Radiation Effects

ICRP Symposium on the International System of Radiological Protection

October 24-26, 2011 – Bethesda, MD, USA

R. Julian Preston
Committee 1
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).
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>J Preston</strong> (Chair)</td>
<td><strong>D Stram</strong></td>
</tr>
<tr>
<td><strong>W Morgan</strong> (Vice-Chair)</td>
<td><strong>A Sigurdson</strong></td>
</tr>
<tr>
<td><strong>J Hendry</strong> (Secretary)</td>
<td><strong>W Ruehm</strong></td>
</tr>
<tr>
<td><strong>S Darby</strong></td>
<td><strong>T Azizova</strong></td>
</tr>
<tr>
<td><strong>R. Wakeford</strong></td>
<td><strong>F Stewart</strong></td>
</tr>
<tr>
<td><strong>R Chakraborty</strong></td>
<td><strong>M Tirmarche</strong></td>
</tr>
<tr>
<td><strong>N Nakamura</strong></td>
<td><strong>PK Zhou</strong></td>
</tr>
</tbody>
</table>
These recommendations are based upon the best available science at the time that they were drafted. As always, scientific research progresses at a rapid pace and so the ICRP is always considering the possible impact of new science on the bases for these recommendations. Committee 1 concentrates on risk estimates for somatic and germ cell effects.
Six relatively recent reports address the issue of risk estimates in the context of the current levels and new information.

- ICRP 2007 Recommendations and Associated Annex on Biology and Epidemiology
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.
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.
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.
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 is using 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.

Currently awaiting availability of a NIOSH document that has an extensive discussion of DDREF
Early and late effects of radiation in normal tissues and organs: threshold doses for tissue reactions in a radiation protection context.

Full members:

Fiona Stewart (Chair): NKI, Amsterdam; Jolyon Hendry: Manchester, UK
Alex Akleyev: Urals Research Centre of Radiation Medicine, Chelyabinsk
Martin Hauer-Jensen: Little Rock, USA; Tom MacVittie: Baltimore, USA
Norman Kleiman: Columbia University, USA

Corresponding members:

Colin Muirhead: HPA, UK; Roy Shore: RERF, Hiroshima
Kiyo Mabuchi: NCI, Bethesda; Berthe Aleman: NKI, Amsterdam
Hamish Wallace & Angela Edgar: Edinburgh, UK
John Cooper: MC
• Review tissue and health effects of radiation, with reference to implications for dose limits in radiation protection and for assessing health risks after accidental or therapeutic exposure

• Review literature on the non-cancer effects of radiation on normal tissues, both in the context of therapeutic doses received by cancer patients, and lower doses sustained during accidental or occupational exposures or during other incidents of unknown magnitude

• Update of ICRP Publication 41 (1984), including new data on cardiovascular effects and the risk of radiation-induced cataracts, and new data on modifiers of radiation responses
Tissue reactions (Deterministic effects)

- ICRP 41 (1984): *non-stochastic* injury in populations of cells
- ICRP 60 (1991): *deterministic effects*, causally determined by preceding events i.e. the dose
- ICRP 103 (2008): *tissue reactions (deterministic effects)*, subject to biological response modifiers (dose modifying factors 1.1 to 2)
- It is now clear that not all non-cancer responses are the result of cell killing and determined directly by the radiation exposure (*deterministic*) but can arise by a number of tissue responses directly and indirectly due to the radiation (*tissue reactions*).
Late Tissue Reactions

• There are some tissue reactions, particularly those involving the lens of the eye (e.g., cataracts) and the cardio and cerebrovascular systems (e.g., circulatory disease), that can occur at very long times after a radiation exposure but can still be related to this exposure.

• New data on these has led to some reconsiderations of the possible impact of tissue reactions on overall radiation risks.
The present report has produced some changes to indicated threshold doses for tissue reactions, compared to those stated in ICRP 103 (ICRP, 2008).

First, the threshold dose for radiation-induced eye cataracts is now considered to be around 0.5 Gy for both acute and fractionated exposures, in line with various recent epidemiological studies. Lower thresholds arise from:

- More sophisticated methods of scoring damage
- Longer follow up (incidence increases with latency)
- More data in low dose region

Second, circulatory disease has been recognised as an important late effect of radiation exposure, both for mortality and morbidity. An approximate threshold dose of 0.5 Gy has been proposed for acute, and fractionated/protracted exposures, although the data to support this are rather uncertain.
Third, the threshold dose values for chronic exposures depend on the exposure duration and the follow-up period after exposure. Differences between these time variables among different studies makes the values more uncertain. The values quoted for both the lens and the circulatory system assume the same incidence of injury irrespective of the acute or chronic nature of the exposure over a working life, with more than 10 years follow-up.
Fourth, much more information has become available regarding the effect of biological response modifiers in mitigating the tissue reactions, which has the effect of modifying threshold doses. These modifications are agent, tissue and schedule specific, and they are likely to have increasing impact in the future, concomitant with increases in scientific and medical knowledge.
As a general conclusion, the ICRP judges on the basis of existing evidence, that acute doses up to around 100 mGy produce no functional impairment of tissues. This includes the lens of the eye regarding the risk of cataract, with the caveat that for this tissue the use of a threshold model remains uncertain.

Hence for most applications of ICRP recommendations in occupational or public situations, the stochastic risks of induced cancer and heritable effects remain the principal risks to consider. At higher doses the risk of tissue reactions (deterministic effects) becomes increasingly important, in particular regarding accidents and medical exposures.
TG was established in 2006 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.

However, during discussions at the 2007 ICRP meeting it was proposed that a concise report be developed 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 (1993) and UNSCEAR (2000) approaches for dose conversion.
• Statement on risk estimates and detriment values and consideration of revised upper reference levels for homes and workplaces (2010)

• Report on radon risks in homes and mines (2011)

• Report on Mayak workers, other workers exposed to internal alpha exposure (Pu or U) and thorotrast and radium studies (2013)
Based on recent results from combined analyses of epidemiological studies of miners, a lifetime excess absolute risk of $5 \times 10^{-4}$ per WLM should now be used as the nominal probability coefficient for radon- and radon progeny-induced lung cancer. It is now concluded that radon and its progeny should be treated in the same way as other radionuclides within the ICRP system of protection; that is, doses from radon and radon progeny should be calculated using ICRP biokinetic and dosimetric models (not using a dose conversion convention based on epidemiological data). ICRP will provide the needed dose coefficients.
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.
• 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.
BTG established to review current state of knowledge of stem cell biology and radiobiology and potential impacts on cancer risk.

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. This effort will involve input from C2 and C4 and should be completed in 2012/13.
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.
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.
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.
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
Conclusions

- 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.