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REVIEW ARTICLE

What are the risks from medical X-rays and other low dose radiation?

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ABSTRACT. The magnitude of the risks from low doses of radiation is one of the central questions in radiological protection. It is particularly relevant when discussing the justification and optimization of diagnostic medical exposures. Medical X-rays can undoubtedly confer substantial benefits in the healthcare of patients, but not without exposing them to effective doses ranging from a few microsieverts to a few tens of millisieverts. Do we have any evidence that these levels of exposure result in significant health risks to patients? The current consensus held by national and international radiological protection organizations is that, for these comparatively low doses, the most appropriate risk model is one in which the risk of radiation-induced cancer and hereditary disease is assumed to increase linearly with increasing radiation dose, with no threshold (the so-called linear no threshold (LNT) model). However, the LNT hypothesis has been challenged both by those who believe that low doses of radiation are more damaging than the hypothesis predicts and by those who believe that they are less harmful, and possibly even beneficial (often referred to as hormesis). This article reviews the evidence for and against both the LNT hypothesis and hormesis, and explains why the general scientific consensus is currently in favour of the LNT model as the most appropriate dose–response relationship for radiation protection purposes at low doses. Finally, the impact of the LNT model on the assessment of the risks from medical X-rays and how this affects the justification and optimization of such exposures is discussed.

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What evidence do we have that low or moderate doses of radiation, such as those involved in diagnostic imaging, are harmful? Some medical X-rays, for example extremity, chest and dental radiographs, involve effective doses of only a few microsieverts. However, organ doses and effective doses can be tens of millisieverts for extensive fluoroscopic or CT examinations [1] and can easily rise to 100 mSv or more when such examinations are repeated through an episode of disease or trauma. Do these levels of exposure result in significant health risks?

The most direct evidence on radiation risks comes from epidemiological studies of increased levels of cancer in exposed human populations. However, these epidemiological studies inevitably suffer from problems of insufficient statistical power at low doses. When these limitations are fully recognized, epidemiological studies are generally unable to provide clear evidence of the effects of protracted low doses of radiation of less than about 50–100 mSv. Judgements about extrapolation to lower doses are made in the light of information from cellular studies and animal experiments that provide radiobiological insights into the basic underlying mechanisms of radiation interaction with living cells and organisms. Radiobiological studies also have some significant limitations, such as the fact that the radiation-induced biological endpoints observed in cells or laboratory animals are not always reproducible and that they are not necessarily directly indicative of radiation-induced carcinogenesis in humans.

Radiation risks are reviewed by international and national organizations, such as the International Commission on Radiological Protection (ICRP), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the UK's Radiation Protection Division of the Health Protection Agency (formerly the National Radiological Protection Board, NRPB) and the National Council on Radiation Protection and Measurement (NCRP) in the USA. It is an important function of these bodies to continually assess and review publications from all over the world on the effects of exposure to ionizing radiation on human health and to reach a balanced view of the risks involved. The current consensus of these bodies is that for radiation protection purposes the most appropriate risk model at low doses is

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one in which the risk of radiation-induced cancer and hereditary disease is assumed to increase with increasing radiation dose, with no threshold. Any increment of exposure above natural background levels will produce a linear increment of risk (the so-called linear no threshold (LNT) model).

The LNT hypothesis is not regarded as immutable law, proven in every circumstance, but rather as a robust working rule. However, the LNT hypothesis has been attacked both by those who believe that low doses of radiation are more damaging than the hypothesis predicts and by those who believe that they are less harmful, and possibly even beneficial (this latter hypothesis is often referred to as hormesis). This paper reviews the evidence for and against the LNT hypothesis, taking particular note of the debates at the UK Radiological Congress in 2004 in which the case for hormesis was strongly argued [2–4]. The LNT hypothesis was, of course, also ably defended in these debates [5, 6].

Finally, we discuss the impact of the LNT model on the assessment of the risks from medical X-rays and how this affects the justification and control of medical exposures to ensure adequate protection of patients without denying them the undoubted clinical benefits that modern diagnostic radiology has to offer.

National and international assessment of the risks at low doses

Reviews of the available information on the effects of low dose radiation are undertaken at regular intervals by national and international organizations. Recent reviews include those conducted by NRPB in 1995 [7], UNSCEAR in 2000 [8] and NCRP in 2001 [9]. The evidence considered by these bodies comprises epidemiological studies of human populations, and radiobiological studies involving laboratory experiments with animals and living cells.

Epidemiological studies

Epidemiological studies of human populations provide the most direct and easily interpretable evidence. Some of the major studies are summarized in Table 1, which is based on data in the UNSCEAR 2000 Report [8]. The epidemiological studies summarized here are of two designs: cohort and case/control. A cohort study involves a large group of individuals who have been exposed to different levels of the agent of interest (here, radiation); the investigators see whether disease levels correlate with the different exposures. A case/control study on the other hand involves a group who have developed the disease being studied and a group of matched controls who did not; the investigators then retrospectively examine whether the cases had been exposed to higher levels of the agent under study than the controls.

Perhaps the most important of the epidemiological studies is the Life Span Study of the Japanese atomic bomb survivors in Hiroshima and Nagasaki. This study has high statistical power because it has followed, for over 50 years, a large cohort of survivors of all ages and both sexes, exposed to a wide range of reasonably well established doses. It is significant that important information also comes from a number of studies of medical exposures, particularly those of children or pregnant mothers, where the low natural prevalence of childhood cancers improved the ability to detect a small increase in cancer rates following paediatric or *in utero* exposures. Studies of occupationally exposed nuclear workers are also beginning to provide information [10, 11]. All of the above reviews [7–9] came to essentially the same conclusions regarding the scientific evidence for the effects of radiation at low doses. They agreed that human epidemiological data demonstrate significantly increased cancer risks from radiation doses above about 100 mGy. Moreover, all the reviews were satisfied that there was good evidence for a significant increase in childhood cancers following fetal doses of 10–20 mGy.

A recent paper by a large group of eminent epidemiologists and radiation scientists from both sides of the Atlantic [12] carefully assessed the latest data from the most recent epidemiological studies including some that were not available to the review bodies listed above. Brenner et al [12] concluded that there is now good epidemiological evidence for an increased cancer risk in humans for acute doses of X-rays down to about 10–50 mSv and down to 50–100 mSv for protracted exposures. In particular, a detailed analysis of the many studies of childhood cancer risk after fetal exposure from diagnostic X-rays [13] demonstrated that a dose of around 10 mSv to the fetus does cause a statistically significant and quantifiable increase in the risk of childhood cancer.

Extrapolation to low doses and dose rates

Despite the fact that epidemiological studies provide direct evidence of the effects of radiation exposure on human populations, there are problems in interpreting the evidence that they provide in the context of radiation protection in general. One of the most important of these problems arises because many of the studies involved populations which received relatively high radiation exposures in a relatively short time. At high doses and dose rates, there is evidence that the effects of radiation exposure are proportionately greater than at the low doses and dose rates which are usually more relevant in radiological protection. This reduction in effects at low doses and dose rates is quantified using a Dose and Dose Rate Effectiveness Factor, DDREF. Animal studies suggest a DDREF in the range 2–10 [8]. The limited human data and cellular studies support values at the lower end of this range. NRPB [7], UNSCEAR [8] and NCRP [9] all suggest a DDREF of two as a reasonable judgement to be used for cancer risks for radiological protection purposes. Consequently the quantitative estimates of the risks per unit dose derived from the epidemiological studies at high doses and high dose rates are halved in order to estimate the probabilities of radiation-induced cancer following diagnostic medical exposures.

While future epidemiological studies in humans will remain of great importance for quantitative risk assessment, it is accepted that they are unlikely to have the

Table 1. Epidemiological studies of the effects of exposures to external low-LET radiation

Study	Type of study	Follow up, years (mean)	Type of exposure	Cancers studied
External high dose rate exposures				
Exposure to atomic bombings				
Life Span Study [53]	Cohort mortality 50113 persons > 5 mSv Japan	5–45 (32.5)	Gamma and neutron radiation from nuclear explosions	various*
Life Span Study [54, 55]	Cohort incidence 37270 persons >10 mSv Japan	13–42 (24.4)	Gamma and neutron radiation from nuclear explosions	various*
Treatment of malignant disease				
Cervical cancer cohort [56]	Cohort incidence 82616 exposed women 8 countries	0–>30 (7.0)	Radiotherapy	various*
Leukaemia following cancer of the uterine corpus [57]	Case-control 218 cases 775 controls 5 countries	1–50	Radiotherapy	Leukaemia*
Lung cancer following Hodgkin's disease (international) [58]	Case-control 98 cases 259 controls 7 countries	1–>10	Radiotherapy	Lung cancer
Childhood cancers (international) [59–61]	Case-control within 9170-member cohort 6 countries	5–48 (5.5)	Adjuvant radiotherapy	Thyroid*, leukaemia, bone sarcoma*
Retinoblastoma [62]	Cohort incidence 962 exposed persons 642 unexposed persons USA	1–>60 (median 20)	Radiotherapy	Various*
Treatment of benign disease				
Childhood skin haemangioma: Stockholm [63–66]	Cohort incidence/mortality 14351 exposed persons Sweden	1–67 (39)	Radiotherapy	Thyroid*, breast*, leukaemia, all other sites
Childhood skin haemangioma: Gothenburg [67, 68]	Cohort incidence 11914 exposed persons Sweden	0–69 (31.1)	Radiotherapy	Various*
Ankylosing spondylitis [69, 70]	Cohort mortality 13914 exposed persons UK	1–57 (17.6)	X-ray therapy	Leukaemia*, other neoplasms* (except colon)
Israel tinea capitis [71–74]	Cohort incidence/mortality 10834 exposed persons Israel	26–38 (25.3)	X-ray induced epilation	Various*
New York tinea capitis [75]	Cohort incidence 2226 exposed persons USA	20–39 (25.4)	X-ray induced epilation	Various*
New York acute post-partum mastitis [76]	Cohort incidence 571 exposed women USA	20–35 (25.1)	X-ray therapy	Breast*
Rochester thymic irradiation [77–79]	Cohort incidence 2652 exposed persons USA	23–>50 (29.5)	X-ray therapy	Thyroid*, breast*, skin
Metropathia haemorrhagica [80]	Cohort mortality 2067 exposed women UK	>5–>30 (~26)	X-ray therapy	Various*
Benign gynaecological disease [81, 82]	Cohort mortality 4153 exposed women USA	0–60 (26.5)	Intrauterine ^{226}Ra	various*
Massachusetts TB fluoroscopy [79, 83]	Cohort incidence 2367 exposed women USA	0–>50 (11.4)	Multiple X-ray chest fluoroscopies	Breast*, skin
Canadian TB fluoroscopy [84, 85]	Cohort mortality 25007 exposed persons Canada	0–57 (30)	Multiple X-ray chest fluoroscopies	Lung, breast*

(*Continued*)

Table 1 Epidemiological studies of the effects of exposures to external low-LET radiation (*Cont.*)

Study	Type of study	Follow up, years (mean)	Type of exposure	Cancers studied
Low-dose or low-dose-rate exposures				
Pre-natal exposure				
Oxford Survey of Childhood Cancers [86, 87]	Case-control 14491 cases 14491 controls UK	16 (max)	Maternal X-rays during pregnancy	Leukaemia*, all solid tumours*
NE USA childhood cancers [88]	Case-control 1342 cases 14292 controls USA	20 (max)	Maternal X-rays during pregnancy	Leukaemia*, solid tumours
Occupational exposure				
Nuclear workers [10]	Cohort mortality 96673 workers Canada, UK, USA	Up to 43 (22.2)	Exposures in nuclear industry	Leukaemia, all other cancers
National Registry for Radiation Workers, UK [11]	Cohort mortality 124743 monitored workers UK	Up to 47 (16.5)	Exposures mainly in nuclear industry	Leukaemia, all other cancers

*Sites for which statistically significant excesses were reported in the exposed group (cohort studies), or for which a higher proportion of the cases were exposed to radiation (case/control studies).
After UNSCEAR (2000).

statistical power to provide direct evidence on radiation effects in humans for doses much below 10–50 mGy. This is because of the difficulty of observing a small number of additional cancers against very high background incidence rates; ever larger study populations would be required to detect ever smaller effects as doses decrease, and this is simply impractical. Moreover, epidemiology is an observational and not an experimental science. Epidemiologists make strenuous efforts to optimize study design, but it is not possible to select the exposed and reference populations on strict statistical grounds and there are likely to be residual effects of confounding factors and possible biases (*e.g.* selection bias), as well as other practical problems such as uncertainties in the dose estimates. UNSCEAR, in Annex I of its 2000 report [8], gives a discussion of the potential problems of bias and confounding, particularly in the low dose region where attempts are being made to resolve very small effects.

The low dose region, where epidemiology is unable to produce clear evidence of risk, provides a fertile area for those who wish to argue that radiation risks have been overestimated or underestimated. The former can conclude, quite correctly, that there is ''no significant evidence for an effect''; this must, however, not be confused with there being ''significant evidence for no effect''. Furthermore, as discussed later, selection effects in epidemiological studies, in particular the ''Healthy Worker Effect'' must be allowed for. Those who believe that radiation risks are greater than the LNT extrapolation suggests can point to selected studies where the play of chance has resulted in apparently elevated risks at low doses, while ignoring studies which contradict this view. It is also true that publication bias will result in studies with significant findings reaching the literature more readily than those which are inconclusive. All this assumes that studies are well designed. Badly designed epidemiological studies, for example, with serious bias in the selection of the study populations, are available in the ''grey'' literature without peer review and are cited as evidence that radiation risks are underestimated or overestimated [14].

Radiobiological studies

The national and international review bodies mentioned above also agreed that increased understanding of biological mechanisms will increasingly underpin judgements about the shape of the dose–response relationship in the low dose region. This increased understanding will come from qualitative and quantitative data from cellular and molecular studies of the biological mechanisms underlying the health effects of radiation. A comprehensive review of recent developments in this area has been undertaken by a Task Group of the International Commission on Radiological Protection [15]. Currently these studies indicate that the carcinogenic effects of radiation are caused largely by double strand breaks and complex lesions in stem cell DNA. Mechanistic modelling of radiation-induced carcinogenesis based on these radiobiological studies is still at an early stage of development. However, data on the role of gene mutations and DNA damage and repair

mechanisms are now sufficiently well established to support the thesis that the risk of radiation-induced cancer at low doses rises as a simple function of dose without threshold for most types of cancer. While some experiments suggest a curve that is concave downwards and others one that is concave upwards, depending on the biological endpoint, there are sound biophysical arguments supporting the LNT model as the most appropriate general model for cancer induction. It should be appreciated that this may not be the most conservative approach and it might result in an underestimation of some radiation-induced cancer risks and an overestimation of others. Those involved in protection should also be alert to the fact that truly low dose experiments are difficult in cellular systems. Also, it remains the case that relatively few studies address directly the effects of low doses. Until the uncertainties are resolved, all the reviews concluded that the current weight of evidence on fundamental cellular processes supports the view that an increase in risk proportionate to the radiation dose is the most scientifically defensible approximation of the low-dose response.

Could radiation stimulate beneficial adaptive responses and hormesis?

It has been suggested [16] that low or moderate doses of radiation might stimulate responses, for example to DNA repair processes, which might counteract the harmful effects of the radiation damage. At its most extreme it has been suggested that these effects are so great as to confer a net benefit, at least in certain dose ranges. The general hypothesis of radiation stimulated beneficial changes is known as the Adaptive Response and the idea of net benefit is called Hormesis. The Adaptive Response was considered by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) in its 1994 report [17] and by NCRP [9]. Explanations for an Adaptive Response tend to involve stimulation of DNA repair processes, although other mechanisms have also been suggested. However, the arguments put forward for adaptive responses and hormesis claim to have supporting evidence from epidemiological, ecological and radiobiological studies.

Epidemiological studies (the Healthy Worker Effect and unintentional bias)

Various epidemiological studies have been conducted of populations exposed to low and/or protracted doses. In its 2000 report UNSCEAR [8] has undertaken a comprehensive review of these studies. Here we will focus on studies of people exposed to radiation either in the workplace or the home, because such studies have often been quoted to support claims of hormesis.

The essence of the epidemiological method is to compare disease rates in two or more populations which differ qualitatively or quantitatively in their exposure to the agent under investigation. However, a common complicating factor is the existence of selection effects, typically factors which mean that those entering the exposed group tend to be more healthy than those in the comparison group. It is a very common finding in epidemiological studies of working populations that death rates are lower than in the general population. Consequently the Standardized Mortality Ratio (SMR) – the ratio (expressed as a percentage) of the number of deaths in the exposed group relative to the number expected based on rates for the general population – is often below 100. This is known as the Healthy Worker Effect [18, 19] and it is generally accepted that this is a reflection of the selection of the fit and healthy into employment and their retention in work. It would be a mistake to interpret low SMRs in such epidemiological studies as evidence for hormesis.

For example, recent issues of an epidemiological journal described three studies of working populations. More examples could be cited, but these are sufficient to make the point. The cohorts were, respectively, workers exposed to ethylene oxide [20], workers in the petroleum industry [21] and workers exposed to formaldehyde in the garment industry [22]. The SMRs were:

- Ethylene oxide exposed workers SMR 90 (95% CI 88–93)
- Workers in the Petroleum Industry SMR 68 (95% CI 63–73)
- Garment workers exposed to formaldehyde SMR 92 (85% CI 88–96).

All three populations thus have significantly lower mortality than the general population. Are we to conclude that exposure to ethylene oxide, to hydrocarbons and to textile fibres or dust (in the presence of formaldehyde) are all beneficial to human health? The investigators who conducted these three studies did not draw such a conclusion, nor would epidemiologists generally. It is clear that what is being seen is the effect of selection factors which mean that working populations are healthier than the population as a whole, which includes the chronically sick and unemployed. It would be perverse to try to impose a different explanation in the case of exposures to radiation.

One of the studies sometimes cited as demonstrating a beneficial effect of radiation exposure is that of mortality amongst British radiologists by Berrington et al [23]. Berrington et al observed significantly lower SMRs for radiologists employed after 1920, when occupational doses had fallen to moderately low levels, compared with other contemporary (unexposed) doctors. It has been suggested that this demonstrates a highly significant beneficial effect of radiation [24]. However, great care has to taken when attributing SMRs for different groups of people (even if they are all doctors) to a particular cause like radiation exposure, when no account can be taken of other possible confounding factors, like smoking. There is evidence in a study of mortality among doctors by Doll and Peto [25] that, during the 1950s and 1960s, GPs smoked more than other doctors and radiologists smoked less. This alone could be the cause of the lower SMRs for radiologists compared with other doctors (a large proportion of whom would be GPs), but without specific smoking habit information for the cohort of British radiologists and the control group of other doctors, it is impossible to be sure. It is because of these problems with external comparisons with other

populations that epidemiologists generally pay more regard to comparisons or trends in mortality (or disease incidence) within cohorts as evidence for radiation risks. Berrington et al focused on internal trends in mortality risks with time since entry into the radiology profession (as an indicator of cumulative dose), rather than relying solely on external comparisons of SMRs with other groups of doctors or the general population. Thus they found evidence for an increasing trend in risk of cancer mortality with time since first registration with a radiological society; for example, such that for those registered for more than 40 years there was a 41% excess risk. This was mostly due to those who registered between 1921 and 1954 when exposures were higher than in more recent years.

As well as the problem of confounding, Brenner and Hall [26, 27] point out that a similar but much larger and more detailed study of male North American radiologists [28] showed a higher SMR for the radiologists compared with other doctors. Moreover, a study in the UK of the mortality of 20 000 NHS consultants employed between 1962 and 1979 [29] showed that SMRs for radiologists and radiotherapists were not significantly different from those for all consultants taken together, either for all causes of death or for cancer. Brenner and Hall suggest that such inconsistent results are entirely to be expected when the doses are so low (a few mSv or less per year after the 1950s), since the radiation effects are likely to be below the limit of detectability for epidemiological methods. In such a situation, most studies would be expected to show no statistically significant effects but there will be occasional ones showing slightly positive or negative results. Such results provide no evidence for health effects one way or the other, they merely rule out large risks or large benefits.

A second study which has been cited [2] as supporting the hypothesis that a moderate dose rate of radiation is beneficial to health is that by Matanoski et al [30] of workers at US nuclear shipyards. This is on the basis of significantly lower SMRs seen in those workers with cumulative effective doses greater than 5 mSv than in those with lower doses, and in the latter compared with non-radiation shipyard workers. However, the authors of the study do not suggest that these results provide evidence for a beneficial effect of radiation, but instead regard selection bias as a more likely cause. Those selected to work on nuclear powered ships were given a physical examination prior to assignment and so are likely to be healthier than those working elsewhere in the shipyard. In addition, those with cumulative doses >5 mSv, mainly through being employed for longer, are further self-selected for enduring good health. Matanoski et al go on to point out that although lower SMRs are seen for all causes of death and for lung cancer, they are not seen for leukaemia where the SMR is 2.17 times higher for the radiation workers with doses >5 mSv than for those with doses <5 mSv. Surprisingly, only an abstract of this study has appeared in the peer reviewed literature [31], but in it the authors recommended an extension of the study population and the application of more powerful methods of analysis. Report 136 of the US National Council on Radiation Protection and Measurements (NCRP) [9], which provides a detailed evaluation of the LNT model, dismisses the suggestion that the nuclear shipyard worker study provides support for the beneficial effects of radiation.

There have been various other studies of nuclear industry workers, reviewed by UNSCEAR [8], where the interpretation of low dose risks is not always clear, for the reasons described previously, but which do not provide any strong support for hormesis. Indeed, such studies provide some evidence of raised leukaemia risks associated with radiation exposure [10, 11]. In the UK's National Registry for Radiation Workers [11, 32], radiation workers had lower SMRs than the general population, not because of any beneficial effect of their exposures, but simply due to the Healthy Worker Effect.

Another study that has been cited as demonstrating radiation hormesis, claimed to show very low cancer rates for residents in Taiwanese office blocks built with Co^{60} contaminated steel [33]. However, it now seems overwhelmingly likely that this study was seriously flawed and grossly underestimated the true number of cancers in the study population [34].

Ecological studies (confounding factors)

Reports of a strong negative correlation between mean natural background radiation levels and cancer mortality in different states of the USA [35] and between mean radon levels and mean lung cancer rates in different US counties [36, 37] have also been cited as further evidence for radiation hormesis [2]. However, it is well-recognized that ecological studies based on aggregated data for large geographical areas, rather than on the individual data used in case-control or cohort studies, have the potential for serious statistical problems [9]. The author of the first study [35] agreed that confounding factors such as smoking, poverty or environmental pollution could be affecting the mortality rates rather than background radiation levels [38].

However, the exceptional strength of the negative correlations between lung cancer and radon levels in the ecological studies reported by Cohen [36, 37] appears to contradict the LNT model. The fact that smoking is responsible for a large majority of lung cancers suggested that different smoking habits between the populations in the US counties might be influencing the results, but no direct data on smoking were available. Indirect evidence finally emerged when Puskin examined correlations between radon levels and a variety of cancers other than lung cancer [39]. Some of these other cancers are related to smoking and some are definitely not. Radon, of course, gives virtually all its dose to the lung so any effect of radiation, beneficial or harmful, could not be expected in cancers of any other organs. For the other smoking-related cancers, Puskin also found negative correlations with radon levels but there was no association between radon and those cancers that are not linked to smoking. He concluded that the negative correlation seen between radon levels and lung cancer in the earlier studies is largely a consequence of a negative correlation between smoking and radon levels across the US counties. Thus the results could be explained in terms of confounding by smoking without invoking any kind of beneficial effect of low level radiation exposure.

Moreover, there have been numerous more recent analyses of cohort and case-control studies of residential radon concentrations and lung cancer incidence throughout the world, where smoking habit information was also available [40]. Most of them observe an excess lung cancer risk from residential radon, though the risks may not always achieve statistical significance. However, recent pooled analyses of case-control studies of radon and lung cancer from Europe [41] and from North America [42] have much more statistical power than the individual studies, and provided unequivocal evidence of the risks of domestic exposure to radon. In particular the European pooling demonstrated a risk of exposure to radon in homes down to concentrations less than 200 Bq m^{-3} which is equivalent to an effective dose of about 5 mSv using the dose conversion convention recommended by ICRP [43].

Radiobiological studies (differences between metabolic and radiation-induced DNA damage and repair)

There is general agreement that DNA lesions are continuously being produced in the body, for example by reactive oxygen species (ROS) generated by normal oxidative metabolism. The vast majority of these lesions are repaired by normal cellular processes. The total number of these endogenous DNA lesions exceeds the number produced by normal background radiation levels by several orders of magnitude.

Proponents of hormesis suggest that acute low doses of radiation induce a temporary protective response against DNA damage that could counteract the ever-present endogenous DNA damage from the ROS. Some cellular and animal experiments suggest that this adaptive response to ionizing radiation appears to increase initially with dose but starts to decrease when the dose exceeds 100 mGy and disappears completely at higher acute doses. By combining such a non-linear model for a protective response with a linear, no threshold (LNT) model for radiation induced cancer, it can be argued that the net risk–dose relationship is more likely to exhibit a threshold than to be linear down to zero dose. It may even result in lower than spontaneous cancer incidence (*i.e.* a beneficial effect) at doses below 200 mGy [3]. However, it should be appreciated that the validity of the predictions of any mechanistic model is critically dependent on the appropriateness of the underlying assumptions.

A fundamental objection that many radiobiologists have to this model is that the DNA damage caused by ROS is believed to consist mostly of base damage and single strand breaks. Ionizing radiation induces these simple DNA lesions but it also induces double strand breaks and more complex lesions [9]. It is only these latter two types of damage that are considered to be the initiating lesions in radiation-induced carcinogenesis [15].

There are also serious doubts about the validity of some of the radiobiological studies that are quoted to provide evidence for a protective effect at low doses. In experiments on chromosome aberrations in human lymphocytes, cells pre-treated with a low (''adapting'') dose of radiation apparently acquired increased resistance to a second high (''challenging'') dose. These studies have been interpreted as giving support for adaptive responses, but serious limitations have been recognized in two of them [44, 45], leading to a subsequent publication by some of the original authors and other scientists who found it very difficult to repeat the results [46]. Another study purporting to show a decreased chromosome aberration score in human lymphocytes *in vitro* after a single acute low dose of about 10 mGy followed by a dose-dependent increase above 50 mGy [47], could also not be repeated by other laboratories. The apparent dip in aberration yield at 10 mGy was thought to be due to an erroneous and unusually high control yield at zero dose [48]. Criticism can also be directed at two other sets of experiments [49, 50], which studied thymidine kinase activity in mouse bone marrow cells and apoptosis in mouse thymocytes, respectively. Both thymidine uptake and the percentage of apoptotic cells observed after different doses of whole body irradiation could be affected by radiation-induced perturbations in the cycling characteristics of the cells as much as by any assumed adaptive response or protective effect.

The 1994 report of the UN Scientific Committee on the Effects of Atomic Radiation, UNSCEAR [17], included an annex which specifically considered evidence for adaptive responses to radiation. However, UNSCEAR decided that ''it would be premature to conclude that cellular adaptive responses could convey possible beneficial effects to the organism that would outweigh the detrimental effects of exposures to low doses of radiation''. Broadly similar conclusions were reached by NCRP [9]. In a recent draft report, an ICRP Task Group has concluded that current understanding of mechanisms and quantitative data on dose and time–dose relationships support a linear dose response at low doses with no compelling evidence for the existence of a threshold dose below which there would be no effect [15].

The impact of the LNT model on the justification and control of medical exposures

One obvious implication of the LNT model is that when the doses are very low, so are the risks. There comes a point when the risks are so low they can be considered negligible, *i.e.* they are so small in relation to the other everyday risks that surround us that they do not need to be considered in any rational decisions about lifestyle choices. There is in a sense a dose corresponding to a threshold risk that, although not zero, is safe enough for the risks to be ignored. Above this ''safe enough'' dose there will be a range of doses where the risks are very small, but are sufficient to require some justification for allowing people to be exposed to them, in terms of an overriding benefit. As the doses and the risks increase so should the concomitant benefits, for the exposures to remain justified. This principle of justification is one of the main planks of ICRP's recommendations regarding radiation protection for medical exposures. In recognition of the substantial potential health benefits to patients from medical exposures, ICRP does not place any restrictions on the levels of exposure that can be used

in diagnostic radiology. It only requires that they be justified in terms of an expected improvement in the clinical management of the patient and that all reasonable steps are taken to keep the exposures as low as possible without compromising their diagnostic efficacy (*i.e.* the exposures should be justified and optimized).

Thus although the LNT model implies that no dose is without risk, in practice there is a dose below which the risks are considered negligible and are of no consequence in decisions regarding the radiation protection of patients. Moreover, precise quantified risk estimates are not critical for the control of medical exposures according to the justification and optimization principles. It is very difficult to quantify the benefits of diagnostic X-ray examinations in any way that is comparable with the radiation risks, so an accurate quantitative weighing of benefits against risks is usually impossible. Justification generally consists of the diagnostic radiology practitioner confirming that the exposure is clinically indicated for the patient and making a mostly subjective judgement that the expected benefits will outweigh the likely radiation risks. For such subjective judgements an approximate estimate of the risks will usually be sufficient. However, in the advice given to practitioners on radiation risks, sources of bias should still be reduced to a minimum, so that the estimated risk lies centrally within the range of uncertainty, which will unavoidably become wider as the doses become lower. Use of the LNT model at the relatively low doses typical of all diagnostic X-ray exposures ($< \sim$100 mGy) and a DDREF of 2 to extrapolate from the effects seen in epidemiological studies, will provide sufficiently robust risk estimates for justification purposes.

As well as the uncertainties in the radiation risk estimates, there are also large variations in the doses delivered to individual patients by the same type of X-ray examination. The risks also depend markedly on the age and sex of the patient and might be quite different for a few individuals in the population who are genetically predisposed to cancer. Consequently, it is usually not appropriate to resolve X-ray examinations into any more than a few broad risk categories, each spanning quite a wide range of risks. This has been done in an information leaflet on the safety of X-ray examinations published by NRPB [51], where all X-ray examinations have been divided into just four risk bands each spanning a factor of ten in risk. This broad classification into negligible, minimal, very low and low risk bands is shown in Table 2 and should be sufficient for most justification purposes.

Those types of examination falling into the highest risk band (still $<$ 1 in 1000 risk of delayed cancer) are those where the potential benefits can be correspondingly high, since many of them are used in the investigation of symptoms that suggest life-threatening diseases and will easily comply with ICRP's justification requirement. It would therefore appear that beneficial medical X-ray exposures need not be unnecessarily restricted by adoption of the ICRP recommendations for patient protection [52]. At the same time, use of the LNT model at low doses provides sufficiently reliable risk estimates to ensure that patients are being adequately protected from unnecessary medical exposures that are either unjustified or not fully optimized.

Table 2. X-ray examinations divided into four broad risk bands

Risk band[a]	Risk range[b]	Typical type of X-ray examination
Negligible	$<$ 1 in a million	Radiography of chest, limbs and teeth
Minimal	1 in a million to 1 in 100000	Radiography of head, neck and joints
Very low	1 in 100000 to 1 in 10000	Radiography of spine, abdomen and pelvis
Low	1 in 10000 to 1 in 1000	CT, angiography, contrast studies of the alimentary, biliary and urinary tracts, and interventional radiology

[a]Nomenclature according to reference [89].
[b]Lifetime risk of cancer per examination for patients aged 30–60 years.

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