited information on neutron dose, and almost none on participants' exposure to radionuclides such as tritium or plutonium or to medical radiation.[9] However, analyses with additional stratification by whether the worker had a known or suspected uptake of radionuclides, or excluding those workers with recorded neutron exposure made little difference.

The failure to take dose uncertainty into account is another weakness, especially because the uncertainties in some organ doses are substantial.[9] Use of all solid cancers as an endpoint is also unfortunate, which includes highly radiogenic cancers (bladder, brain, breast, colon, liver, lung, and oesophagus) as well as cancers with much lower radiosensitivity (prostate, small intestine, uterus, and rectum). Correlation of this endpoint with a cumulative dose to the colon—which could adequately represent doses to deeper organs within the trunk but possibly not other body sites (brain, breast)—is another weakness.

Use of all solid cancers as an endpoint also complicates comparisons with the Life Span Study of Japanese atomic bomb survivors. This study had much lower proportions of certain highly radiogenic cancer sites than the INWORKS study; among men exposed between ages 20 and 60 years in the Life Span Study,[2] lung cancer accounted for 17.9% of solid cancer deaths, compared with 32.3% in INWORKS.[7] It would have been better to use analyses stratified by cancer type with the relevant organ doses used for each stratum, which would also have allowed for tests of heterogeneity by cancer type.[10]

The present analysis of all solid cancers[7] and a parallel analysis of leukaemia and lymphoma[11] both estimate radiation risks that are slightly above those in corresponding subsets of the Life Span Study.[2] Should we conclude, as Richardson and colleagues do,[7] that exposures at lower dose rates are just as risky as those at higher dose rates (that is, DDREF=1)? This conclusion may be unwarranted: apart from the endpoint heterogeneity within the Life Span Study and INWORKS cohorts discussed above, the radiation received by the workers in INWORKS had energy ranging from 100 kiloelectron volts to 3 megaelectron volts.

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This energy level would have been about twice as risky (per unit dose) as that received by atomic bomb survivors in the Life Span Study, who received most of their dose from gamma rays with an energy range of 2-5 megaelectron volts.[12] Allowing for this and the statistical uncertainties would be consistent with a DDREF of 2.

Other uncertainties must also be taken into account when comparing risks between INWORKS and the Life Span Study. The most important uncertainty is the method by which one transfers risk estimates from one population to another. Despite the relatively large quantity of data on radiation risk,[1] the question of how to transfer risk estimates between different populations remains unanswered.

In summary, the study by Richardson and colleagues[7] adds to a growing body of evidence suggesting associations between exposure to moderate or low dose radiation and risk of cancer.[4-14] The study is consistent with risks previously derived from the Japanese atomic bomb survivors[2] and other groups exposed to moderate or high doses,[1 15] which form the basis of the regulatory limits applied to nuclear workers and other radiation exposed groups. As such, the excess solid cancer risks associated with radiation in this cohort are modest: for the average worker, the lifetime risk of cancer death is likely to be increased by about 0.1% from a baseline risk of cancer death of about 25%.[1 5] However, it is equally clear that the excess risks are unlikely to be zero. This body of evidence does not suggest, and indeed is not statistically compatible with, any large “no risk” threshold for dose, or any possible beneficial (hormetic) effects.

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1 United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). UNSCEAR 2006 report. Annex A. Epidemiological studies of radiation and cancer. United Nations, 2008:13-322.
2 Ozasa K, Shimizu Y, Suyama A, et al. Studies of the mortality of atomic bomb survivors, report 14, 1950-2003: an overview of cancer and noncancer diseases. *Radiat Res* 2012;177:229-43.
3 Tubiana M, Feinendegen LE, Yang C, et al. The linear no-threshold relationship is inconsistent with radiation biologic and experimental data. *Radiology* 2009;251:13-22.
4 Little MP, Wakeford R, Tawn EJ, et al. Risks associated with low doses and low dose rates of ionizing radiation: why linearity may be (almost) the best we can do. *Radiology* 2009;251:6-12.
5 International Commission on Radiological Protection (ICRP). The 2007 recommendations of the International Commission on Radiological Protection. ICRP publication 103. *Ann ICRP* 2007;37(2-4):1-332.
6 Jacob P, Rühm W, Walsh L, et al. Is cancer risk of radiation workers larger than expected? *Occup Environ Med* 2009;66:789-96.
7 Richardson DB, Cardis E, Daniels RD, et al. Risk of cancer from occupational exposure to ionising radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). *BMJ* 2015;351:h5359.
8 Cardis E, Vrijheid M, Blettner M, et al. The 15-Country Collaborative Study of cancer risk among radiation workers in the nuclear industry: estimates of radiation-related cancer risks. *Radiat Res* 2007;167:396-416.
9 Thierry-Chef I, Richardson DB, Daniels RD, et al. Dose estimation for a study of nuclear workers in France, the United Kingdom and the United States of America: methods for the International Nuclear Workers Study (INWORKS). *Radiat Res* 2015;183:632-42.
10 Little MP, Hawkins MM, Shore RE, et al. Time variations in the risk of cancer following irradiation in childhood. *Radiat Res* 1991;126:304-16.
11 Leuraud K, Richardson DB, Cardis E, et al. Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. *Lancet Haematol* 2015;2:e276-81.
12 National Council on Radiation Protection and Measurements (NCRP). Report no 104. The relative biological effectiveness of radiations of different quality. NCRP, 1990:1-218.
13 Kendall GM, Little MP, Wakeford R, et al. A record-based case-control study of natural background radiation and the incidence of childhood leukaemia and other cancers in Great Britain during 1980-2006. *Leukemia* 2013;27:3-9.
14 Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. *Lancet* 2012;380:499-505.
15 Little MP. Comparison of the risks of cancer incidence and mortality following radiation therapy for benign and malignant disease with the cancer risks observed in the Japanese A-bomb survivors. *Int J Radiat Biol* 2001;77:431-64.

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