

## Effects of Low-Dose Ionising Radiation

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### ABSTRACT

Recent years there have been a number of discussions about the magnitude of the health risks resulting from the exposure to low levels of ionising radiation mainly within the American Health Physics Society, the French Academy of Sciences and the Canadian Radiation Protection Association. Essentially, the debate has centred on the question of linearity, i.e., whether to assume that the probability of radiation-induced cancer at low doses is proportional to the radiation dose received, without any threshold below which there is no risk, or to assume that a threshold does exist. In view of the current status of knowledge and of the established ethical precautionary principle, the use of the LNT assumption and the current "ICRP system of protection" is justified according to the author's view *for radiation protection purposes*. It has also a good acceptance among the health physicists all over the world. However, this approach to limiting the radiation risk should be used with great care. The collective dose should not be used to predict future detriment in the form of mortality numbers at very low doses say below a few millisieverts to large segments of populations.

Recently, there have been a number of discussions about the magnitude of the health risks resulting from the exposure to low levels of ionizing radiation mainly within the American Health Physics Society, the French Academy of Sciences and the Canadian Radiation Protection Association. Essentially, the debate has centered on the question of linearity, i.e. whether to assume that the probability of radiation-induced cancer at low doses is proportional to the radiation dose received, without any threshold below which there is no risk, or to assume that a threshold does exist. The International Atomic Energy Agency (IAEA) has in its Nuclear Safety Review 1996 provided a survey of present knowledge in the field (Ref. 1).

Radiation protection standards assume that radiation doses over natural background doses cause additional health risks, notably an increase in the induction of cancers, that is proportional to the additional doses. The biological foundation for the standards includes the results of epidemiological investigations and fundamental studies on the cellular and molecular mechanisms involved in radiation damage and response. Furthermore, the results of studies with experimental animals provide further guidance.

Taking radiation such as X rays, gamma radiation and beta particles with a low energy transfer (low-LET radiation), epidemiological studies have, for some time, provided a substantial amount of direct, quantitative information on radiation risk. The main source of data is the Life Span Study of the survivors of the nuclear explosions at Hiroshima and Nagasaki in Japan 1945. These populations show a pattern of increasing mortality with an increasing dose for leukemia and most solid cancers, with a significant increase in the risk of cancer fatalities following acute doses in the range 200-500 mSv. With respect to cancer incidence, more recent data indicate a significantly increased risk at doses down to between 50 and 100 mSv (Ref. 2).

Information on cancer risks is also available from a number of epidemiological studies of patients irradiated for medical reasons. Many patients have received high doses to particular organs. Results from pooling several studies have suggested a significant increase in the risk of thyroid cancer at doses down to 100 mSv, received in childhood.

A number of studies provide information on the risk of childhood cancer following exposure of the mother's abdomen during pregnancy. Detection of an elevated cancer risk after irradiation in utero is helped by the low background cancer rates that normally exist among children. These studies suggest that irradiation in utero increases the cancer risk. The Oxford Study of Childhood Cancer showed a 40 per cent increase in childhood cancer rate in children up to 15 years of age following in utero radiation doses within the range of about 10-20 mSv (Ref. 3).

Direct information on the effects of low dose chronic irradiation is becoming available from studies of radiation workers. Some of these studies provide indications of excess cancer risks, notably for leukemia. Although the data are not strong enough to allow for quantitative risk estimates, the findings are consistent with ICRP risk estimates in Publication 60 and the assumption of a cancer risk even at low doses (Ref. 4). However,

below 10 mSv, it is not expected that epidemiological studies will alter the shape of the dose-effect curve for stochastic effects.

Experimental studies on animals cannot be used to obtain quantitative estimates of cancer risk for application to human populations because of the differences in sensitivity between species. They can, however, be used for examining the form of dose-response relationships and biological and physical factors that influence the radiation response. In a number of studies, the lowest acute dose to have a significant effect on the tumor yield falls within the range of about 100-200 mSv. This is similar to that found in studies on adult human populations. The lowest dose to result in a significant increase in risk following chronic irradiation is generally higher than that for acute exposure because of the reduced effectiveness of low dose rate radiation in inducing cancers. Animal studies, therefore, provide a broad support for the results of human epidemiological studies of the cancer risk of radiation at low to intermediate doses.

Studies at molecular, cellular, tissue and whole-animal level have made substantial contributions to our understanding of the radiation risk. In particular, they have demonstrated that the radiation damage increases with the dose and that, at least for low-LET radiation, it is often greater at high dose rates than at low dose rates, per unit of exposure. A Dose and Dose Rate Effectiveness Factor (DDREF) is commonly used to allow for the reduced effectiveness of radiation in inducing cancer in man at both low doses and low dose rates. However, only limited data are available on the effects of dose rate on the induction of tumors in human populations.

The available experimental animal data and limited human information have led ICRP to use a DDREF of 2 (Ref. 4).

The developing understanding of the process by which damage to DNA may cause cancer has increasingly influenced the understanding of epidemiological and experimental studies. Neoplasia in tissues is now seen as a complex multistage process that may be subdivided into four phases: neoplastic initiation, promotion, conversion and progression. Although these are simplifications of the overall process, they do provide a framework for interpreting the changes involved at the biochemical and cellular levels.

Neoplastic initiation encompasses the irreversible cellular damage, which provides the potential in cells for neoplastic development. There is good evidence that this initiation process results from damage to DNA leading to gene or chromosomal mutations in single cells in tissues. The critical event in relation to ionizing radiation is likely to be DNA double-strand breaks for which error-free repair is not likely at any dose.

Once the necessary gene mutation is present in a cell, further neoplastic development is believed to be highly dependent upon the cellular environment. Promotional events, influenced by growth factors in cells, dietary constituents, hormones, or other environment agents, may increase cell proliferation and may, in some instances, interfere with communication processes between cells that act to maintain cellular stability in tissues.

Conversion of these pre-neoplastic cells to a form in which they are committed to be malignant is believed to be driven by further gene mutations.

Progression of the disease, once the potential for a malignancy has been established, may depend upon further cellular changes that allow for the invasion of adjacent normal tissues, the circulation of neoplastic cells in the blood and lymphatic systems and the establishment of metastases at other sites in the body.

Radiation-induced mutations may influence all stages of the neoplastic process. Consequently, at the level of DNA damage, there is no basis for assuming that there is a dose threshold below which the risk of tumour induction is zero. For radiation protection purposes, it is appropriate to assume a progressive increase in risk with an increasing dose, with no threshold (the LNT hypothesis).

However, there is also some experimental evidence that low dose radiation may induce or activate cellular DNA repair functions, the so-called adaptive response. This effect is believed to be the result of the activation of signaling pathways. The majority of effects seen to date have essentially been short-term and act to modify the response to radiation rather than eliminate it (Ref. 5).

Although the ICRP does not employ the term precautionary principle, it does use the concept, at least implicitly (Ref. 6). In fact, the whole philosophy of protection against stochastic effects is not based on proven harm at low doses from radiation, because cancer and hereditary diseases from radiation have not yet been

demonstrated conclusively, either in humans or animals at doses below 10 mSv. Experimental, ethical and practical reasons have led the ICRP and some other international agencies (FAO, ILO, OECD/NEA, PAHO, and WHO) to adopt the LNT hypothesis for low dose ionizing radiation.

The experimental molecular biology studies are broadly consistent with the thesis that, at low doses and low dose rates, the cancer risk of ionizing radiation increases as a simple function of dose and does not have a threshold-like component. Taken together with the epidemiological information, there is no basis for arguing that low radiation doses below about 10 mSv would have no associated cancer risk at all.

In view of the current status of knowledge and of the established ethical precautionary principle, I believe that the use of the LNT assumption and the current "ICRP system of protection" is justified for radiation protection purposes. It is also largely accepted by health physicists over the world.

However, this approach to limiting the radiation risk should be used with great care. The collective dose should not be used to predict future detriment in the form of mortality numbers at very low doses, say below a few millisieverts to large segments of populations. In all cases, experts should use the best scientific information available concerning a given exposure situation. They may choose not to use the LNT assumption in their assessment. I refer, for example, to the Auger electron emitter isotopes bound to a chemical compound entering the DNA of cells and to radon in homes and workplaces.

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