Radioprotection 2017, 52(3), 211–212
© EDP Sciences 2017
DOI: 10.1051/radiopro/2017019

Available online at:
www.radioprotection.org

Editorial Comment

Editorial Comment on: Mortality in the French cohort of nuclear workers

***Radioprotection* 52(3), DOI: 10.1051/radiopro/2017015**

B. Grosche*

Retired, formerly Department Radiation Protection and Health, Federal Office for Radiation Protection, Oberschleissheim, Germany.

Received: 22 May 2017 / Accepted: 22 May 2017

In this issue of *Radioprotection*, K. Leuraud *et al.* present a comprehensive update of the main results obtained on mortality in the French cohort of nuclear workers. The publication of this article offers the opportunity to make a point on the current radiation protection system and on the strengths and limitations of epidemiology regarding the health risks associated to ionizing radiation exposure at low doses.

The quantitative assessment of radiation risk is based on knowledge gained from epidemiological studies of radiation-exposed populations, complemented by data from animal experiments, as well as fundamental *in vitro* cellular and biophysical studies. Epidemiology is currently the most informative approach for the assessment of health risks to humans from ionizing radiation. To carry out such an assessment in the best possible manner it is necessary to use information from as many well conducted studies as possible.

As pointed out by MELODI, a European platform dedicated to low dose radiation risk research, in its 2016 statement, the current system of radiation protection has been developed and evolved on the basis of an understanding of the magnitude of health risks associated with radiation exposure together with knowledge of the mechanisms of radiogenic disease pathogenesis to inform risk extrapolation. The accurate assessment of health risks is fundamental to striking an appropriate and an acceptable balance between the benefits of use of ionizing radiation and the associated health risks. Accordingly, the 2016 draft of MELODI's Strategic Research Agenda puts first the dose and dose-rate dependency of cancer risk and second non-cancer risks. These topics are of relevance to answer the question about the robustness of the radiation protection system, *i.e.* is it adequate, does it overprotect, or does it miss to include relevant risks.

Today, the major source of information on radiation risk related to external radiation exposure is still the Life-Span Study of the Japanese atomic bomb survivors. Since decades there is a continuing discussion whether the exposure pattern of the atomic bomb survivors, which was high dose-rate exposure with low to high doses, could be used for risk extrapolation to doses from low and low dose-rate exposures, *e.g.* as among nuclear workers. ICRP introduced in its 1990 recommendations (ICRP Publication 60) the Dose and Dose-Rate Effectiveness Factor (DDREF) to the radiation protection system. This DDREF is probably challenged by new findings. Consequently, ICRP started recently a task group to look at this question in as much detail as possible, taking into account findings from epidemiological, experimental and *in vitro* studies.

This issue of *Radioprotection* includes the findings of to-date's largest cohort study among French nuclear workers. This cohort was part of the joint INWORKS cohort, encompassing nuclear workers from France, the UK, and the US. Nonetheless, it is important to have the results from the French cohort presented separately. One major result is that the French cohort basically reveals the same results as the joint INWORKS cohort does. This is insofar of relevance since it shows that the overall result of the joint cohort is not driven by the larger cohorts from the UK and the US, but it is consistent over the different workforces.

When looking at the results, it has to be kept in mind that the French cohort is a young cohort being aged 56 on average at the end of follow-up. Accordingly, 89% of the cohort were alive at the end of the study period. The cohort shows a strong healthy worker effect, as it observed in almost all occupational cohorts. Nevertheless, as it is known from other occupational studies, the healthy worker effect will get less strong with extended follow-up. The authors looked at this in more detail, and already in this young cohort, the healthy worker effect seems to disappear with longer time since first employment. Thus, it looks as if this effect would more likely be a healthy hire effect.

The healthy worker effect is also seen for cancer deaths, though a bit lower than for all causes of death. What is striking is the fact that cancer accounts for 40% of all deaths observed in the cohort, compared to approximately one third in the general French population (https://www.ined.fr/).

* Corresponding author: bgrosche@t-online.de

It is a relevant and important point that the authors looked at the healthy worker effect in much detail. Nonetheless, the most important point regarding the knowledge about health effects from exposure to ionizing radiation at low doses and low dose-rates, *i.e.* chronic exposure, is the analysis of the dose-risk relationship.

Though the statistical power is limited, the French study indicates a dose-related risk of malignancies, and the results do not contradict the assumption of a linear dose-response without a threshold, the so-called Linear-no-Threshold (LNT) hypothesis, which is one of the bases of the current radiation protection system. The other relevant finding is the fact that the results regarding the risk per unit dose, given the low doses (with a mean of 26 mSv) and the low dose-rates in the French cohort, are compatible with those found among the Japanese atomic bomb survivors. The central risk estimates do not differ, but the confidence intervals in the French cohort are large and might be compatible with a DDREF for low Linear Energy Transfer (LET) radiation of 2 as suggested by ICRP or 1.5 as suggested by the US National Research Council in its BEIR VII report.

What is missing in the paper is a discussion about attributable risk, *i.e.* which fraction of deaths from malignancies could be attributed to the fact of radiation exposure assuming the central estimate for the dose-risk relationship is true. Given the low doses the workers received this fraction should also be low, and based on the results from the INWORKS study it can be assumed that it is approximately 1%.

As said above, not only the risk of malignancies is of importance for the radiation protection system, but other diseases as well, in particular circulatory diseases. The French study showed a positive, though statistically not significant, dose-risk relationship. This is in line with results found in other studies, and it will be interesting to see the respective findings from the joint INWORKS cohorts.

It is important to mention that other risk factors certainly play a role in cancer induction and that this role is more important than the low occupational exposures to ionizing radiation. The major risk factor for lung cancer is smoking, and when no information on smoking is available, a way forward is excluding lung cancer from the analysis. When doing this for the French cohort, the central estimate for the risk per unit dose was lower than for all solid cancers combined, but still positive and thus indicating a dose-risk relationship.

It can be assumed that for some members of the study population medical exposures to ionizing radiation exceed occupational exposures. In terms of risk analysis this would be important when medical exposures were a confounder, *i.e.* medical exposures correlate with occupational exposures, *e.g.*, the higher the occupational exposure the higher the medical exposure or the opposite. It is highly unlikely that this is the case, and thus it is justified to assume that taking other sources of exposures to ionizing radiation into account would not change the overall results. The same accounts for other risk factors, which are – based on the fact that approximately 1% of all cancer deaths in the French cohort are due to occupational exposures to ionizing radiation – responsible for 99% of all cancer deaths. I cannot think of any other chemical or physical risk factor that has the potential to induce almost all kinds of malignancies, which plays a role in the working environment of nuclear workers, and which is correlated to radiation doses.

If more research on other risk factors would be needed so-called nested case-control studies would be a step forward. In such studies as much information as possible is collected from persons who suffer or died from a certain disease and from a comparable group of non-diseased persons. Such studies allow to take the role of other risk factors into account in much detail. What might be important is to also consider the genetic disposition of individuals and to look in more detail into possible gene-environment interactions. In recent years, it was shown that not only genetics, but also epigenetics play an important role in disease induction. Here, a link between epidemiological and biological research is of great importance.

Epidemiology can demonstrate a correlation between the exposure to a certain risk factor and the occurrence of a disease and – wherever possible – a dose-risk relationship; but the results from one single study do not allow to draw any final conclusion. Only when a series of independent studies demonstrate the same dose-risk relationship this relationship can be considered as true. Since the radiation exposure to a cohort like the French nuclear workers is low it is of major importance to compare the results with those from other studies and to combine data from as many well designed and well conducted studies as possible. These efforts allow to see whether or not there is still a small risk at low doses and as a consequence, whether or not there is a need to alter the current radiation protection system.

To sum up, the findings from the French cohort show the importance of adherence to the basic principles of radiation protection, *i.e.* to continuously optimize protection measures aimed at keeping exposures as low as reasonably achievable.

Taking into account the results from the French cohort (young, indications for dose-risk relationships for cancer and circulatory diseases, high proportion of malignancies among all causes of death) and having MELODI's questions regarding the robustness of the radiation protection system in mind makes a further follow-up absolutely necessary. It would be beneficial for future analyses if not only information on causes of death could be used as study endpoints, but also incidence data; and I wonder if in future studies it would be possible to use biological material from diseased or deceased workers for bridging epidemiology and biology and to integrate epidemiological, molecular and systems biological approaches.

Cite this article as: Grosche B. 2017. Comment on: Mortality in the French cohort of nuclear workers. *Radioprotection* 52(3): 211–212