

What's New with Radiation-Induced Cancer and Non-Cancer Effects from an ICRP Perspective

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Radiation Risk

Initial approaches for estimating risk were not based on quantitative human or experimental data but on general observations of biological harm.

Cancer Risks

- Atomic bomb survivor data began to provide evidence for increases in leukemia and later in solid cancers in the exposed group. The outcome was the need to estimate the risks of cancer from radiation exposure at low doses (and dose rates). This had to be done by extrapolation from high dose and dose rate studies. Such extrapolations were considered to adhere to a linear non-threshold hypothesis.

Risk-Based Approaches (I)

- 1977 – ICRP adopted a more formal risk-based approach for setting standards. Based on cancer mortality, radiation risk was 1×10^{-4} per rem, and so a maximum annual dose limit for a radiation worker was recommended as 5 rem (50mSv) per year (average dose would be less than 10mSv per year)

Risk-Based Approaches (III)

1991 ICRP (*Publication 60*)

The occupational limit was set at 20mSv per year (averaged over defined periods of 5 years). The public limit was set at 1mSv per year. No revisions were considered until the recently published 2007 Recommendations.

What is the Latest on Radiation Risk and Dose-Response?

Four new reports address the issue of risk estimates in the context of the current levels and new information.

- Health Risks from Exposure to Low Levels of Ionizing Radiation – BEIR VII Phase 2 (2006)
- ICRP Report 99 – Low-Dose Extrapolation of Radiation-Related Cancer Risk (2005)
- Tubiana M et al. Dose-effect relationships and estimation of the carcinogenic effects of low doses of ionizing radiation, Institut de France Academie des Sciences (2005)
- ICRP 2007 Recommendations and Associated Annex on Biology and Epidemiology

ICRP Committee 1 (C1)

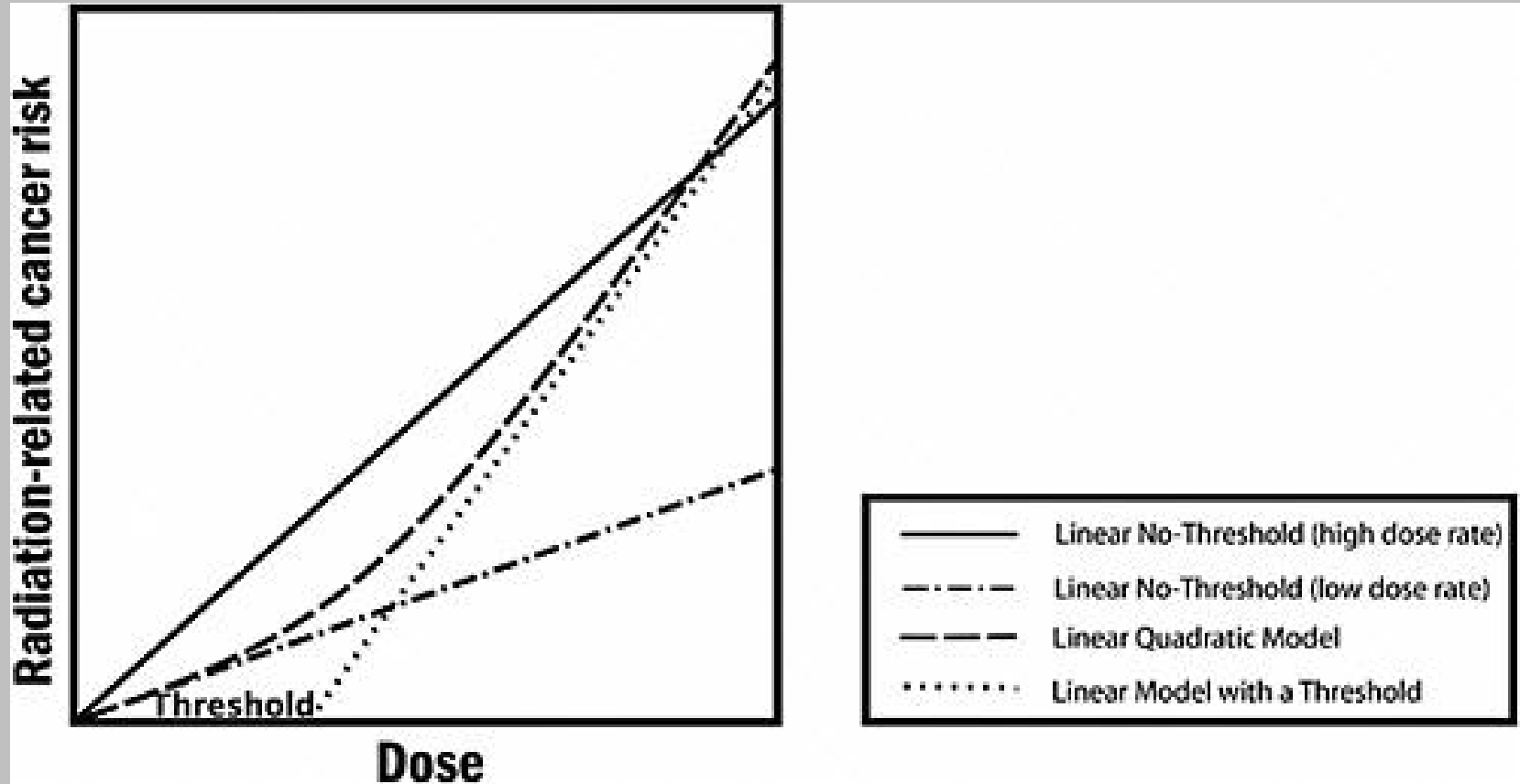
Radiation effects

- Committee 1 considers the risk of induction of cancer and heritable disease (stochastic effects) together with the underlying mechanisms of radiation action; also, the risks, severity, and mechanisms of induction of tissue/organ damage and developmental defects (tissue reactions; deterministic effects).

Committee 1 Members

RJ Preston (Chair)	O Niwa
R Ullrich (Vice-Chair)	DL Preston
JH Hendry (Secretary)	E Ron
AV Akleyev	W Ruehm
M Blettner	RE Shore
R Chakraborty	FA Stewart
W Morgan	M Tirmarch
CR Muirhead	PK Zhou

Linear Nonthreshold Model



From BEIR VII, NAS, 2006

Principal Conclusions and Recommendations

- For the induction of cancer and heritable disease at low doses/low dose rates the use of a simple proportional relationship between increments of dose and increased risk is a scientifically plausible assumption; uncertainties on this judgment are recognized

C1 Activity

- Continue to monitor the data from the LSS (atomic bomb survivors) both for cancer and deterministic effects, particularly for incidence. Consider the use of biologically-based dose-response models for assessing effects at low doses.

Principal Conclusions and Recommendations

- A dose and dose-rate effectiveness factor (DDREF) of 2 recommended in *Publication 60* should be retained for radiological protection purposes; the effect of introducing the possibility of a low-dose threshold for cancer risk is judged to be equivalent to that of an uncertain increase in the value of DDREF.

DDREF

The BEIR VII Committee took a computational approach to the estimation of DDREF that was based on a Bayesian analysis of combined dose-response data. The Committee considered the following data sets: solid cancer incidence in the LSS cohort of Japanese atomic bomb survivors; cancer and life-shortening in animals; chromosome aberrations in human somatic cells.

DDREF

The BEIR VII Committee found a believable range of DDREF values for adjusting linear risk estimates from the LSS cohort to be 1.1 – 2.3. A value of 1.5 was selected for solid tumors.

ICRP proposes to continue to recommend a value of 2 while appreciating the need to continue to consider lower values based on new research.

C1 Activity

- C1 will use a working party to develop a position on the most appropriate data set for calculating a DDREF and establish if the BEIR VII approach is valid.

Principal Conclusions and Recommendations

- New radiation detriment values and tissue weighting factors (w_T) have been proposed; the most significant changes from Publication 60 relate to breast, gonads, and the treatment of remainder tissues. The w_T changes in question are; breast (0.12 from 0.05); gonads (0.08 from 0.20; remainder tissues (0.12 from 0.05 using a new additive system).

C1 Activity

- No specific activity is proposed at this time. As always review of epidemiological studies is maintained. The tissue weighting factors will be revisited as new data become available that would appear to impact risk estimates.

Principal Conclusions and Recommendations

- Based upon cancer incidence data, detriment adjusted nominal risk coefficients for cancer are $5.5 \times 10^{-2} \text{ Sv}^{-1}$ for the whole population and $4.1 \times 10^{-2} \text{ Sv}^{-1}$ for adult workers; the respective *Publication 60* values are $6.0 \times 10^{-2} \text{ Sv}^{-1}$ and $4.8 \times 10^{-2} \text{ Sv}^{-1}$.

C1 Activity

- Continue to monitor epidemiological studies for possible impacts on the risk estimates currently used.
- In a related activity a Task Group has been established to consider the current status of risk estimates for radon and other alpha emitters.

TG on Alpha Emitters (II)

- TG was established in 2006 and is due to produce a report on assessment of recent published literature in 2 years and, if agreed, a consideration of risk estimates in 2 additional years.
- During discussions at the 2007 ICRP meeting proposed to develop a concise report by the end of 2008 on radon and lung cancer with specific emphasis on discussion of reference levels, dose conversion factors and dose limits – to be developed with significant input from C2 and C4.
- The need is to reconcile the ICRP and UNSCEAR approaches for dose conversion.

TG on Alpha Emitters (III)

- The report on recent literature on cancer and alpha emitters (excluding radon) will be developed over the following 2 years.
- Radon in homes and in the mining environment (Report1)
- Mayak workers
- Other workers exposed to internal alpha exposure (Pu or U)
- Thorotrast and radium studies.

Principal Conclusions and Recommendations

- Detriment adjusted probability coefficients for heritable disease up to the second generation are $0.2 \times 10^{-2} \text{ Sv}^{-1}$ for the whole population and $0.1 \times 10^{-2} \text{ Sv}^{-1}$ for adult workers. The respective *Publication 60* values are $1.3 \times 10^{-2} \text{ Sv}^{-1}$ and $0.8 \times 10^{-2} \text{ Sv}^{-1}$ but these relate to risks at a theoretical equilibrium and no longer seem justified.

C1 Activity

- Working party that will continue to monitor human studies of germinal effects of radiation.

Principal Conclusions and Recommendations

- Cancer risk following in utero exposure is judged to be no greater than that following exposure in early childhood.

C1 Activity

- Continue to monitor LSS (and other epidemiological studies) for any data that might change this conclusion. Currently, there are rather few data available on in utero exposures.

Principal Conclusions and Recommendations

- Knowledge of the roles of induced genomic instability, bystander cell signalling and adaptive response in the genesis of radiation-induced health effects is insufficiently well developed for radiological protection purposes; in many circumstances these cellular processes will be incorporated in epidemiological measures of risk.

C1 Activity

- Working Party will provide regular updates of research in the area of non-targeted effects.
- UNSCEAR has just completed a review of this topic
- On this general topic, C1 has a Task Group on stem cell radiobiology.

Task Group on Stem Cell Radiobiology

TG established as a Working Party in 2006 to review current state of knowledge of stem cell biology and radiobiology and potential impacts on cancer risk. Converted into a TG in 2007.

There has been an enormous increase in knowledge of stem cell biology in the past 3-5 years although not nearly as much new information on radiation effects on stem cells. The emphasis of the TG will be on stem cell radiobiology in relation to carcinogenic radiation risk. In addition, there will be an emphasis on non-targeted effects. The TG will review the topic and produce a report in 2-3 years. This effort will involve input from C2 and C4.

Principal Conclusions and Recommendations

- Genetic susceptibility to radiation-induced cancer involving strongly expressed genes is judged to be too rare to appreciably distort estimates of population risk; the potential impact of common but weakly expressing genes remains uncertain.

C1 Activity

- Working party established to review the literature on associations between single nucleotide polymorphisms (SNPs) and enhanced radiation cancer risk. Also, to review data on other susceptibilities and cancer induction. Not clear what will come from this activity in terms of risk estimates.

Principal Conclusions and Recommendations

- Dose responses for radiation-induced tissue reactions (deterministic effects) in adults and children are, in general, judged to have true dose thresholds which result in the absence of risk at low doses; further consideration of the extent of the dose threshold for cataract induction (visual impairment) is recommended.

C1 Activity

- C1 has formed a Task Group to address this issue.

TG on Tissue Reactions and Other Non-cancer Effects of Radiation

The TG will revisit the basis and the new data available for establishing revised dose limits for non-cancer effects. ICRP has not addressed this issue for about 30 years and there are some indications that there is a much greater sensitivity for some tissues (e.g., lens of the eye) that must be considered. The TG was formed in 2006 and the aim is to complete a report by 2009.

TG on Tissue Reactions (II)

Outline of Report:

Chapter 1: Introduction and General Principles

Section 2: Responses of Organs and Tissues

- **Hemopoietic System**
- **Digestive System**
- **Cardiovascular System**
- **Eye**
- **Urinary Tract**
- **Musculoskeletal System**
- **Reproductive System**
- **Respiratory System**
- **Skin**
- **Endocrine System**
- **Nervous System**

Section 3: Modifying Factors Influencing Tissue Reactions

TG on Tissue Reactions

- *Time scale for completing Report:*
 - ✓ The plan is to complete drafts by September 2008
 - ✓ Complete report by end of 2009

Principal Conclusions and Recommendations

- Dose responses for in utero radiation-induced tissue reactions, malformations and neurological effects are also judged to show dose thresholds above around 100mGy; uncertainty remains on the induction of IQ deficits but at low doses the risks are judged to be of no practical significance.

C1 Activity

- The Task Group on Tissue Reactions will consider any new data on these topic areas.

Principal Conclusions and Recommendations

- Risks of non-cancer disease at low doses remain most uncertain and no specific judgement is possible.

C1 Activity

- Epidemiological review group will provide updates on non-cancer effects. UNSCEAR has just completed a review of the topic. If significant new data become available C1 will consider forming a Task Group.

Epidemiology Reviews

- One point of note is that there are still a large number of new reports each year on cancer and non-cancer effects in radiation exposed populations and groups. In general summary, these provide support for the conclusions and judgments developed in the ICRP Recommendations

Reviews

Additional reviews are provided in the following areas:

- Tissue reactions and non-cancer effects
- Susceptible populations/Susceptibility
- Dosimetry and exposure
- Radiobiology
- Heritable effects
- **Epigenetics**
- DNA repair and non-targeted effects

Mini Reviews

- Discussion of developing relatively short update reports on issues pivotal to ICRP/C1 mandate – e.g., susceptible subpopulations, heritable effects
- New data on significant genomic variations among humans have real possibility of changing the way we view individual versus population effects

Conclusion

- C1 is addressing a number of the 2007 Recommendations because there are always new data and there remain important uncertainties.
- If you would like additional information, please contact me (preston.julian@epa.gov) or any C1 member.

TG on Cancer Risk from Alpha Emitters

- **Chair : Margot Tirmarche** , IRSN, France

Other Full Members:

- **Maria Blettner**, University of Mainz, Germany, C1 member
- **Betsy Ellis**, Oak Ridge Assoc Universities, USA
- **Natasha Shilnikova**, SUBI Mayak, Russia
- **Dominique Laurier**, IRSN, France

From C2 :

- **John Harrison**, HPA-RPD, UK
- **François Paquet**, IRSN, France