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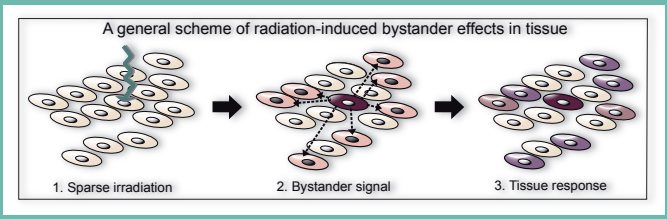
Scientific Issues and Emerging Challenges for Radiological Protection

Report of the Expert Group on the Implications of Radiological Protection Science



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NUCLEAR ENERGY AGENCY
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

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NUCLEAR ENERGY AGENCY

The OECD Nuclear Energy Agency (NEA) was established on 1st February 1958 under the name of the OEEC European Nuclear Energy Agency. It received its present designation on 20th April 1972, when Japan became its first non-European full member. NEA membership today consists of 28 OECD member countries: Australia, Austria, Belgium, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Luxembourg, Mexico, the Netherlands, Norway, Portugal, the Republic of Korea, the Slovak Republic, Spain, Sweden, Switzerland, Turkey, the United Kingdom and the United States. The Commission of the European Communities also takes part in the work of the Agency.

The mission of the NEA is:

- to assist its member countries in maintaining and further developing, through international co-operation, the scientific, technological and legal bases required for a safe, environmentally friendly and economical use of nuclear energy for peaceful purposes, as well as
- to provide authoritative assessments and to forge common understandings on key issues as input to government decisions on nuclear energy policy and to broader OECD policy analyses in areas such as energy and sustainable development.

Specific areas of competence of the NEA include safety and regulation of nuclear activities, radioactive waste management, radiological protection, nuclear science, economic and technical analyses of the nuclear fuel cycle, nuclear law and liability, and public information. The NEA Data Bank provides nuclear data and computer program services for participating countries.

In these and related tasks, the NEA works in close collaboration with the International Atomic Energy Agency in Vienna, with which it has a Co-operation Agreement, as well as with other international organisations in the nuclear field.

FOREWORD

In 1993, the CRPPH held a workshop entitled *Radiation Protection on the Threshold of the 21st Century*. This followed the preparation and issuing of ICRP Publication 60, and took place at the beginning of a period of adaptation, implementation and change. As such, the CRPPH felt that it would be useful to scan the horizon to see what types of issues could arise in the near future, and to study their possible implications. The intention of this effort was to help member country governments to be better prepared to guide their national policy and its application through this period of flux. As a result of this workshop, the CRPPH published, in 1994, a summary document entitled *Radiation Protection Today and Tomorrow: A Collective Opinion of the CRPPH*. In addition to the value that this work brought to NEA member countries, it also served as a list of issues and areas to be further studied by the CRPPH. The Collective Opinion, in effect, became the blueprint of the Committee's programme of work for almost ten years. Since its publication, the CRPPH has strived to address the topics and areas that were identified, and has published reports and studies in all of them.

Twelve years later, in 2006, radiation protection was again at a turning point. Within the NEA, a renewal process was undertaken, and a new Strategic Plan was established in 2004. As part of this effort, all the NEA standing technical committees, including the CRPPH, updated their mandates. The radiological protection community was also in the process of renewal, with new ICRP recommendations under development.

In the context of this atmosphere of renewal, the CRPPH agreed to begin to identify topics and areas that, in the mid- to long term, would or could have significant influence on radiological protection policy, regulation and application. The ultimate objective of this work is to develop a new CRPPH Collective Opinion that will provide the Committee with programmatic direction for at least the coming five to ten years. To accomplish this work, the CRPPH held a topical session during its 62nd meeting in March 2004 to develop preliminary thoughts on this subject. However, unlike the previous Collective Opinion, the CRPPH felt that specific efforts should be put towards the study of radiological protection science. This was in part due to the significance of the

Committee's earlier work on *Developments in Radiation Health Science and their Impact on Radiation Protection* (NEA, 1998), but also due to the results of the topical session. Discussions during the latter indicated that challenges in radiological protection science seem to be growing, particularly in areas such as genetic susceptibility, bystander effects, long-term effects of chronic exposures and non-cancer effects. Preliminary discussions regarding how to develop a new CRPPH Collective Opinion noted that developments in RP science could potentially have key mid- and long-term influences on radiological protection policy, regulation and application. In order to most effectively focus and orient national and international resources, the Committee agreed to establish the Expert Group on the Implications of Radiological Protection Science (EGIS) to address science at the service of mid- and long-term policy needs.

The CRPPH agreed that EGIS should in priority survey ongoing projects in radiological protection science, and discuss the possible implications that their results could provoke. This was to focus on projects expected to yield results in the short and mid-term, e.g. the coming three to ten years. In addition, the Group was to attempt to identify scientific questions that need to be answered in order to support policy decisions concerning current or emerging trends in radiological risk assessment and management.

The structure of the report is as follows:

- Part 1: Possible Scientific Issues and their Implications,
  - Challenges from Non-targeted and Delayed Effects,
  - Individual Sensitivity,
  - Epidemiology,
  - Challenges to the Concept of Dose as a Surrogate for Risk.
- Part 2: Possible Emerging Challenges in the Application of Radiological Protection,
  - Radiological Protection in Medical Exposure,
  - Radiological Protection of the Environment,
  - Health Impacts of Radiological Terrorist Attacks.
- Possible Areas of Collaborative Research.
- Policy Implications.

The CRPPH would like to note the significant contribution of Dr. Masahiro Doi to this report, and to offer its most profound condolences to his family and colleagues on their loss.

H. Métivier and T. Lazo

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EXECUTIVE SUMMARY

In 1998, a Working Group of the NEA Committee on Radiation Protection and Public Health (CRPPH) performed a survey of the state-of-the-art research in radiological protection science, and the possible implications that research results could have (NEA, 1998). This report hinted at possible changes in our understanding, just emerging at the time, but ten years more were needed before the fruits of research could more clearly point towards significant, possible implications for the system of radiological protection. Existing and ongoing research results will impact on the way the system is perceived and on the confidence society has in it. In addition, changes in society will continue to affect the expectations of stakeholders on the system.

Since 1998, our biological understanding has considerably grown. Non-targeted (indirect) effects have challenged the existing paradigm that DNA is the prime target of concern, and that the dose-effect relationship is linear. However, although non-targeted effects are today accepted as scientific fact, their significance to radiological protection remains unclear. In view of the possible significance of these effects, radiological protection experts are already trying to assess their implications.

Our current assessment of overall risks to the entire population from radiation exposure has been developed based on the study of general cohorts, such as the A-bomb survivors, which necessarily included a representative range of individual sensitivities. However, in 1998, variations in individual sensitivity to ionising radiation were noted in the NEA report as potentially having policy and regulatory significance. Since this report, significant advances have been made in molecular biology, providing us with new tools for genetic studies of possible variations in radio-sensitivity.

It is recognised that there are gaps in the knowledge base underpinning today's system of radiological protection. The science is also complex, thus of necessity the system at least in part is based on a series of assumptions and simplifications in order to be practicable for public and worker protection. Among the most important of these simplifications are the use of a linear non-threshold hypothesis (LNT) which assumes that there is risk at any dose, and of effective dose, that dose is a surrogate for risk and that all doses can be simply

added to represent the overall detriment caused by irradiation. However, science contradicts some of the assumptions and simplifications used for the current system of practicable radiation protection.

Although many scientific challenges have emerged to this simplistic, generic approach, no other overall system has been suggested other than for public exposure to radon. Here, protection is based on radon concentration in air rather than dose and the conversion of exposure to dose has been unnecessary. This does, however, provide an example of how known scientific expertise can be used in place of the generic approach when sufficient, recognised scientific knowledge exists. This also provides an example of how exceptions to the system of protection can be used when science or expediency demand. The management of risks for geologic disposal may also be facilitated by the use of an alternative approach. Similarly, the NEA proposed an approach for the radiological protection of the environment (NEA, 2003) which suggested focusing the application of the universal system at the most appropriate level for the situation at hand; local, national or international. If accepted, such an approach could reinforce the confidence of stakeholders in the system of radiological protection.

Eight years after the publication of the first NEA report on the status of radiological protection science, scientific knowledge continues to challenge the unified system of radiological protection. But before abandoning this system (or rather parts of it), the advantages and disadvantages of any change should be fully analysed. The system has in the past, and will need in the future, to be responsive to new scientific findings – without this credibility would be lost and the system would fall into disrepute. Where necessary, some deviations may be needed in those cases where the unified system for general application is not sufficiently robust or too divergent from the underlying science. This represents a natural evolution of the current system and would show the maturity of the system, capable of adjusting itself to best meet many diverse needs, while not fundamentally questioning the precautionary approach that has largely been the source of its robustness.

Notwithstanding the continuing challenges it faces, the system of dose limitation has progressively evolved to accommodate them. The system remains robust in its practical implementation and affords a high level of protection for both the public and workers. Consequent upon the underlying goals of the system of coherence and ease of implementation, many simplifying assumptions have been made that are neither rigorous nor defensible in a narrower scientific context. In general, however, a cautious approach has been followed thereby affording a higher level of protection than might rigorously be justified in these situations. This, however, is judged to be an acceptable compromise given the overwhelming desire for simplicity and coherence.

Nonetheless, such matters need to be kept under continuous review, in particular in the context of emerging scientific knowledge, to avoid undue caution which would result in the inefficient or ungrounded allocation of resources to protection.

The report discusses identified key challenges to the scientific bases and the application of the system of radiological protection; key findings from each topic are reported here.

Non-targeted effects

The current paradigm in radiobiology holds that the deposition of ionising radiation energy in the cell nucleus results in damage to DNA, which is responsible for the harmful biological effects of radiation. A range of evidence has now emerged, particularly relating to non-targeted effects, that challenges the universality of this target theory of radiation-induced effects. This therefore raises the possibility that the assumptions of the LNT hypothesis may not be appropriate in all circumstances.

A better understanding of non-targeted effects may have important consequences for health risk assessment and, consequently, for radiation protection. These non-targeted effects may influence cancer and other risks from occupational, medical and environmental exposures. In particular, they may have implications for the applicability of the LNT hypothesis in extrapolating high dose and high dose-rate radiation risk data into the low-dose and low dose-rate region. This challenge to the current paradigm includes the adequacy of the concept of dose to estimate risk, the concepts of summing doses over time, particularly of summing doses of different types of radiation (e.g. alpha, beta, gamma…) or at different dose rates, and the concept of summing doses delivered internally and externally. A new paradigm may also provide new mechanistic explanations for the development of non-cancer diseases following exposure to low doses and dose rates. Further research is required to determine if these results, typically measured in cells in culture and some animals, are generally applicable in all animals, and ultimately in humans.

Extensive new data will likely be available within the next 10 years and may have profound implications for risk assessment of ionising radiation. It remains to be determined how this would apply to low-level radiation and whether it would increase, decrease, or leave unaltered, current assessments of risk. This can impact on policy concerning human radiation protection and protection of the environment, waste management, remediation of contaminated sites, and operational concepts such as ALARA. In the medical field, the challenge will for example impact on justification and patient acceptability of diagnostic procedures, and advice to pregnant women.

Possible policy challenges

Development of a new radiation biology paradigm (combining targeted and non-targeted effects) may require changes to the current system of radiation protection, with possible implications for radiation risk assessment, the system of dose limitation and the management of radiation protection in all fields.

Individual sensitivity

Variation in individual sensitivity to ionizing radiation exposure has emerged as an important consideration in protection of patients, workers and members of the public. Identifying radiation sensitive workers and patients (through medical screening or disease diagnosis) and providing adequate protection raises important policy questions. Most evidence for enhanced radiation sensitivity has been identified in individuals who have undergone high dose radiation therapy for cancer who subsequently expressed unusually severe normal tissue reactions (i.e., ataxia telangiectasia). Evidence of increased radiation sensitivity to cancer in individuals exposed to low doses of radiation is more limited but recent research is highly suggestive of increased radiosensitivity (to breast cancer) among BRAC1/2 mutation carriers exposed to chest X-rays. While these findings need to be confirmed, the existence of radiosensitive subpopulations, exposed at low doses, should be taken seriously.

Scientific advances over the past years, particularly in molecular biology, have increased our ability to identify variations in genetic susceptibility to various toxic agents. It is based on this that it is prudent to consider the possible implications of the identification of sensitive sub-groups, based on their genetic make up, could have on radiological protection.

If the increased sensitivity of mutation carriers to low dose is confirmed by further research, it may have significant clinical consequences. More importantly, differences in individual sensitivity for exposures to low doses could pose problems in terms of the employment of radio-sensitive individuals in certain jobs, and would require some rethinking in terms of protection norms. In view of the current state of our current knowledge, some reflection on possible issues and approaches (e.g. ethical issues and questions of employment, insurance and social discrimination) would be worthwhile today.

Possible policy challenges

- Development of ability to link radiation exposure to susceptibility at an individual level would pose questions for how dose or risk controls are set and applied e.g. different restrictions for different susceptibilities or restrictions based on the most susceptible group.

- Assessment of wider social, ethical and legal implications of linking individual susceptibility to radiation through genetic testing e.g. right to require testing, right to refuse testing, risk of social discrimination or exclusion.
- New guidance or approaches to radiotherapy of patients may be required.

Epidemiology

So far, the main source of information on radiation-induced human cancer risk has come from epidemiological data on exposed populations. However, direct information is available for doses in excess of about 100 mSv, and linear extrapolation from these data (albeit with some allowance of dose and dose rate) is applied to estimate the human cancer risk at lower doses, which are more typical of exposure to the general population and radiation workers.

The shape of the dose response curve for cancer at the low doses, below 100 mSv, is a matter of constant debate. Arguments range from beneficial effects of small radiation doses (hormesis), to a threshold response, to non-threshold supra-linear responses. Therefore, there is a strong motivation to extract additional information in this dose range.

The main issues in radiation epidemiology today are:

- The estimation of risk at doses below 100 mSv.
- The effects of different types and qualities of radiation.
- The effects of different exposure patterns (e.g. chronic or acute exposure, internal or external exposure).
- The effects of modifiers, both genetic and other, of radiation risk.
- The effects of age and gender on risk.
- The consideration of non-cancer effects (i.e. cardiovascular diseases, immune response, cataracts…).
- The integration of radiobiological information in the design, analysis, interpretation of studies.
- The follow-up of current epidemiological studies over the full lifetime of the cohorts under investigation.

A key issue in “modern” radiation epidemiology today is the greater use of molecular epidemiology to better estimate the risk, particularly at low doses.

For a variety of reasons, epidemiology is currently the most informative approach for the estimation of health risks to humans from ionising radiation, and much remains to be learned. However, classical epidemiological studies are severely limited in statistical power, because of their need for large study populations for the estimation of the effects of doses below 100 mSv.

Possible policy challenges

Maintaining and/or developing long term, perhaps collaborative, epidemiological studies. Such studies require long-term financial commitment yet are a vital part of understanding harm from radiation.

Adequacy of the concept of dose to estimate risk

The current paradigm assumes that doses of all types and natures can be summed as an indicator of overall detriment. This is a key assumption in the unified system of dose limitation.

However radiation biology studies show that cellular and tissue responses differ depending upon the type of exposure or exposure situation, mainly for internal exposure at low doses and low doses rates to high LET radiations. Observations suggest that the biological processes occurring in cells in response to low doses and dose rates or to fractionated doses could be fundamentally different from those that result from exposure to high doses.

Research further indicates that the ability of radiation to produce tumours varies according to the irradiated organ, the type of tumour, the absorbed dose and the exposure pathway. Although not compromising the broad application of the system of dose limitation, these results do suggest that the use of generalised radiation weighting factors may in some cases lead to erroneous conclusions as to the consequential level of risk.

While there is broad consensus within the EGIS group on the contradictions/incompatibilities between the underlying science and the development and use of effective dose, there are divergent views on the practical implications of these contradictions for the unified system in particular with respect to chronic, internal exposures to long-lived nuclides. It is thus important to use radio-toxicology studies, adapted to different relevant scenarios, to further understand these issues so as to provide appropriate information and tools to better inform radiological protection decisions.

It is prudent to base the estimation and management of risks to the greatest extent possible on sound, scientific knowledge. In situations where the use of the unified system may be inappropriate (i.e., in terms of it not being sufficiently robust) or its application would incur costs that are grossly disproportionate with the actual reduction in risk, alternative more specific approaches will need to be adopted. The skill of the radiation protection profession will be to identify such conditions and respond in a timely manner. For such situations, stakeholder concerns (e.g. governmental, scientific, affected

populations) could be addressed through relevant toxicological studies (either completed or newly proposed) in order to develop case-specific protection solutions. Such an approach is fully consistent with the principles underlying the system of dose limitation.

Possible policy challenges

A consensus should be sought on those situations where the use of the unified system may be inappropriate (i.e., in terms of it not being sufficiently robust) or its application would incur costs that are grossly disproportionate with the actual reduction in risk; in such cases, alternative more specific approaches will need to be developed and adopted.

Radiation protection in medical exposure

Medical exposures represent a clear benefit for the patients when these exposures are justified and optimised. However, medical exposures represent the largest man-made dose and they are increasing rapidly. Individual doses can be high from some procedures, and stochastic risks can be particularly relevant in children and young adults. Patient doses need to be known by doctors (especially for the new techniques) to help in the justification and optimisation of diagnoses and treatment and to give the appropriate information to the patients. Industry should collaborate with researchers and practitioners in this effort.

New regulations and standards for medical exposures are being published and scientific data should be available to support their needs and applicability. Development of “referral criteria for imaging” and “methodology to optimise medical procedures with ionising radiation” guides for new technology will be necessary. New technology in medicine requires periodic re-evaluation of diagnostic reference levels (which indicate typical dose levels for certain medical procedures).

The aspects related to radiation doses (to the patients and to the staff) should be a substantial part of the clinical audit process for medical exposures. Industry should be advised of the need to implement dosimetric tools and electronic archives of the data in new equipment for radiology. Physicians and practitioners should be assisted in understanding the risks associated with medical exposures and in optimising the use of the new technology.

Multidisciplinary collaboration between the medical exposures and other areas of activity in radiation protection (e.g. dosimetry, epidemiology, radiobiology, radiation pathology, etc) should be promoted to take advantage of medical data for epidemiological studies.

Possible policy challenges

- Studies suggest increasing exposures of both patients and medical workers and imply the need to ensure that exposures are justified and optimised e.g. through better dose information via equipment that measures and displays patient dose as well as through the development of new optimisation approaches, etc.
- Sharing of knowledge between medical and other types of exposure should be encouraged, so all can benefit from each others' experiences.

Radiological protection of the environment

Contrary to the previous topics, it is not the results of scientific research that have driven interest in RP policy, regulation and application in the radiological protection of the environment, but rather a political, societal demand for better scientific understanding of possible radiological harm to non-human species and their related ecosystems, in particular from chronic exposure.

There is international consensus on the need to protect the environment. However, given the complexity of the situation (e.g. large variations in natural background, relationship between individuals and ecosystems, etc.) the research necessary to respond to these questions must be well targeted, guided by social answers to "framing questions" (e.g. What is pollution? What is the aim of protection? What is harm? What "gap" should be filled? etc.), and aimed towards concrete results to assist policy makers, regulators and practitioners.

To date, there have been no observed harmful effects to the health of ecosystems that can be attributed to radiation exposure in situations that are in compliance with the protection system for humans. The data published to date have led to the finding that no significant harmful effects that could put whole species at risk or promote irreversible imbalances between species have been observed for radiation exposure below 1 mGy per day. However, closer examination shows that these data mostly relate to external and acute exposure to gamma irradiation with observations made at the level of individuals, a context that is at variance with chronic exposure situations.

Possible policy challenges

Ensuring that (current) tools and technical approaches developed for protecting the environment from adverse effects of ionising radiation are suitably compatible with broader principles and conceptual approaches in other areas of environmental protection.

Health impacts of malevolent actions

It is widely agreed that radiological terrorist acts could occur.

There is a general consensus that while most dispersion scenarios would not have significant public health effects, they would cause significant public concern. More significant public health effects could, however, result from the use of high-activity sources hidden in public places.

In preparing to address such events, it is important to have effective detection systems ready for use and to be prepared for scientific training of early response teams (e.g. firemen, paramedics, and medical doctors), psychological support for victims and advice to pregnant women.

It is also necessary to develop rapid triage techniques for dose estimation, and a "standard" approach to post-accident health and epidemiological studies. It will also be important to use the relevant stakeholder-involvement lessons from previous experience to develop an effective rehabilitation strategy.

Possible policy challenges

- Maintaining public confidence in the event of an accident or attack and in any post-incident rehabilitation strategy.
- Developing a capacity for rapidly giving information to the public; this capacity will also need to be able to address concerns of a high number of people with low or no exposure.
- Developing a well-organised, effective medical response system, capable not only of handling direct medical effects but instilling confidence in, and supporting, the community.

Suggested new areas of international research and collaboration

Given important interfaces with other disciplines (for example, in medicine, the environment and malevolent acts) and shrinking radiological research communities, collaboration will be a key theme for radiological protection and its supporting science. Where appropriate, suitable collaborating organisations are suggested. However, for these initiatives to be truly successful, a useful starting point could be doing "catalogue" existing RP research resources (i.e. animal study facilities, radio-biology / toxicology laboratories).

In view of the conclusions of this report, suggested collaboration is proposed in three forms: meetings, fora and discussions; establishment of information and experience exchange networks; and specific collaborative research projects.

Meetings/Fora/Discussions

1. International workshop on “non-targeted effects: Unified response or not - consequences for the current paradigm”. With collaboration of EC and US DOE.
2. Individual sensitivity and risk in modern society: technical, ethical, legal issues.
   - Possible implications of individual sensitivity.
   - Individual risk assessment.
   - RP, chemical, biological, medical.
   - Genetic screening.
3. Forum on Management of risks from radon isotopes.
   - Discussion of national approaches.
   - Discussion of how radon and smoking risks can be addressed.
   - Include WHO programme.
4. Forum on Sustainability of radioecology and radiological protection of the environment (with IUR).
   - RP and chemical aspects.
   - Waste issues (long-term).
   - Establish an International Observatory of Effects (see next section).
5. Forum on the limitations of the use of RP protection quantities for risk management involving ICRU and ICRP.
   - Use of quantities and units in radiological protection.
   - Dose response variations for internal exposures.

Establishment of information and experience exchange networks

1. An “ISOE like system” for medical exposure. Collaboration with WHO, UNSCEAR, EC, Industry, IAEA.
   - Definition phase to begin.
   - Patient and occupational exposures.
   - Access to data/patient confidentiality.

2. An “ISOE like system” for NORM exposure? Collaboration with ILO, UNSCEAR, EC work, Industry, IAEA.

3. International data registry and assessment for environmental radiological protection, an international “Observatory” (with IUR).
   - Centralised data registry from contaminated areas, from areas of high background, from experimental investigations, also other contaminants.

- Network of experimental facilities.
- Network of existing research and experimental programmes (bio-geo-chemical cycles).
- Network for database collection and assessment of environmental measurement data around nuclear installations.
- Assess current data collection.
- Identify additional measurements that could be added to better characterise environmental protection (as opposed to human protection).

4. Network for emergency-response for biological dosimetry in case of terrorist acts.

5. Network to integrate capabilities for collaborative animal research.
   - Standard approach to ethical approval of experiments.
   - Identification and co-ordination of capabilities.

6. Consolidation of the French-German initiative for a data bank on Chernobyl, for health effects, radio-ecology (and status of the sarcophagus), in collaboration with epidemiology and environmental protection programmes.
   - Discuss data collection and access rules and processes.
   - Tissue banks (follow biological example).
   - Data.

Collaborative research

1. Epidemiology of chronically exposed people, internal and external. Consolidation of EC programmes by co-operation with US and Japan (and others).

2. A specific sub-case of particular importance is that of paediatric exposures. These doses should be registered and made available for epidemiological studies, in that this population is at particularly elevated risk.

3. Research of links (or not) between molecular or cell modifications and observed pathologies (animal experiments and epidemiology).

4. The Ultra-Low Level Radiation Biology Laboratory, proposed by the US DOE, should be opened for international collaboration, including scientific and technical oversight, collaborative funding, and collaborative research.

5. Sound scientific evaluation of non cancer diseases by new mechanistic explanations.

6. Common definition of an international programme of radiotoxicology linked to internal exposure:
   - Chronic exposure vs. acute exposure,
   - Biokinetics,
   - Late-effects,
   - Wider exploitation and exploration of the EC data bank (in collaboration with EC).

INTRODUCTION

In 1998, the OECD Nuclear Energy Agency published a report titled *Developments in Radiation Health Science and their Impact on Radiation Protection*, summarising the state of the art in radiological protection science. The focus of this report was on what, at that time, was known, and what was not known in the area of radiological protection science. Now, nine years later, the NEA Committee on Radiation Protection and Public Health has revisited this issue, focusing more on the nature of current research and on the possible implications that this could have on radiological protection policy, regulation and application.

Since the 1998 report, many studies have been completed, tending to confirm the trends or tendencies of previous research. As such, the unified nature of the current system of radiological protection continues to be challenged.

To study this challenge in more detail, this report is divided into two sections. The first examines scientific issues, including non-targeted effects, individual sensitivity, epidemiological results, and adaptive response. These provide a basis for assessing the degree to which the current system is under scientific challenge.

The second section examines the key areas where radiological protection is applied, and which, due to technological evolution or socio-political changes, may require new thinking in order to optimise protection. The most important of these are medical exposures, the radiological protection of the environment, and protection against malevolent uses of radiation or radioactive material.

PART 1
SCIENTIFIC ISSUES AND THEIR IMPLICATIONS

Non-targeted and delayed effects

Individual sensitivity

Epidemiology

Other challenges to the unified system of dose limitation

NON-TARGETED AND DELAYED EFFECTS

1. What is the issue?

The current paradigm in radiobiology holds that the deposition of ionising radiation energy in the cell nucleus results in damage to DNA, which is responsible for the harmful biological effects of radiation. The radiation-induced DNA changes are believed to become irreversible by the first cell division following the radiation exposure, and cancer risks are considered to be the consequence of a clonal proliferation of cells carrying the resulting mutations in specific genes. Since the initial damage induced in DNA has been shown to be directly proportional to dose, risk is also be considered to be directly proportional to dose (of a given radiation type). Risk from multiple exposures is considered to be additive, and risk from high and low LET radiation exposure is assumed to be qualitatively the same, albeit taking due account of their differing radiobiological effectiveness. These assumptions are incorporated into the Linear-No-Threshold (LNT) hypothesis that is used in all radiation protection practices.

A range of evidence has now emerged that challenges the universality of this target theory of radiation-induced effects, and therefore raises the possibility that the assumptions of the LNT hypothesis may not be appropriate in all circumstances. These effects have been termed “non-(DNA)-targeted” and include radiation-induced bystander effects, genomic instability, adaptive response, low-dose hyper-radiosensitivity, abscopal (out-of-field) effects, premature differentiation of cells, induction of clastogenic factors, delayed reproductive death and induction or suppression of gene activity by radiation. Two important features of non-targeted effects are that they do not require a direct radiation dose to the cell nucleus and that they are particularly significant at low doses. This new evidence suggests a need for a *new paradigm* in radiation biology. The new paradigm should cover both the classical (targeted) and the non-targeted effects. New aspects include the role of cellular communication and tissue-level responses.

A better understanding of non-targeted effects may have important consequences for health risk assessment and, consequently, for radiation

protection. These non-targeted effects may influence cancer and other risks from occupational, medical and environmental exposures. In particular, they may have implications for the applicability of the LNT model in extrapolating high dose radiation risk data into the low-dose region. This challenge to the current paradigm includes the adequacy of the concept of dose to estimate risk, the concepts of summing doses of different LET or dose rate and the concept of summing doses delivered internally and externally. The new paradigm may also provide new mechanistic explanations for the development of non-cancer diseases. Further research is required to determine if these results, typically measured in cells in culture, are generally applicable in whole animals, and ultimately in humans.

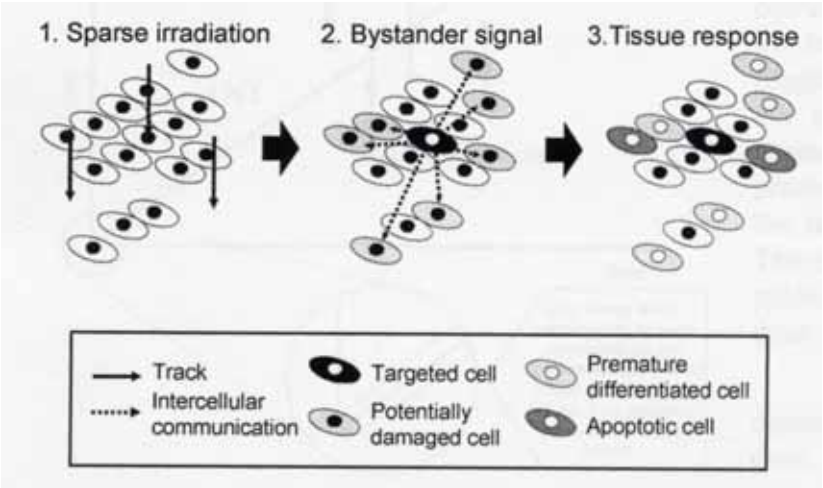
2. Scientific evidence

2.1 Bystander effects

Radiation-induced bystander effects are generally demonstrated very rapidly after irradiation in cells that were not directly hit by radiation but were nearby. The bystander signal can be transferred via the culture medium ("clastogenic factors") or by direct cell-to-cell communication (inhibition of cell communication prevents some bystander effects). Bystander effects have been reported in a variety of cellular systems. Early bystander responses include increases or decreases of damage-inducible and stress-related proteins and increases or decreases in reactive oxygen species. At more delayed time points, effects such as cell death or cell proliferation, cell differentiation, induction of mutations, chromosomal instability and radioadaptation are observed. Bystander effects are the most likely drivers for the more delayed non-targeted effects such as genomic instability and adaptive response.

Bystander effects are not new. Starting from the 1960s, there is extensive literature on clastogenic factors and other "compounds" that stimulate or modify responses in cells that were not damaged. Modern microbeam exposure systems capable of exposing single cells or even defined cellular organelles to charged particles or ultra soft X-rays have facilitated research on bystander effects. Such irradiation facilities also make it possible to target sub-cellular structures, such as nucleus, cytoplasm or mitochondria with either a single or an exact number of alpha particles. The dose-effect relationship for both protective and harmful bystander effects invariably shows a plateau below one Gray. Harmful effects appear to be determined by dose per hit cell, rather than number of cells hit, and high and low LET radiations appear to be equally effective.

Figure 1. **A general scheme of radiation-induced bystander effects in tissue**

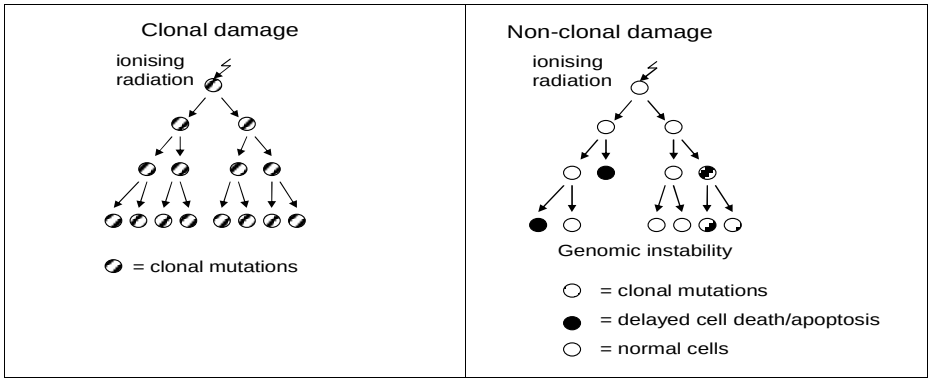


2.2 Genomic instability

Radiation-induced genomic instability means that the progeny of irradiated cells show, for many generations, an increasing occurrence and accumulation of new mutations and/or new chromosomal aberrations or other genomic damage. Affected progeny also demonstrate high levels of lethal mutation, which may be measured as delayed reproductive cell death and/or delayed apoptosis. These effects also occur in cells that were not exposed to radiation. Genomic instability occurs in the progeny of irradiated cells at a frequency that is several orders of magnitude higher than would be expected for a mutation of a specific gene. Therefore a mutation in, for example, a repair gene is not a likely explanation, and the induction of genomic instability is more likely a second order event. Genomic instability is induced both by high-LET and low-LET radiation, but not all cell lines show this effect. The dose-effect relationship for genomic instability invariably shows a plateau but is a function of time at which effects are scored. High LET is more effective than low LET, but LET also influences the temporal pattern of expression.

Animal studies indicate that some mouse strains are genetically more susceptible to genomic instability induction than others. These strains also show a higher susceptibility to radiation-induced malignancy. Individual sensitivity seems to play a role both in genomic instability and bystander effects. Genotypes that have a less effective apoptotic response seem to be more predisposed to the development of malignancy. The human genetic basis for this variability requires further research, but in animals, Tp53 gene function and its response to radiation exposure are known to play a major role in some of these effects.

Figure 2. **Diagrammatic representation of genomic instability in comparison to the clonal mechanism**



Animal experiments have shown that the phenomenon of radiation-induced genomic instability is not restricted to somatic cells but may also manifested in the germ line, resulting in elevated somatic and germline mutation rates in the offspring of exposed parents. The observed transgenerational increases in cancer predisposition and mutation rates are attributed to some yet unknown signal transmitted via a single sperm from irradiated males to their offspring. The mechanism appears to be epigenetic.

2.3 Adaptive response

The term adaptive response refers to a biological response whereby the exposure of cells or animals to a low dose of radiation induces mechanisms that protect the cell or animal against the detrimental effects of other events or agents, including spontaneous events or subsequent radiation exposure. Low doses (typically 10-100 mGy) have been shown to increase cellular DNA double-strand break repair capacity, reduce the risk of cell death, reduce radiation or chemically-induced chromosomal aberrations and mutations, and reduce spontaneous or radiation-induced malignant transformation *in vitro*. Elevated DNA repair capacity after low dose exposure is a response that has been tightly conserved throughout evolution, appearing in single-cell eukaryotes, simple eukaryotes, insects, plants, amphibians, and mammals including human cells, suggesting that it is a basic response critical to life.

Adaptive response occurs in situations where the dose is too low for all cells to be hit, but the protective effect is amplified by induction in the bystander cells. For low LET radiation, the first ionisation track through the cell (a dose of about 1 mGy to the cell) appears to produce the maximum increase in DNA repair capacity, and further tracks, if delivered at low dose rate, neither increase nor decrease that maximum response. For malignant transformation in human and

rodent cells, the protective effect of low doses appears dose independent for all doses up to about 100 mGy, when given at low dose rate. Above about 300 mGy, these protective effects give way to an increased risk of malignant transformation, suggesting detrimental bystander effects outweigh protective effects at this point. Like bystander effects, the (unknown) signal(s) for adaptation can be transmitted through the medium that surrounds the cells. In human cells, there was no difference between gamma rays and tritium beta particles for the induction of the adaptive response, and low doses of low LET radiation protect against the detrimental effects, including detrimental bystander effects of high LET exposure. At least some types of high LET radiation can also induce the adaptive response in mammalian cells but, in a lower eukaryote (yeast), where, unlike in mammalian cells the magnitude of the induction is proportional to dose, the efficiency per unit dose of neutrons was lower than with gamma radiation.

For low doses to induce an adaptive response, cells or animals require a functional copy of the Tp53 gene, responsible for the control of several processes critical to the risk of carcinogenesis and teratogenesis. In animals with full Tp53 function, and in cancer-prone animals with partial Tp53 function a single low, whole body dose of low LET radiation increased cancer latency and restored a portion of the life that would have been lost due to either spontaneous or radiation-induced cancer in the absence of the low dose. An increase in tumour latency but not frequency, suggests that adaptation to radiation *in vivo* acts primarily by slowing the process of genomic instability. In genetically normal foetal mice, a prior low dose also reduced the extent of birth defects resulting from a subsequent large dose. In genetically normal adult-male mice, a low dose prior to a high dose protected the offspring of the mice from heritable mutations produced by the large dose. Low doses delivered to foetal mice earlier in gestation have been shown to rescue from death foetuses that would otherwise die due to radiation damage. However, these rescued mice show a higher frequency of mental defects.

In Tp53 normal mice, protective effects against radiation-induced cancer occur up to at least 100 mGy. In the cancer prone mice protective effects give way to increased risk between about 10 and 100 mGy. However, different tissues appear to have different thresholds at which protection turns to detriment, indicating that radiation sensitivity is not constant, but varies from zero to positive values as dose increases; this has implications for the derivation and use of tissue weighting factors (W_T) in the unified system of dose limitation. The results suggest that protective adaptive responses may predominate at typical public and occupational exposure levels, but that at doses around 100 mGy detrimental bystander effects may overcome the protection. High doses at high dose rates do not induce the protective response, although relatively high total doses received at low dose rates may be effective.

2.4 Combined effects (radiation and other agents)

Induction of genomic instability or bystander effects is not unique to ionising radiation since exposure to UVA, genotoxic chemicals or heavy metals can also cause such effects. Therefore, the non-targeted effects may represent a more universal damage/external stress response system. Ionising radiation is, however, a good model for studying delayed effects, because no extra substance is left in the cells after external irradiation. In the case of chemicals, interpretation of delayed effects is more complicated because of the possibility that traces of chemical may remain in the cells and cause effects in subsequent cell generations.

2.5 Non-cancer effects

Since non-targeted cellular responses to radiation are the products of cell signalling which result in the modulation of a variety of genes, including those that produce free radical scavengers and enzymes to repair DNA damage, it is expected that such exposures could impact on the risk of non-cancer effects as well as on the risk of cancer. Research to date indicates that both of these cellular responses show an "all or nothing" type of response to dose, suggesting that the first track of radiation produces the maximum gene response. If this is so, then the radiation protection concept of an effect that is proportional to dose is inaccurate at low doses, and this difficulty may apply equally to non-cancer and cancer endpoints.

Recent publications indicate that individuals who were exposed to radiation in the nuclear bombing of Hiroshima and Nagasaki may be at higher risk of cardiovascular diseases, as well as to other non-malignant health conditions. Published results on the influence of radiation on cardiovascular disease in animals are sparse and, in general, only some of the laboratory animal models are good models for human cardiovascular diseases. However, a review of the occurrence of cardiac and vascular diseases in life-span experiments in which animals were exposed to relatively low doses of ionising radiation indicates that such exposure did not increase the risk of cardiovascular disease. On the contrary, in the pooled data, risk reduction appears statistically strong. In a recent study, exposure at either low or high dose rate reduced the severity but not the frequency of aortic lesions in animals genetically susceptible to coronary disease. It will be important to understand the reasons for these apparently opposite results in animals.

There is a considerable amount of research data that addresses the influence of low doses on longevity in mammals. A review of radiation effects in laboratory mammals exposed to low-dose radiation clearly indicated a trend of increasing longevity with exposure to low doses, especially prevalent at doses below 250 mGy. The type of ionising radiation used to irradiate the animals did not significantly affect this increase.

2.6 Relationship between biological effects and health effects

An adverse biological effect at the cellular level does not necessarily mean that there would be adverse health consequences.

A key question is the evolutionary origin and meaning of the non-targeted effects: why are the cells exchanging messages on the radiation exposure and what can be gained by the tissue-level responses? Non-targeted effects have been described not only in vertebrates, like mammals and fish, but also in invertebrates, like crustaceans. The evolutionary conservation would suggest that these effects are basically protective and that they would enhance the survival of the individual. However, this rescue of the individual might well carry a price: survival with damage. The very first direct in vivo demonstration of bystander response showed that soluble factors from non-irradiated bone marrow cells were capable of rescuing lethally irradiated mice by protecting endogenous haematopoietic stem cells. This means that signalling takes place not only from irradiated to the non-irradiated cells, but also back to the hit cells.

The balance between the harmful and protective effects may well be the key in understanding the in vivo health consequences of the non-targeted effects. The interrelationship between bystander response, genomic instability and adaptive response needs to be determined. At the cellular level, it has been recently shown that all three effects may be observed at time points distant from the initial radiation exposure. These results extend the adaptive response to include environmentally relevant exposure situations, i.e. where the challenging radiation dose or other stress may be far removed from an initial dose, and may affect cells that were not themselves originally irradiated.

3. Possible research results

The cancer risk at low doses typical of current public and occupational exposures will probably never be fully elucidated by epidemiological studies, as this would require very large populations and accurate individual dosimetry. Currently, the lowest dose of X- or gamma-radiation for which good epidemiological evidence exists of increased cancer risk in adult humans is about 50-100 mSv. Human data suggests that cancer risk in children may be elevated at exposures significantly lower than for adults, and this appears particularly true for *in utero* exposures. Biological modelling of radiation carcinogenesis may offer a tool to study risk in the low dose region. The input data should contain not only the classical direct radiation effects but also non-targeted effects, which may be important modifiers of risk at the low dose region. It remains to be determined how this would apply to low-level radiation and whether it would increase, decrease, or leave unaltered, current assessments of risk.

Genomic instability and bystander effects are observed after very low tissue doses. Using a microbeam exposure system, it has been shown that a single alpha particle is able to induce chromosomal instability in the progeny of cultured human cells. In fact, the dose response data indicate that the relative contribution of these indirect effects as compared to damage caused by direct hits may well be more pronounced in the low dose region, thus giving some support for a potential supralinear response at the low-dose region. Such supralinear responses are not observed in animal studies, which rather indicate an apparent threshold.

The genomic instability and bystander endpoints are both transmissible (mutational) and non-transmissible (lethal). The balance of these in different cellular systems may lead either to an increased or decreased risk. Some scientists indeed argue that these non-targeted radiation effects are in fact part of the adaptive response to ionising radiation and therefore protective. More research is needed on the delayed damage response systems, such as adaptive response and premature differentiation. An increase in cancer risk can be argued by amplified genomic damage, genomic instability and also by increased proliferation of cells due to cell killing. A decrease in cancer risk can be argued by cell killing removing damaged cells and adaptive response and increased differentiation of cells, which may protect. During embryonic and foetal development, however, any changes altering the normal pattern of cell proliferation, cell differentiation and cell migration are likely to be harmful.

New research to address the problem of non-cancer-effects is highly desirable. At the molecular level, future research on gene activation analysis may provide insight into the biological processes being influenced by high and low LET exposure. At the whole animal level, comparative and combined effects of high and low LET radiation on cardiovascular responses, particularly at low doses in susceptible animals, would also be informative.

4. Possible policy challenges

Low-dose cancer risk

The main source of information on radiation-induced human cancer risk comes from epidemiological data on exposed populations. Direct information is available only at relatively large doses, and linear extrapolation from this data is applied at lower doses, which are more relevant in terms of exposure to the general population and radiation workers. The shape of the dose response curve for cancer at low doses is a matter of vigorous debate. Arguments range from a beneficial effect of small radiation doses (hormesis) to a threshold type response and to non-threshold supralinear responses (implying that small doses are more

hazardous than previously assumed). However, if the underlying biological responses to high versus low doses, or high versus low dose rates, or high versus low LET exposures are each fundamentally different from each other, it will be difficult to simply add such doses to estimate risk. Understanding the contributions of genomic instability, bystander effects and adaptive responses to overall risk under these various situations provides new insight into the risk assessment of low dose exposure. While the evidence is not yet conclusive, current and further research on non-targeted effects appears likely to lead to the formulation of a new radiation biology paradigm combining both the classical (targeted or direct) and the non-targeted (indirect) radiation effects. Radiation protection systems may have to be modified to accommodate both individual responses and exposure under different situations of dose, dose rate and LET.

Extensive new data will likely be available within the next 10 years and may have profound implications for risk assessment of ionising radiation. It remains to be determined how this would apply to low-level radiation and whether it would increase, decrease, or leave unaltered, current assessments of risk. This can impact on policy concerning human radiation protection and protection of the environment, waste management policy, remediation of contaminated sites, and operational concepts such as ALARA. In the medical field, the challenge will have an impact on patient acceptability of diagnostic procedures and advice to pregnant women.

Non cancer-effects

Non-targeted effects may provide a potential mechanistic explanation for the development of non-cancer diseases. Increased oxidative stress seems to be a long-term characteristic of the progeny of irradiated cells and animal studies have suggested that inflammatory-type responses are involved. The well-documented increases in malignancy in the Japanese A-bomb survivors have recently been supplemented by reports of increases in cardiovascular, digestive and respiratory system diseases. Such effects are very difficult to explain on the basis of the conventional target theory, but could be linked to oxidative stress and inflammatory-type of responses.

The contrast between the protective effects of radiation observed in experimental animals and the detrimental non-cancer effects in persons exposed to radiation from nuclear bombing suggests that some other variable may be important. If the data from the survivors of the Japanese bombing is to be used to form the basis for estimating non-cancer risks from radiation, then it will also be important to be sure that that data actually reflects the risk from current public and occupational exposures. The incidence of radiation-induced non-cancer diseases among the A-bomb survivors is less than that for cancer.

However, even a small excess risk could mean a significant public health impact as these diseases, especially cardiovascular diseases, are so common in the population. The number of cases could well outnumber the cases of leukaemia, the signature disease for ionising radiation.

Possible implications include:

- The conceptual basis of the present system may be undermined.
- Effective dose and the weighting factors underpinning its derivation may need revision.
- The apparent coherence of the present system and its ease of implementation (consequent upon the additivity of dose) may be lost.
- Dose limits and constraints (and standards or reference levels more generally), to the extent that they are based on risk considerations, may need to be revised.
- The relevance of dose and the target at risk may need to be re-examined.
- The belief that the LNT assumption is cautious and embodies the "precautionary principle" could prove unfounded and the claimed robustness of the present system undermined – alternatively, this assumption could be shown to be grossly over-cautious, unduly constraining the use of radiation in industry and medicine and wastefully allocating scarce resources to protection.

The levels of dose at which uses of radiation in industry and medicine were judged to be justified and optimised may change

The current evidence is not sufficient to justify a radical departure from the current system of dose limitation. However, it would be prudent for the policy community to begin to explore the possible implications of the emerging science now.

The scientific evidence challenging the current system is accumulating and it would be remiss were it to be met with a policy vacuum. As a minimum, the rudiments and practical implications of a system or systems of dose limitation, better able to accommodate a non-linear dose-risk relationship, should be investigated and contingency arrangements developed.

5. Possible approaches to improve the situation

In general, there is need to investigate the link between non-targeted effects and various radiation-induced health effects, like cancer, hereditary effects, reproductive/developmental effects and non-cancer diseases. Furthermore, it is important to explore the mechanisms involved in the non-targeted effects of

ionising radiation, to determine the dose-effect relationships of non-targeted effects in space and time, to address individual susceptibility and to determine whether non-targeted effects are protective or harmful depending on the level of radiation. The linkage between bystander response, adaptive response and genomic instability needs to be studied. In the longer term, a conceptual framework for the generation of a new radiobiological paradigm, that covers both targeted (direct) and non-targeted (indirect) effects of ionising radiation, should be established.

Some questions can be addressed by employing a range of low-dose broad field and microbeam irradiation approaches to investigate both high- and low-LET responses, and by employing well-defined biological systems, such as human cell cultures, 3-D artificial tissue systems and *ex vivo* tissue explants. At the cell and molecular levels, new research should focus particularly on identifying the signals and signal receptors for the non-targeted effects. It will be important to understand whether such signals are produced by all cell types and whether reception and response is general or limited by cell type or organ. Considerable evidence now indicates that the cell signalling processes and outcomes observed with isolated cell types in tissue culture are considerably modified when other cell types, typical of the organ of origin are included. These data suggest that it is extremely important to test mechanistic conclusions in whole tissue. Identifying and understanding the action of the signalling process could lead to a means of predicting the outcome of an exposure in an individual.

While research at the cellular, molecular and *ex vivo* tissue levels will be critical for understanding the mechanisms of these processes, their influence on risk must also be determined more directly. To properly assess the net impact of targeted and non-targeted radiation effects, new research should specifically employ whole animal models, using both strains that are genetically normal and strains that are suspected to be radiation sensitive or cancer prone. Overall measures of risk should be accompanied by tissue specific measures, and these tissues should be assessed for cell and molecular changes. These results will also be important in understanding the relationship between dose and tissue weighting factors (W_T) as dose decreases. The animal models could additionally provide clarification on interrelations between non-targeted effects as a possible part of inflammatory-type response to radiation-induced stress under *in vivo* conditions. Long-term clonal variability of non-targeted responses and cell type differences need to be studied. More information is required on the influence of LET, and on simultaneous exposures to radiations of different LET. More information is also required on the relationship of dose rate and total dose for induction of these responses. Systems biology perspective, as well as mathematical modelling is likely to improve the understanding of the potential role of non-targeted effects in the development of different pathologies.

Teratogenic and carcinogenic endpoints in foetal and young animals should receive particular attention. Measurement of non-cancer endpoints should be included in all studies, including studies of heritable effects, and particularly in studies with animals selected for genetic propensity for cardiovascular diseases. The study of the influence of the adaptive response to radiation in organisms in the environment, and its influence when those organisms are also exposed to other stresses, will be important in future environmental assessments.

Radiation biology has identified, and continues to study several significant mechanisms for cellular responses that do not follow the classic "single target paradigm". Non-targeted effects, including radiation-induced genomic instability, adaptive response and bystander effects are now well established and incontrovertible. The universal use of deterministic language of cause and effect, resulting from DNA damage, seems now inappropriate, and may sometimes be misleading. The practical implication is that the classic paradigm may become an insufficient basis for both research and the protection of human health.

Our understanding of non-targeted effects is still growing, and much of the data have been obtained from *in vitro* studies. Since there are observed discrepancies between *in vitro* and *in vivo* experiments, the significance of these indirect effects on human health remains to be elucidated. Recent research and new data on both *in vitro* and *in-vivo* non-targeted effects suggest that the concept of radiation dose as a surrogate for risk will in due course need to be re-examined to incorporate both direct and indirect effects. The outcome of such research could seriously put into question the generic use of a simple linear extrapolation of radiation risks from high to low doses.

It would be prudent, therefore, for the policy-forming community to address the possible implications of the emerging science now.

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INDIVIDUAL SENSITIVITY

1. What is the issue?

An individual's sensitivity to ionizing radiation has emerged as an increasingly important consideration in the protection of workers and members of the public. Identifying radiation sensitive workers and patients (through medical screening or disease diagnosis) and providing adequate protection raises important policy questions. Enhanced radiation sensitivity has been identified in individuals who have undergone high dose radiation therapy for cancer and subsequently expressed unusually severe normal tissue reactions (e.g., ataxia telangiectasia). Several cancer genes have now been identified (including the one for AT) that may increase an individual's predisposition to certain cancers. There is less evidence of increased radiation sensitivity to cancer in individuals exposed to low doses of radiation. There is, however, emerging evidence of increased radiosensitivity (to breast cancer) among BRAC1/2 mutation carriers exposed to chest X-rays. While these findings need to be confirmed by further research, the existence of radiosensitive subpopulations, exposed at low doses, should be taken seriously**.**

Should worker and population dose limits be made more restrictive to account for more sensitive individuals? Should workers be treated differently because of increased radiation sensitivity? What are the social and economic costs associated with identifying sensitive individuals and providing additional protective measures? How should clinicians manage patients with known radiosensitivities? Should dose prescriptions be modified downward to account for heightened radiosensitivity? Should high dose interventional procedures be modified to limit patient dose?

The framework for radiation protection has historically been based on radiation responses of the average individual in an exposed population. There is now considerable interest in shifting emphasis away from the average response to individual responses. Recent advances in medicine and radiobiology indicate that certain genetic mutations and diseases are characterised by increased sensitivity to ionising radiation exposure. In the near future methods (including new DNA techniques) will be available to detect many of these mutations through simple blood tests.

The percentage of workers and the public who have increased risk of radiogenic cancers because of genetic susceptibility to cancer is not known but has been estimated to be in the range of 1-10%. This estimate is highly uncertain because it is based on limited epidemiologic and scientific data. Further, a definition of radiosensitivity for the purposes of radiation protection has not been clearly established; the number of radiosensitive individuals in the population will depend on how radiosensitivity is defined. Although little evidence is available at this time, sensitivity to radiation may also imply sensitivity to certain cancer-causing chemicals if sensitivity is determined by common damage pathways.

Individual radiosensitivity presents challenging problems in radiation protection and medicine. For workers, do we treat all radiosensitive individuals in the same way or do we recognise that some health outcomes are more serious than others? Individuals who are at increased risk for non-melanoma skin cancers are likely to require different risk management strategies than individuals at higher risk for colon cancer or lung cancer.

Medical management of patients with known radiosensitivities is particularly challenging because patient doses from radiotherapy for cancer and certain interventional procedures (e.g. angiography, angioplasty) can be as high as 70 Gy (to specified areas of the body)[1]. There is considerable interest in identifying sensitive individuals who are candidates for cancer therapy. Screening cancer patients for radiation (and chemotherapy) sensitivity could be useful in identifying optimum treatments. For example if a patient with prostate cancer has the option of surgery or radiotherapy, information about radiation sensitivity would be important in the treatment decision. Radiosensitivity status should be carefully considered by the clinician in the diagnosis and treatment of diseases requiring management by radiation.

2. Scientific evidence

Evidence for enhanced radiosensitivity comes mainly from high dose medical exposures. A small number of human diseases such as ataxia telagiectasia (AT) are associated with increased radiation sensitivity. Patients with AT express severe normal tissue reactions during radiotherapy that are not observed in the general population. Radiobiological studies indicate that cells from AT patients are more sensitive to the cytotoxic effects of radiation because of defects in DNA repair capacity. However, it is unknown whether enhanced radiosensitivity also includes increased sensitivity for cancer. The fact that cytotoxic sensitivity is enhanced does not necessarily mean that cancer sensitivity is also increased.

1. Medical exposures are expressed in grey (Gy) where 1Gy =1 Sv for x and gamma radiation. For the purposes of this document Sv is used to compare with doses encountered in occupational settings.

There is less evidence of enhanced radiosensitivity following exposure to low doses of radiation. This is due, in part, to the difficulty of detecting small differences in risk epidemiological studies of populations exposed to low doses, let alone detecting differences between sub-groups in such populations. A recent study, however, of the effect of chest X-rays on the risk of breast cancer among BRCA1/2 mutation carriers is highly suggestive of enhanced radiosensitivity among such women. While these findings need to be confirmed by further research (in particular with better dosimetry), they indicate the importance of further investigations of individual sensitivity at low doses.

If enhanced radiosensitivity is an important consideration, it is at least partially accounted for in current risk estimates used in radiation protection. Estimates are based principally on epidemiological studies of the Japanese survivors of the atomic bombings. The Japanese populations were large and heterogeneous. In estimating risk across populations, it is also assumed that any genetic differences are accounted for by utilising population-specific baseline cancer data. Controlling for genetic differences that influence spontaneous risk does not, however, control for genetic differences (e.g., in different populations) that control radiation risk.

It is well known that individual cancer risk is determined by a number of host and environmental factors including age, gender, smoking and diet. But there is now growing evidence that genetic differences add to the individual variability in radiation response. A large number of diseases have now been identified that are associated with increased cancer risk. Inherited predisposition for cancer associated with these diseases is due to specific germ-line mutations in one or more cancer genes. These mutations may cause an increase in radiosensitivity because they impact a cell's capacity to repair damage to DNA or affect cell growth and division. Examples of genetic diseases characterised by enhanced radiation sensitivity include familial breast cancer, ataxia telangiectasia and Bloom's syndrome.

The accumulation of mutations in cancer genes (i.e., oncogenes and tumour suppressor genes) promotes cancer. A critical cellular response that counteracts the carcinogenic effects of DNA damage is DNA repair. There are several known pathways of DNA repair, all of which act to remove DNA lesions and prevent mutations, thereby restoring genetic integrity. The importance of DNA repair pathways is illustrated by a number of hereditary diseases, in which individuals with defects in DNA repair genes are highly susceptible to cancer. For example, reduced activity of various DNA repair mechanisms predisposes individuals to lung cancer. Smokers with reduced DNA repair activity have a greater than 100 fold risk for lung cancer compared to non-smokers with normal DNA repair capacity. However, defects in a particular DNA repair system that may predispose

an individual to cancer by specific chemicals may or may not always predispose the individual to radiation-induced cancer, i.e., cancer-proneness does not necessarily equate to radiosensitivity.

Radiosensitive individuals are not predisposed to the same cancers. Depending on the genetic mutation, the affected individual may be at increased risk for lung cancer, breast cancer, colorectal cancer, thyroid cancer or other cancers. Because these tumours have different incidence and mortality rates and present different clinical management challenges, enhanced radiosensitivity may be more severe in one person than in another. For example, lung cancer has a very high mortality rate whereas basal-cell cancer of the skin is easily treated and very rarely leads to death.

3. Possible research results

There has been a rapid evolution in molecular and cell biology during the last decade. The human genome has been sequenced and data on individual genetic variation is emerging. These results will be important since much of human variation in response to both external and internal agents and stimuli is thought to result from individual gene variations due to single nucleotide polymorphisms (SNPs), specific gene codon variations that result in a change of a single amino acid inserted at a specific site in the protein product of the gene. New biomedical approaches are helping to clarify our understanding of the impact of SNPs on gene products and how they affect cell and tissue function; research results will continue progress in this area and also provide new possibilities to look at the genetic basis of individual radiosensitivity and radio-resistance. An example of the importance of such results in understanding human variability, particularly relevant to radiation response, is a recently described substitution of proline for the normal arginine in the p53 protein, the product of the Tp53 gene. This change impairs the ability of the p53 protein to initiate apoptosis and results in those persons with this variation being cancer prone and 2.5 fold more likely to die from spontaneous cancer. Paradoxically, if the cancer prone persons with this variation survive to 85 years of age, they are 40% more likely to outlive persons with the normal p53 protein. This human situation exactly parallels the observations in mice with functional variations in Tp53 and the animal results are, therefore, likely to predict the human response and risk.

Several epidemiologic studies have shown that the rate of chromosomal aberrations in peripheral blood lymphocytes is predictive of cancer risk. This association holds true not only for chromosomal aberrations induced by genotoxic agents such as ionising radiation, but it is also seen in unexposed persons, implying that part of the risk is explained by inherent (genetic) factors. Future research may investigate whether part of this individual variability can be

explained by repair gene variants, other gene polymorphisms or dietary factors. There is currently very little information on the interaction of ionising radiation (and chemical carcinogens) and DNA repair gene variants on the population level and even less on the effect of different combinations of gene variants.

4. Possible policy challenges

Although age, gender, smoking and diet are the principal determinants of cancer risk, individual radiosensitivity may also be important in some circumstances. Radiosensitive individuals working in radiological environments may be at higher risk for cancer. It may be prudent, where possible, to identify such individuals and provide additional protective measures.

If it is decided that radiosensitive individuals should have enhanced protection what risk management strategy should be adopted? Should an egalitarian approach be taken in protecting radiosensitive individuals or should radiosensitive groups be stratified in accordance with the severity of the cancer predisposition? Should current dose limits be reduced to protect sensitive workers or should separate limits for radiosensitive groups be established? The current radiation protection framework includes special considerations for pregnant workers. These workers are subject to more restrictive dose limitations during pregnancy because of increased embryo/foetus radiosensitivity.

Genetic testing, whether voluntary or involuntary, raises a number of ethical questions and also implications for radiation protection policy. The rapid evolution in DNA technologies will soon make it possible to obtain quite detailed genetic information on individuals. Some tend to think that genetic information is like Pandora's Box – don't open it or we'll be in big trouble! At the individual level, one can argue between the right-to-know vs. the right-not-to-know. Some people do not want to know if they carry genes that predispose them to a certain disease, whereas others want to know so that they can do something about it (e.g. engaging in risk avoidance behaviours like not smoking or eating a healthy diet).

Genetic testing of employees is also a sensitive issue, and can be interpreted either as worker discrimination or as a prudent procedure in the best interests of the individual. Individuals with (false or true) positive screening tests may be subject to employment, insurance and social discrimination. Should radio-sensitivity be considered a legitimate pre-employment condition that requires testing? Should genetic testing for radiosensitivity be left up to the individual only or are there certain employment situations when such personal information would be legitimately required by the employer. Should employees be allowed to "declare" radiosensitivity much like workers may declare pregnancy? Are current policies for protecting pregnant workers a useful model when dealing with radiosensitivity of workers?

In developing policies for protection of radiosensitive individuals several key issues must be addressed. It should be emphasised that the question of worker sensitivity extends beyond radiological protection. Individuals with enhanced radiosensitivity may also be sensitive to other carcinogens particularly if cellular damage pathways are common. Accordingly, many of the issues raised here will need to be addressed in the context of occupational health more generally, and radiological protection policy will need to be developed in a broader framework. Three specific issues are highlighted below.

Defining radiosensitivity

- How should radiosensitivity be defined in terms of measurable criteria and standards?
- Evidence of radiosensitivity comes largely from medical exposures at high dose. Is radiosensitivity an equally important problem at low dose?
- Is radiosensitivity fundamentally a dose problem?
- Do all radiosensitive individuals require specific protection?

Guidelines for screening

Should guidelines be developed for screening tests to identify radiosensitive individuals? Should screening tests meet certain standards for sensitivity, specificity and predictive value? What are the implications of a positive or negative screening test? Ethical issue and questions of employment, insurance and social discrimination are important consequences of screening and genetic testing. Ideally screening tests should have a low false negative rate. Should compensation policies be established to address false positive and false negative testing claims?[2] Does it matter whether testing is voluntary or involuntary? Are there situations in which the employer may require testing because of business necessity?

Setting dose limits

If screening tests and other information is readily available, should individual risks be taken into account in setting dose limits?

2. A false negative screening test may result in a radiosensitive employee being assigned to a high risk radiological environment. A false positive screening test may result in a worker with average sensitivity being placed in an undesirable work environment.

5. Possible approaches to improve the situation

Improving understanding of variations in population sensitivity

Basic molecular biology has increased our understanding on the responses of cells to ionising radiation and mechanisms of radiation action. However, regardless how refined a picture emerges from human and animal experimental models, large-scale work in human populations will be required to confirm effects in realistic settings and to quantitatively address public health implications. The feasibility of such studies is rapidly improving with the evolution of high throughput screening techniques such as DNA chips and proteomics. Potential genes capable of modifying the radiation response are genes involved in DNA repair and cell cycle control. Association of relevant gene variants with cancer, chromosomal aberrations and mutations should be carried out in radiation exposed and control populations to evaluate their role in individual radiation sensitivity. Development of functional phenotype assays should be carried out in parallel with the genotype analyses. Biosample banks of radiation-exposed populations are needed to carry out the studies.

The assessment of SNP variations in genes of particular relevance to radiation response, like Tp53, will be extremely valuable in assessing individual variations in radiation risk. Since, in this example, the influence of Tp53 after high doses appears different from its influence after low doses, such understanding may have different implications for patient protection in a therapy setting than for radiation protection in a public, occupational or diagnostic radiology setting. It seems likely that (paralleling the case for many known, genetic diseases in humans) SNP variations will be unlikely to be distributed normally across the entire human population, but will be biased towards a regional or ethnic basis. It is possible, therefore, that ethnic or regional differences in SNP distributions could reduce the efficacy of broadly based epidemiological studies unless those differences were accounted for in the study design. Ethnic and regional differences may also give rise to ethical issues with policy implications, not least issues of discrimination. In the future coupling molecular epidemiology with classical epidemiology is desirable.

Developing screening tests

Molecular epidemiology, whereby radiation exposure is linked to genetic susceptibility and effects, may help in assessing the variability in radiation sensitivity in the population. Such studies could lead to the development of simple screening tests for the identification of individuals who are inherently more sensitive to radiation induced cancer. Such tests would not, however, eliminate the uncertainty of who actually gets cancer. Nevertheless individual sensitivity has potential implications for radiation protection and use of radiation

in medicine (diagnostic and interventional radiology and radiotherapy). Development and implementation of screening tests and interpretation of screening results must proceed with caution because they can have serious social, ethical as well as economic consequences. A false positive test result for an otherwise healthy individual with no increased risk for cancer may lead to employment and health insurance discrimination and to expensive follow-up tests to confirm absence of enhanced radiosensitivity. Even if the test result is true positive (i.e., the test detects actual increased radiosensitivity) radiation exposure does not necessarily mean that the radiosensitive individual will get cancer – merely that they are at increased risk.

Major advances in cellular and molecular biology are providing a basis for building a more complete understanding of variations in radiosensitivity within the population. Enhanced radiosensitivity has been identified following exposures to high doses. There is less direct evidence following exposures to low doses but recent studies are highly suggestive of increased sensitivity among carriers of particular genetic mutations. In the future, it is likely that individuals at increased risk for radiation induced cancer may be identified through simple, genetic screening. These developments may have important implications for the current system of dose limitation and radiation protection, particularly for workers and for patients.

These findings indicate:

- The need to better understand the variations of radiosensitivity in the population.
- The need to identify who is radiosensitive.
- The need to investigate whether protection would be better achieved through a single dose limit or dose limits customised to groups with differing radiosensitivity.
- The need to explore the ethical issues raised by genetic screening.

In light of the pace of these developments, it would be prudent and timely for the policy community to begin examining these implications in the near term. This issue is well suited to being addressed through broad stakeholder involvement, particularly at a formative stage. This will enable the concerns of those most affected by these developments (in particular, employers, employees and regulatory bodies) to be fully identified and accommodated within any new policy framework. Many of the issues to be addressed are common to genetic screening more generally (e.g., in other occupations, for insurance, liability, and employment purposes, etc) and benefit should be taken of developments elsewhere.

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EPIDEMIOLOGY

1. What is the issue?

So far, the main source of information on radiation-induced human cancer risk has come from epidemiological data on exposed populations. However, direct information is available mainly for effects seen at medium to large doses, and linear extrapolation (albeit with correction for dose and dose rate) from these data is applied to estimate the human cancer risk at lower doses, which are more relevant in terms of exposure to the general population and radiation workers. The shape of the dose response curve for cancer at low doses is a matter of considerable debate. Arguments range from beneficial effects of small radiation doses (hormesis), to a threshold response, to non-threshold supralinear responses (implying that small doses are more hazardous than previously assumed, possibly because of the heterogeneity of human populations with respect to their risk of radiation-induced cancer).

The main issues in radiation epidemiology today are:

- The estimation of risk at relatively low doses.
- The study of different types and qualities of radiation.
- The study of different exposure patterns.
- The study of modifiers, both genetic and other, of radiation risk.
- The integration of radiobiological information in the design, analysis, and interpretation of studies.

Epidemiology is currently the most informative approach for the estimation of health risks to humans from ionising radiation and much remains to be learned on the effects of low doses of radiation from further epidemiological studies. Such studies are severely limited, however, and methodologically complicated, for the estimation of the effects of doses at levels typical of environmental and occupational exposure and much of diagnostic radiology.

2. Scientific evidence

Among the biological effects of concern when human beings are exposed to low-to-moderate doses of ionising radiation (1 Gy or less), the most important long-term effects are the induction of cancer and, to a lesser extent,

vascular diseases. Much can be learned about the nature of the cancer-induction process from laboratory experiments in cellular systems and animals. Even some insights into the mechanism of cancer induction may be obtained in this way. Nevertheless, until now, the most informative approach to the quantification of radiation-induced cancer risk in humans is the epidemiological study of exposed human populations. Only epidemiology is able to determine the types of cancer induced in humans, their frequency as a function of dose and time after exposure and the many factors, such as age and sex, which modify their expression. Furthermore, only epidemiology is able to quantify these responses and, as a result, derive estimates of the risks of cancer induction as a function of dose.

Classical epidemiological studies (as opposed to the emerging field of molecular epidemiology) are not intrinsically expected to contribute directly to the knowledge on radiobiological mechanisms as the only measurable outcomes of such studies are disease occurrence (in particular cancer) or, in some instances, relatively stable biological markers of damage or effect. However, epidemiological studies can provide valuable information about the applicability to humans of dose response and other information suggested by data obtained in experimental systems. For example, molecular epidemiology can be used to test the influence of the combined, overall effect of all relevant radiobiology mechanisms (i.e. DNA damage and repair, bystander effects, genomic instability, and adaptive response) on the risk of radiation-induced cancer in humans. Adaptive response, for example, would be expected to lead to lower estimates of risk per unit of dose in populations with low-dose protracted exposures than in populations where exposure was received acutely at a high dose rate.

Further, epidemiology has provided, and will continue to provide, important information on effects of age at exposure, time since exposure, and various host and environmental factors that may modify radiation risk and thus be of importance for radiation protection of sensitive groups. Information from these studies therefore needs to be taken into account in any theory of the mechanisms of radiation-induced cancer. Particular examples include studies of breast cancer, thyroid cancer and leukaemia, which indicate that children and adolescents are especially vulnerable to environmental insult. Studies of A-bomb survivors and of uranium miners also provide information about the joint effect of smoking and acute and protracted exposures to radiation on the risk of lung cancer. As another example, the roles of iodine deficiency and of dietary supplementation in the months and years after the exposure in the estimation of the risk of thyroid cancer following exposure to radioactive iodines can only be assessed by means of epidemiological studies.

As successful as epidemiology has been in contributing to a broad understanding of radiation-induced cancers in humans and the quantitative risks of the process, it has some inherent limitations. When the dose is high, epidemiological studies have identified clear-cut responses, and risk estimates for many types of cancer have been derived and their dependencies on other factors explored. However, when the dose is low and the effect to be detected is very small compared with the natural occurrence of cancer in the irradiated population, the precise quantification of risk is difficult and may, at very low doses, be impossible. To maintain statistical significance and power, the necessary sample size increases approximately as the inverse square of the dose: for example, if a sample size of 1 000 persons were needed to quantify the effect of a 1 000-mGy dose, then a sample size of 100 000 would be needed for a 100-mGy dose, and about 10 million for a 10-mGy dose, assuming that the risk is proportional to the dose. For the assessment of risks at low doses and dose rates, it has been customary to rely on the combination of direct evidence from populations exposed at high dose and dose rates and extrapolations; the latter is made on the basis of an assumed linearity between dose and effect, albeit making an allowance for the levels of dose and dose rate.

In recent years, epidemiologists have increasingly been attempting to evaluate the health effects of doses below 100 mGy by studying ever larger populations with reliable individual dosimetry (for example multinational cohorts of nuclear industry workers) or individual dose reconstruction (case-control studies of residential radon) to reduce statistical uncertainties. Progress has also been made in characterising and quantifying errors in doses and in accounting for dosimetric uncertainties in the assessment of the risk estimates through sophisticated statistical models.

Current ongoing epidemiological investigations of the health effects resulting from low dose exposures include studies of people receiving radiologic diagnostic examinations or treatments with ^{224}Ra, radiation workers, A-bomb survivors, persons exposed to radiation from accidental or routine emissions from nuclear facilities, people exposed to fallout from past nuclear testing, and people resident in areas of high natural background radiation (including radon).

At present, significant increases in cancer risk have been found in epidemiological studies following acute radiation doses of mixed radiations (γ-rays and neutrons) as low as about 50-100 mSv for solid cancers and about 200 mSv for leukaemia among atomic bomb survivors; about 100 mSv for thyroid cancer following treatment of children with external radiation and about 10-20 mSv for children exposed *in utero* to diagnostic X rays. For residential radon, a significant increased risk of lung cancer has been observed for radon concentrations in the range 100-200 Bq m^{-3}. It should be noted that lack of

statistical significance at lower doses should not be interpreted as proof of the existence or the absence of a risk: indeed, the level at which a significant increase is found in a study is a function of the statistical power of the study (including the size of the population studied, the length of the follow-up, the adequacy of the dosimetry and the spread of doses).

Nevertheless, some studies of populations exposed to high-LET, alpha-emitters do seem to indicate a threshold response. For example, no excess risk of osteosarcoma was found in radium dial painters that received average skeletal radiation doses below 10 Gy and a similar lack of osteosarcoma (and liver tumours) has been noted in Mayak workers with plutonium body burdens estimated to be below 7.4 kBq (corresponding to doses to bone surfaces of a few Gy). Since the latency period for osteosarcoma may increase with decreasing radiation dose, one possible explanation is that at low doses the latency period for the tumour is longer than the remaining period of life.

Other problems associated with the epidemiological studies include:

- The uncertainties attached to the dose estimates, which may be reconstructed in all studies related to environmental exposures and in many studies related to medical exposures. The uncertainties are generally larger for internal than for external exposures.
- The confidence limits quoted in most studies do not take account of uncertainties in dose estimation, etc.
- The exposure to mixed LET radiation.
- The comparison of the results obtained for different exposure patterns (for example, acute external irradiation versus protracted internal irradiation) and/or for different types of radiation (for example, γ rays versus α particles).

3. Possible approaches to improve the situation

The efforts that have been undertaken during the last decade to improve the knowledge on dose response at low and/or protracted doses (< 100 mSv) should continue. Of particular interest are the epidemiological studies involving large populations that are currently under study or that are under consideration. It is, however, recognised that these studies will often necessitate very long-term commitments. Moreover, because cancer is a late onset disease, a trend to truncate existing cohort studies, such as the radium-dial painter study, before the death of all subjects should be reversed. Indeed with the increasing interest in trans-generational effects it could be argued that funding for some studies should be extended beyond the lifespan of the exposed subjects.

Estimates of radiation risk in the low dose and dose rate region are expected to be refined as a result of epidemiological studies that have just been completed (for example, the pooled analysis of 600 000 nuclear workers gives the most precise direct risk estimates to date related to protracted low-dose external radiation exposure) or that will be completed in the near future (for example, the Chernobyl studies of thyroid cancer among individuals who were exposed as children or *in utero*). Follow up of these populations over long time periods will yield more comprehensive information. However, the power of classical (as opposed to molecular) epidemiological studies will never be great enough to determine the risk of specific diseases at very low doses.

New insights are expected into the effects of modifying factors and different radiation types and exposure patterns. The importance of iodine deficiency and of long term dietary supplementation with stable iodine on the risk of thyroid cancer following exposure to radioactive iodines in childhood has already been mentioned. Studies of carriers of mutations in BRCA1 and BRCA2 also indicate that such persons may be at an increased risk of radiation-induced cancer; studies are starting to evaluate the joint roles of low dose radiation exposure and genetic susceptibility in the aetiology of breast cancer in young women.

Populations of specific interest for future research on cancer include:

- Bomb survivors. It is important that the follow-up of this cohort is continued until the extinction of the cohort, in order to fully characterise and quantify risks. Because of its long follow-up and relatively high number of medium to highly exposed individuals, this cohort forms a unique data source to study time and age related patterns of radiation-induced risk.
- Medically exposed populations (including populations exposed to low doses of alpha-emitters). Studies of such populations will continue to be extremely valuable, both for the radiation protection of patients – on which they provide direct information – and for radiation protection in general. They can and do provide information about inter-individual variations in radiation sensitivity, and will do so even more with the increasing widespread use of molecular markers. They provide information on other potential risk modifiers – including sex, age and exposure fractionation – and on risks for specific tumour types.
- Mayak workers. Continuation of the study of this population and improvement in the quantification of internal doses is likely to provide valuable information on the effects of exposure to alpha emitters and of exposure protraction in the relatively high dose range. Valuable information on the risk related to neutron exposure may also be obtained.

- Nuclear workers. Studies of workers in the nuclear industry are particularly well suited for the direct estimation of the effects of protracted, low-level ionizing radiation exposure. Many of the existing nuclear workers cohorts are still young, and continued follow-up will therefore lead to important further improvements of the precision of direct estimates of risk at low doses. Studies of the effects of radionuclides on specific types of cancer (i.e. lung cancer) can be nested within appropriate nuclear workers cohorts to provide information on the effects of internal radiation.

- Chernobyl. Studies of Chernobyl accident recovery workers may provide important information concerning the effects of exposure, and possibly of exposure-protraction, in doses of 0-500 mSv. Further studies on the risk of thyroid cancer and possibly breast cancer in subjects residing in the most contaminated districts and exposed in childhood and adolescence may also provide important information about risk of these diseases and about possible modifiers – both environmental and genetic – of these risks.

- Residents of the Techa River basin. Studies of long-term exposure (mainly to ^{137}Cs and ^{90}Sr) may provide valuable insights into the effects of protracted and internal exposures.

- Radon. Further studies of residential radon isotope exposures (in particular combined analyses of European, North American and Chinese cohorts) and of miners are likely to refine our estimates of risk following low dose protracted exposure, enhance our understanding of possible reverse dose-rate effects and provide important information on the possible modifying effects of smoking. Given the levels of exposures in dwelling, residential radon is an important public health and radiation protection problem, with recent estimates indicating that 9% of all lung cancer deaths and 2% of all cancer deaths may be attributable to radon-222 in Europe.

- Residents in areas of high background natural radiation. Studies of the health of populations living in areas of high levels of natural radiation are a potentially important source of information on the effects of chronic low-dose rate exposures to ionising radiation. Given the very low doses in general and thus the small size of the expected risk, it is critical to identify health effects that can reasonably be studied in such populations, to assess carefully the feasibility of informative studies and, if they are judged feasible, to use appropriate and sensitive epidemiological study designs. The conduct of nested case control studies – with individual dose assessment to various targets from both

external and internal radiation and collection of individual information on known and possible risk factors for the diseases of interest – will be a useful tool for the evaluation of health risks from low-level chronic radiation exposures.

In addition, it is important to expand the studies of non-cancer effects, in particular of cardiovascular diseases. To maximise the information that can be drawn from studies of low dose exposures, it is important that the following methodological issues be addressed in future studies:

- The combination of studies with similar exposures and endpoints. Pooling of studies will, in principle, lead to more precise estimates of risk and offer an opportunity for understanding differences and similarities between the studied population groups.
- The reduction of dosimetric uncertainties. The assessment and validation of doses by means of different methods and the involvement of dosimetrists with diverse background and experience might help to better determine the main sources of uncertainty and their magnitude and how the latter can be decreased.
- The further improvement of the methods of analysis, so that the uncertainties in dose estimates and other factors and those resulting from exposure to different types of radiation can be taken fully into account in establishing confidence levels on risk estimates derived from epidemiological studies.
- The use of radiobiological information in the design, analysis, and interpretation of the studies.

4. Possible policy challenges

Ongoing and future epidemiological studies, combined with radiobiology involving non-targeted effects, may eventually contribute to the formulation of a new radiation biology paradigm combining both the classical targeted and the new evidence on non-targeted radiation effects. This may have profound implications on the risk assessment of ionizing radiation, and, consequently, on radiation protection policy and standards.

Radiobiology, epidemiology and genetics have contributed to our understanding of radiation sensitive subpopulations, and, as more is learned, the question of how to protect these groups will become an issue for radiation protection. For example, exposure *in utero*, even at very low doses, appears to be especially tumorgenic.

Within the coming decade there will be a significant increase in epidemiological studies of risks from exposure to protracted radiation, of risks from internal exposures, of risks of diseases other than cancer (in particular vascular diseases), of risks to sub-groups of mutation carriers and of risks to those exposed in infancy and childhood. Only time will tell what impact these studies will have on the risk estimates that currently underpin radiation protection standards – some change is, however, almost inevitable. Policy makers need to remain abreast of developments in this area and be prepared to respond appropriately to new findings.

Our main source of information on radiation-induced human cancer risk has come from epidemiological data on exposed populations. However, direct information is available mainly for effects seen at doses around 50 to 100 mSv for solid cancers in adults, and 10 to 20 mSv for children exposed *in utero*.

The main issues in radiation epidemiology today are the estimation of risk (of cancer and other health effects) at relatively low doses, the influence of different types (e.g. α, β, γ, n, X-ray) and qualities (high LET and low LET) of radiation, the influence of different exposure patterns (e.g. chronic or acute exposure, internal or external exposure), how risk varies with age at exposure (particularly in childhood and infancy) and how risk is increased for carriers of particular genetic mutations. However, classical epidemiology studies are limited (statistically) in terms of their ability to quantify the effects of doses at levels typically encountered in the environment, the workplace and generally in diagnostic radiology and this should be recognised.

Another area of study is that of molecular epidemiology. Although such studies may identify risks at the cellular level, it will be important to link any cellular detriments to risks and detriments at higher levels; at the organ/tissue level, and more importantly at the level of the entire organism.

Lastly, it is important to expand the studies of non-cancer effects on the basis of sound science, linking mechanistic studies and epidemiological evidence. The emerging issue of cardiovascular disease resulting from radiation exposure exemplifies the need for a more integrated approach to its resolution.

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OTHER CHALLENGES TO THE UNIFIED SYSTEM OF DOSE LIMITATION

The system of dose limitation is founded on knowledge in the radiological sciences. It has been developed to provide a practicable and largely coherent approach that is able to provide a high level of protection irrespective of the nature or source of radiation. Inevitably, in achieving practicability and coherence, many simplifying assumptions had to be made, some of which contradict or are not fully compatible with the underlying science. These contradictions or incompatibilities are generally recognised, yet tolerated, by those responsible for developing and applying the system in the interests of the overriding goals; sadly they are often less well recognised in the broader practicing radiation protection community. Nonetheless, the system, if it is to be sustainable, must remain responsive to emerging scientific evidence – otherwise it will lose credibility and fall into disrepute. This is an ongoing process and there will be differences of view as to the adequacy of the system in terms of how and when it accommodates the underlying science. This is inevitable given the value judgements that need to be exercised in establishing a system that is practicable, largely coherent and broadly compatible with the science. Finding the right or more exactly the best balance is a continuing challenge.

The unified system has had a long gestation and much experience has been gained from its application over the past three decades. It can be shown to be robust for most applications and the coherence it offers (relative to the system in place prior to ICRP 26) has led to a more consistent and optimal allocation of resources to protection than before. The degree of robustness is less for internal exposures but, even here, is broadly sufficient, in particular given the relatively low levels of exposures now experienced in populations and at the workplace consequent upon improved occupational hygiene in most industries involving radiation.

Nonetheless, contradictions and incompatibilities with the science remain and need to be recognised; moreover, further contradictions will emerge as scientific understanding advances. Where these are of sufficient import to invalidate the applicability of the system (i.e., in terms of it not being sufficiently robust or its application would incur costs that are grossly disproportionate with the actual reduction in risk), alternative more specific

approaches will need to be adopted. This is fully in accord with the principles underlying the system. The skill of the radiation protection profession will be to identify such conditions and respond in a timely manner.

In the previous chapters, a number of emerging scientific challenges to the radiation protection system have been identified, in particular in relation to non targeted effects, adaptive response, genomic instability, individual sensitivity, etc. In this Chapter consideration is given to other scientific challenges to the system that have been identified since its inception. Only those which appear to be of sufficient import to warrant consideration of the development and application of more specific approaches to protection, or in a more fundamental review of their implications for the current generalised system, are addressed. Some of these issues are related to or may have their scientific origins in matters addressed in the previous chapters; consequently, there is some repetition of material between this and previous chapters with a view to making this Chapter largely self contained but not unduly repetitive.

Many of the issues addressed in this Chapter are concerned with the appropriateness of the use of effective dose as the unifying quantity in the system of dose limitation, in particular its use as a surrogate for risk or harm. While there was broad consensus within the EGIS group on the contradictions/incompatibilities between the underlying science and the development and use of this quantity (and in some cases the relevance of dose more generally), there were divergent views on their practical implications for the unified system. The following sections are intended to inform and stimulate further discussion on this latter issue.

1. What are the issues?

The linear, no threshold (LNT) hypothesis, in which the predicted risk of harm is assumed to be a linear function of radiation dose, along with the concept of dose additivity, underpin and are central to the justification of the current risk-based radiological protection system. This system is used as the basis of protection in most situations where man is exposed to ionising radiation and embodies a unified approach through the use of effective dose – where weighting factors are employed to account for the variable toxicity of different radiation types and the variable response of different tissues. However, evidence is increasingly accumulating, which suggests that at low doses and at very low dose rates typical of most public and occupational exposures, effective dose may not be an appropriate surrogate for risk.

Major challenges to the scientific basis of the current risk-based system are considered most likely to emerge in areas related to:

- The shape of the dose effect relationship for stochastic effects at low doses (below 100 mSv) and at low dose-rates similar to those experienced in the workplace and the environment.
- Dose additivity and the concept of effective dose as an appropriate tool for adding doses.
- The difference in risks from chronic and acute exposures.
- The assessment of risks from internal exposure to high LET and low LET radiation.
- Variation in individual sensitivity to radiation.
- Dose-related changes in latency period and apparent dose thresholds for the induction of some cancers (e.g., bone cancer).
- The combined effects of mixed LET radiations and radiation with other carcinogens or other stressors.
- The emerging evidence of non-cancer effects.

These issues are discussed in the following sections.

2. Scientific evidence

2.1 Shape of the dose effect relationship for stochastic effects at low doses

Following exposure to acute doses of energetic gamma rays from external irradiation, epidemiological evidence indicates that the risk of mortality and morbidity in adults from all solid cancers combined is not inconsistent with a linear relationship with dose down to approximately 50-100 mSv, below which loss of statistical power obscures evidence in epidemiological studies of radiation risk. Evidence from children and from studies of *in utero* exposures is not inconsistent with a linear relationship with risk down to the order of 10 to 20 mSv. The extrapolation of risk estimates to low doses, based largely on observations at moderate-to-high doses continues to be the primary basis for estimation of radiation-related risk at low doses and dose rates of interest to the radiation protection community.

In organisms thus far studied, low doses of ionising radiation induce protective effects against spontaneous damage as well as damage from further radiation exposure. Studies using low dose and low dose rates of low LET radiation in mammalian cells and in adult animals have shown that below a threshold dose (about 100 mGy in human cells, rodent cells and normal mice)

the detrimental effects of a radiation exposure disappear and are replaced by protective effects, manifested in cells by decreases in transformation frequency and in animals by increases in cancer latency. Moreover, different tissues seem to display different dose thresholds. However, when considered as a whole, the emerging results with regard to a radiation-related adaptive response, genomic instability, and bystander effects suggest that the risk of low-level exposure to ionizing radiation is complex and uncertain. As such, a simple extrapolation from effects at moderate to high doses is unlikely to be correct. However, a better understanding of the mechanisms for those phenomena, the extent to which they are active in vivo, and how they are inter-related is needed before they can be included in the estimation of potential risk to the human population of exposure to low levels of ionizing radiation. It should be recognized that information from direct epidemiological measure of cancer risk will, by definition, include any potential contribution from these processes, but because of the constraints of low statistical power at low doses, will not provide information on either the mechanisms or their influence on risk.

All of these observations suggest that the biological processes occurring in cells and tissues in response to low doses and dose rates or to fractionated doses could be fundamentally different from those that result from exposure to moderate to high doses. However, resolving uncertainties on the existence or otherwise of a true low-dose threshold for cancer risk of low-LET radiation will never be resolved by epidemiological studies, and must necessarily rely on cell and animal experiments.

2.2 Dosimetry and biological effects after internal and external exposure

The radiological protection system assumes that the risk induced by radiation exposure is independent of the position of the radiation source (internal or external to the body). It thus considers that the risk of cancer occurring after an internal exposure may be derived from the risk coefficients calculated for populations exposed to external radiation sources, like the Hiroshima and Nagasaki A-bomb survivors. This approach seems to work for some types of radiation and some types of cancer, but for other irradiation scenarios it does not. For example, application of the current system to estimated risk would imply a large overestimate of the risk of leukaemia following bone marrow irradiation by alpha-emitting radionuclides.

Using standard radiological protection models (which underpin the application of the unified system) and risk estimates, leukaemia is predicted to be an important consequence of skeletal irradiation by ^{226}Ra and plutonium isotopes, but it has never been observed in exposed populations. One possibility is that bone marrow cells lying close to radionuclide contaminated bone

surfaces have no leukaemogenic potential. Another possibility is that the irradiated marrow cells are so sensitive to alpha-irradiation that they are killed rather than transformed. Whatever the explanation, it is clear that the current radiological protection system is flawed with respect to its ability to estimate the risk of post-irradiation leukaemia.

Another problem is that human and other experimental experience suggests that the risk of cancer following internal contamination by alpha emitters seldom, if ever, conforms to the LNT hypothesis. This would not be important for radiation protection dosimetry if the deviations from LNT were small. However, the relationships found between dose and bone sarcoma in female radium dial painters, between dose and both bone cancer and liver tumour in Mayak radiation workers, and between lung cancer and plutonium exposure in rodents show apparent dose thresholds, below which no excess of cancer is detected. A similar threshold has been observed for bone cancer in dogs fed ^{90}Sr. In the latter case it was suggested that the reason for this threshold was that, as skeletal dose decreased, then the latency period between irradiation and detectable bone tumours increased; at a certain dose the latency period exceeded the life expectancy of the dogs and no cancer was seen. An alternative or perhaps even a linked explanation is that the induction of some tumours, by alpha-irradiation in particular, may be linked to the onset of tissue damage, such as fibrosis, rather than to a primary effect of radiation on the DNA within identified target cells. This would certainly seem to be true for the unusual leukaemia seen in radium chemists which occurred only at very high bone marrow doses and was linked to the onset of bone marrow failure.

It is important to recognise that the assessment of internal doses from alpha emitters and from Auger emitters may be particularly difficult because of the very short range of these particles in human organs and tissues and the uncertainty on the location of the emitters with respect to the radiosensitive cells. After internal contamination, radionuclides can concentrate with different patterns in different tissue and cellular structures, leading to a heterogeneous deposition of energy, which may distort the dosimetric estimate and the evaluation of biological effects. Moreover, radionuclides commonly concentrate in macrophages, which by secreting cytokines are key cells in regulating tissue and body responses to injury and toxins. Consequently, it might be expected that doses resulting from radionuclides deposited in these cells might result in non-targeted effects; these may have a quite different effectiveness in producing macrophage-mediated responses than the same doses evenly distributed across a tissue. Neither the heterogeneous distribution of dose within most tissues nor the possibility of non-targeted effects appears to be adequately accounted for in the current radiological protection system.

The universal use of the existing radiological protection system (and in particular the effective dose) will consequently result in unnecessarily restrictive limits on the intake of some nuclides. There is, however, no evidence to suggest that application of the existing system is inadequately protective.

2.3 Dosimetry and biological effects after chronic and acute exposure

The effects produced by chronic exposures to radiation should be predicted by summing the effects predicted to be produced by an infinite number of acute exposures during a defined exposure period. In this way acute and chronic radiation doses differ only in the rate at which the dose is delivered. However, it is widely accepted that a radiation dose delivered at a low dose rate produces fewer late effects than the same dose delivered at a high dose rate. This is probably because dose protraction facilitates the more effective repair of cells, including DNA damage. Similarly, fractionation of doses – where dose is delivered at the same dose rate, but as a number of small duration discrete doses, spread in time, rather than during one single longer exposure – produces fewer late effects than single acute exposures. Again this is probably a function of repair facilitation. It follows that the ICRP defines a Dose and Dose Rate Effectiveness Factor (DDREF) to take account of the reduced effectiveness of chronic and fractionated radiation doses. For such radiation the DDREF factor is taken to represent the ratio of the slope of the linear no threshold fit of high dose, high dose-rate data to the slope of the linear no threshold fit of low dose, low dose-rate data. For radiological protection the ICRP recommend a DDREF factor of 2. This use of a single factor is a compromise and is not well founded in science. Several problems exist.

The utility of the DDREF depends upon the assumption that, for exposure to low doses at low dose-rate, the dose-response is linear with a slope that is less than that for high dose, high dose rate exposures. However, in contrast to the situation with low LET radiation, fractionated doses of high LET often produce either a similar number, or even more late effects, than high acute doses. In this case fractionation may reduce the effectiveness of cell killing as a mechanism for reducing effects.

In contrast, some low dose and low dose rate studies using low LET radiation in cells and in adult animals have shown that below a threshold dose (about 100 mGy in human cells, rodent cells and normal mice) the detrimental effects of a radiation exposure disappear and are replaced by protective effects, manifested in cells by decreases in transformation frequency and in animals by increases in cancer latency. Moreover, different tissues seem to display different dose thresholds. Observations also suggest that the risk induced by exposure to low doses of high LET radiation, and even low LET radiation, may be

underestimated when risk coefficients have been derived from observations at high doses. All of these observations suggest that the biological processes occurring in cells in response to low doses and dose rates or to fractionated doses can be fundamentally different from those that result from exposure to high doses, calling the concept of DDREF and its universal application into question.

It has been shown that chronic exposure may also influence the deposition and redistribution of radionuclides within the body. At the experimental level, some studies have compared the kinetics of the same amount of radionuclide after either acute or chronic intake and found differences. For example, it has been demonstrated that the rate of lung clearance of nickel oxide in rats is inversely proportional to the exposure duration. Similarly, the biokinetics of uranium in rats is different after chronic and acute exposure. Finally, the excretion of ^{90}Sr from individuals contaminated over tens of years in the vicinity of the Techa River (close to the Mayak nuclear fuel facility in Russia), appears to be much slower than expected based on the excretion measured for individuals subject to acute contamination. Dose rate related differences in metabolism are not accommodated by existing radiological protection models and it is axiomatic that where such differences occur they impact upon the accuracy of the estimated radiation doses and consequential risks.

These data suggest that the linear no threshold hypothesis, and the associated dose and dose rate reduction factors and tissue weighting factors derived from high dose experiments may be inappropriate for universal use at low doses and low dose rates.

2.4 Biological effectiveness at low and high LET: RBE and WR

Effective dose is a function of absorbed dose, radiation type and sometimes particle energy. To take account of radiation type and energy the ICRP recommends weighing the absorbed dose with a factor reflecting the relative biological effectiveness (RBE) of the radiation to induce stochastic effects (cancer). Values of this factor, known as the radiation weighting factor (W_R), have been specified for photons, electrons, neutrons, protons and alpha particles. As yet, factors for other particulate radiations, including the heavy ions encountered during space flight, have not been specified. The W_R values recommended are dose independent and the same for all tissues, but it is acknowledged that this is a simplifying assumption. The values specified are also taken to be independent of photon-, electron-, proton- and alpha-particle-energy. An exception is accepted for neutrons, for which energy-dependent values of W_R are recommended for radiological protection dosimetry. The values of W_R are, therefore, taken to depend only on the radiation type, and, in the case of neutrons, of its energy. There are, however, many problems with this approach:

- Data collected from a number of sources show that RBE varies as a function of tumour type and, therefore, of organ or tissue. For example, as described above, human data with radium and thorium isotopes show that alpha radiation is little more, or even less, effective than gamma radiation in producing leukaemia, but is a much more effective producer of liver tumours. The W_R values do not reflect these differences.
- The currently accepted W_R factors have largely been determined by comparisons of RBE at high doses, where all cells are hit by radiation and each cell receives multiple tracks of radiation. Since the dose to a single cell from a single high LET track is much higher than the dose from a single low LET track, these measurements of RBE (and therefore W_R) are valid only when there are sufficient tracks of low LET per cell to provide enough physical dose to match the effect, at a minimum, of one high LET track per cell. At lower doses, however, these concepts break down. At lower doses of high LET most cells are not hit, yet those that are hit still receive the high dose delivered by one track. At similar doses of low LET radiation all cells may still receive multiple tracks. At even lower doses, low LET radiation, like high LET radiation, will not hit all cells. At these levels, typical of public and occupational exposures, the use of W_R derived largely from high dose exposure assumes that the biological mechanisms responsible for the observed difference in biological response to different radiation types are the same mechanisms that operate at low doses. This ignores differences in the effects of high and low LET for induction of bystander effects, adaptive responses and genomic instability, which are discussed in the chapter on non-targeted and delayed effects. These results call into question the universal use of current W_R factors at low doses.

These examples show that the ability of radiation to produce tumours vary according to the type of tumour, absorbed dose, type of radiation, and radiation energy. It follows that, particularly at low doses, current predictions of radionuclide toxicity, made using the ICRP specified W_R values, may be substantially in error for some nuclides. Moreover, the individual biological variability may contribute further to the overall uncertainty. If so, the application of the concept of the effective dose as the unifying quantity in radiological protection is at best questionable. Nevertheless, there is little evidence to suggest that application of the current radiological protection system fails to be adequately protective, due to the use of generalised radiation weighting factors. It does, however, indicate that the use of these factors may seriously impair the ability of the system to quantify risk and, more importantly, lead to undue allocation of resources to protection in particular circumstances.

2.5 Non-cancer effects

The spectrum of health effects resulting from exposures to chronic (and perhaps also acute) irradiation includes non-cancer effects that impact upon life-expectancy, but these are not explicitly taken into account in the current system of dose limitation. Chronic expose to ^{226}Ra has been shown to cause impaired vision, tooth breakage and impaired body growth in adolescents. Exposures to such radionuclides also induce tissue fibrosis that impacts both on radiation dosimetry and health, but none of these health effects are currently modelled. Claims have been made in Belarus that long-term exposure to ^{137}Cs deposited as a result of the Chernobyl accident is the cause of a wide range of health effects (disorders of the cardiovascular, central nervous, digestive, respiratory, immune and reproductive systems as well as thyroid and kidney disorders). These claims have not been authenticated but, if they were and they could unequivocally be attributed to radiation, it would impact the current system of dose limitation.

Exposure to natural radiation

Radon gas (^{222}Rn) is the single largest natural source of ionising radiation exposure of human populations. The short-lived decay products of ^{222}Rn account for about half of the total average annual dose from natural background radiation and represents about 40% of the exposure from all sources including medical uses. For several decades radon gas has been known to cause lung cancer. However, significant hazard was commonly believed to be restricted to underground hard rock, mine settings where very high concentrations of radon could accumulate. More recently, it has been realised that high concentrations of this gas could accumulate in homes and other buildings, particularly if they are poorly ventilated.

[Suggest we delete this as it has caveats which are not necessary when we quote in the following the direct residential results, i.e., why confuse the issue with caveted statements based on occupational exposure?] Recent pooled studies in Europe, North American and China of residential radon exposures and risks suggest that up to 9% of lung-cancer deaths may be due to radon. These studies have seen statistically significant risks at radon concentrations at levels as low as about 100 Bq/m^3, with risk coefficients generally being consistent with linear extrapolations from studies of risks in higher radon concentrations found in uranium mines. If these risk estimates are correct, radon is near the top of the list of important human carcinogens.

Risk estimates (when expressed in terms of dose) for radon are made uncertain by difficulties in estimating dose because of the highly non-uniform distribution of radon decay products in lung tissue (it is the alpha emissions from inhaled radon and its decay products that contribute most to lung dose).

Accordingly equivalent dose is neither a meaningful nor useful quantity for the measurement of risk and is not used for exposure limitation in radiological protection. Instead radon concentration in air (measured in Bq/m3) is measured directly and used as a surrogate for dose in risk assessment, with the understanding that the relationship between radon concentration in air and absorbed dose in lung tissue is complex.

2.6 Adequacy of the current system to estimate risk

It is clearly stated by the ICRP that its system (and underlying guidance on its application) is to be used only for radiological protection purposes and not for risk assessment. Notwithstanding this, such uses are commonplace both within the profession and elsewhere and are likely to remain so in future. While the system is based on estimates of human risk, there are many examples where the use of the system fails to accurately predict "field-generated data". Examples include: the failure of current models to predict the excess of liver cancer, relative to bone cancer, in Russian nuclear workers; the lack of predicted leukaemia in Russian workers exposed to plutonium and women exposed to $^{226}Ra/^{228}Ra$; the failure to see predicted lung cancer in Thorotrast patients exhaling significant quantities of ^{220}Rn; failure to see detectable levels of radiation-induced disease in populations resident in areas with high natural background radiation, where annual radiation doses may exceed the ICRP recommended public dose limit by several orders of magnitude. In addition, the current system does not take explicit account of late non-stochastic effects of radiation such as liver cirrhosis and circulatory effects that may also impact upon longevity.

These types of problems are particularly of concern with regard to very-low exposures, where direct evidence of detriment is not available from epidemiological studies, uncertainties are very high, and risk estimates can only be derived based on models and hypotheses. The difficulty of this situation manifests itself clearly in the ongoing discussion of the validity of summing small doses over large populations to predict risk and the expected number of resulting deaths. This approach can be seen as a simple, mathematical outgrowth of the LNT hypothesis. At the same time, it assumes the literal validity of the LNT hypotheses, and masks the high level of uncertainty associated with risk assessment at low doses, low dose rates, and perhaps even far into the future.

While there is broad agreement on the scientific limitations of the use of effective dose as a surrogate for harm or risk, there are divergences in view on the extent to which these limitations compromise the system of protection in practice. It is noteworthy that an alternative approach has been used in one area where the unfied system has to date not proved practicable; this concerns protection against exposure to radon. Here, concentration of radon in air has been used as the

quantity for radiological protection decision making (see accompanying text box). Further deviations from the unified system may need to be considered in future, in particular if were demonstrated that its use would result in large deviations from the level of risk implicit in its application. There is little evidence to suggest that use of the current system is inadequately protective but more which indicates that, in particular circumstances, disproportionate resources may be being allocated to protection.

3. Possible approaches to improve the situation

3.1 Shape of the dose effect relationship for stochastic effects at low doses

The experiments currently being conducted in the areas of genomic instability, bystander effects and the adaptive response will shed light on the dose-effect relationship for stochastic effects at low doses. The emerging data suggest that the impact of these non-targeted effects may be greatest in the dose region where not all cells are hit, typical of public and occupational exposures. Moreover, non-targeted effects may have an additional effect on risk by modifying the response of tissues to damage by radiation or other stressors such as chemical carcinogens. Such results will be particularly important in assessing the concept of dose to estimate risk, since non-targeted effects amplify both protective and detrimental responses in a way that appears independent of average dose, but which may be more dependent on the dose received by any cell that is actually hit. Since non-targeted effects of low LET doses appear able to reduce the non-targeted effects of high LET doses, the current concept of dose additivity for radiations of different LET (the use of effective dose) may need revision. The physical extent of these non-targeted effects, that is whether bystander and adaptive effects can be disseminated only to like tissue or to a whole organ or even the whole animal is yet to be determined.

3.2 Dosimetry and biological effects after internal and external exposure

Research should be undertaken on the dosimetry and effects of specific internal contaminations. Uncertainties in dose coefficients for some radionuclides such as α- and auger-emitters are large and more work should be undertaken to reduce these *uncertainties.* That implies a better understanding of the biokinetics and microdistribution of some radionuclides. A specific effort should be put on determining both dose and effects from radionuclides binding to DNA. Moreover, epidemiological studies should be continued for groups exposed to radiation from internally deposited radionuclides. These groups should include not only nuclear industry workers, but also residents living near nuclear and other facilities, populations exposed to fallout, residents and miners exposed to radon and populations living in high natural radiation areas.

Experiments currently performed on animals after internal contamination will allow a precise determination of the biokinetics and, therefore, the dosimetry of incorporated radionuclides. Furthermore, most of these experiments now measure both cancer and non-cancer effects and, therefore, complete the current database. All these data will serve to improve the current radiological system for assessing the effects of internal contamination. Similarly, new data is being collected on the biokinetics of radionuclides in man. These also will help to improve the predictive quality of current biokinetic models.

Few studies of health effects related to internal exposures are currently in progress, but those that are (e.g., studies of Russian nuclear workers) may have a big impact on our understanding of risk. Some of the studies in progress are aimed at defining the health effects within populations living in the contaminated areas surrounding Chernobyl. Other studies, as indicated above, are examining health detriment in Russian nuclear workers that, unlike those in western countries, were commonly exposed to significantly high levels of both low- and high-LET radiation. These studies could, provided that good dosimetry is achieved, provide data that is complementary to those from Hiroshima/Nagasaki and will serve to either improve or challenge the current radioprotection system. Case-control studies are also being undertaken to look at the risk of leukaemia in high natural radiation areas of central Asia.

Some important qualifications are needed here. In particular, any such research should focus on nuclides or components that are potentially significant sources of public or occupational exposure. For example, the International Generation IV programme is studying the development of new reactor and fuel-cycle options that may generate novel radionuclides for which little or no radio-toxicological data exist. These are the types of situations that should be studied.

3.3 Dosimetry and biological effects after chronic and acute exposure

Research to address the comparison of effects following acute and chronic exposures should focus on both animal experiments and opportunities to acquire human data. Animal experiments must include actual measures of general and specific tissue cancer risk, accompanied by pertinent molecular data such as measures of changes in gene activation, adaptive response, bystander effects and genomic instability. Human epidemiological data should focus on situations with exclusive exposure to low LET radiation and include a consideration of both the dose rate and the dose. One opportunity to acquire such data may be from the residents of Taiwan living for many years in apartments constructed using ^{60}Co-contaminated steel reinforcing bars in the concrete. To test this question for high LET exposure, the uranium miner data could be re-examined on the basis of dose rate.

3.4 Biological effectiveness at low and high LET: RBE and WR

To be applicable to typical human public and occupational doses, future experiments will need to focus on using exposure levels where not all cells receive a radiation track. Since human exposure to high LET radiation is almost always accompanied by exposure to low LET radiation, it will also be important to understand the biological responses to such mixed field exposures. Micro-beam irradiation facilities have begun to address these problems at the level of single cells, and this will provide the opportunity to elucidate the contributions of the various molecular mechanisms that contribute to the effects of high versus low LET exposure, and to the net effect of combined exposures. These single cell experiments will need to be extended to three-dimensional arrays of cells, to test the influence of the various non-targeted effects in a model tissue system. It will be particularly important to extend these experiments to real tissues at the whole animal level to assess the differences in response of different tissues, so that appropriate tissue weighting factors can be determined for different exposure scenarios.

In addition, further work is being undertaken, which is specifically designed to derive better RBE values. This includes recent work that is investigating the RBE of protons and heavy ions about which nothing is currently known. New work is also on the point of publication concerning the relative toxicity of α- and β-particles.

Human data may be obtained from individuals living in high natural background areas. Since exposures to high natural background include exposure to both high and low LET radiation, populations living in these areas represent an opportunity to study combined effects using both molecular epidemiology and conventional epidemiological approaches. Such studies could include populations exposed to different ratios of high and low LET doses. An additional opportunity exists to study cancers other than lung cancer in uranium miners, who are typically exposed to high LET, but also to other carcinogens and to relatively large external doses of low LET radiation from uranium ore, for significant times each day.

3.5 Non-cancer effects

There is a strong need to conduct studies on non-cancer effects (or to critically review the observations made by some investigators of the consequences of the Chernobyl accident) in order to determine their contribution to the overall detriment caused by exposures to ionizing radiation at the levels of interest for the radiation protection community.

3.6 Adequacy of the current system to estimate risk

As indicated above, the radiation protection professionals use the ICRP models and methods to calculate risks at low doses for specific cancer sites and specific population groups, though this is not recommended by the ICRP. The current system and the concept of effective dose may not be appropriate for predicting risk in every situation where man is exposed to radiation. The assessment of risk after radon exposure is one of the cases where the current system does not formally apply. Another example is that of internal exposure to plutonium and radium isotopes, for which dose thresholds seem to exist for several important cancer endpoints. More generally, it seems that internal contamination with internal emitters may produce different biological effects and dose responses than those expected after external irradiation. Radiation exposure responses may also modify/be modified by co-exposures to other stressors, including, but not exclusively, other carcinogens. The best known example of this is the apparent synergistic effect between cigarette smoke and radon with respect to lung tumour induction, but other interactions are likely – for example between benzene and radiation with respect to leukaemia. This presents a particular future challenge to a risk-based system because it requires linkages to be established between radiological protection and chemical protection.

For risk assessment purposes, it is therefore recommended to search for specific solutions for specific problems when the use of effective dose and the application of the ICRP models and methods lead to results that are not adequate. There are some cases (i.e. radon isotopes) where the effects observed are directly linked to the air concentration, without any use of the dose concept. Similarly, effects derived from uranium exposure are sometimes expressed linked to mass intake, rather than to effective dose, which is reliable only for cancer induction. It should also be recognized that radiation protection is a socio-political process, responsive to the interests and perceptions of stake-holders with different points of view, and relying upon a knowledge base that is extensive, but also uncertain. In this light, it should be noted that the ICRP has already introduced mechanisms for stakeholder input into its recommendations. Acceptance of the political aspects of radiation protection implies that it is important, for the benefit and information of participants and stakeholders in the radiation protection process, to establish a consensus with all parties involved that takes into account all sources of uncertainty in the estimated risk, but that is not entirely based on scientific considerations. Such an approach could be internal exposures from long-lived radionuclides from such situations as waste disposal, site release, or effluent release; radiotoxicology studies would be used to assess the magnitude of the risk for the radionuclides and the site that are considered, while constructive communication efforts with all stakeholders would determine the level of risk that would be acceptable. This implies that

further targeted human and animal research would be necessary in order to provide support for a risk-based radiological protection system. For example, there is a clear need for further animal experiments including life-span toxicity studies. However, the policy of most OECD member governments in recent years has been to decrease financial support for research in these areas and to close down the facilities where such research could be conducted. These trends should be reversed in order to conduct the necessary research.

4. Possible policy challenges

The system of radiation protection was developed on the basis of measured and estimated risks in human populations, and is seen by policy makers, radiation protection professionals, and the public as a risk based system. Confidence in the system by all these groups exists because it is believed that the practical application of the system, which is to manage exposures, is an appropriate strategy for limiting those known risks. Challenges to the system occur because, when the system is used to predict risk, particularly at low doses or from internal exposures, those risk predictions are impossible to validate with epidemiological studies or in fact fail on occasions to explain actual results. This is not surprising since public and regulatory interest is usually with exposures at radiation doses far lower than those at which useful information about risk can be obtained by studying populations with such exposures.

The discussions here raise several specific policy challenges:

- *The concept of effective dose may not be sufficiently rigorous for all applications.* There is mounting evidence that challenges the concept of dose as an indicator of risk for low dose and dose rate radiation, and suggest that the uniform application of a constant DDREF, regardless of dose, may be inappropriate. If true, then associated concepts of dose independent radiation and tissue weighting factors (W_R, W_T) are also inappropriate at low dose and dose rates. If true, most of the basic assumptions of radiation protection, including dose additivity, dose normalisation for radiations of different LET (the use of effective dose) and the lack of dose thresholds for harm may need to be reconsidered. If different exposures (e.g. internal / external, chronic/acute, low/high, low LET/high LET, etc.) can NOT be summed to estimate an individual's total detriment/risk, or even if, more simply, several specific types of exposure can not be summed, then a new approach (at least for some specific situations) to radiation protection may need to be developed, in order to protect against each specific type of exposure separately. This in turn suggests that the risk or benefit of exposure to radiations of different quality needs to be understood and assessed independently.

- *Dose limitation may not, in some circumstances, equate with risk reduction.* Many cell and animal based experiments indicate that low doses of low LET radiation induce a protective effect that reduces the risk from spontaneous cancer and the risk of cancer from further exposure. If this is also true for humans, then radiation protection policies that endeavour to reduce exposures to the lowest possible dose, or entirely eliminate the exposure, may need to be reconsidered since they may prevent the induction of this protective response. For persons who may be occupationally exposed, prevention of the induction of protective responses would result in a higher than necessary risk if that person were then accidentally exposed to a high dose. In this circumstance, such a radiation protection policy could be viewed as increasing occupational risk.
- *Exposures in high natural background areas do not increase risk.* The apparent absence of significant radiation-induced health effects in populations living in high natural background areas is challenging. These observations appear inconsistent with current estimates of radiation risk, particularly since the exposures include individuals exposed during the entire in utero period and during all of childhood, stages at which humans are postulated to be particularly radiation sensitive.

The current radiation protection system is generally believed to be a risk-based system but functions practically on the basis of dose limitation. When used to predict risk, it frequently fails, giving rise to challenges to the system.

The current assumption that at low doses risk is directly proportional to dose without a threshold is being challenged.

A keystone assumption of the system of radiological protection is dose additivity. The current paradigm assumes that physical doses (Grays) of all types and natures can be normalised for radiation type and biological effectiveness and summed (as Sieverts) as an indicator of overall detriment.

Radiation biology studies suggest that this assumption is not rigorous and cellular and organism responses can differ depending upon the type of radiation exposure or exposure situation, for both external and internal exposure at low doses and low doses rates, and to both low and high LET radiations.

These data show that, for many exposure scenarios, the scientific basis of the radiological protection system, as a risk based system, is insecure. For the intake of some nuclides, the biological effects and dose responses differ from those expected after external irradiation. It is thus important to use radiotoxicology studies, adapted to different relevant scenarios, to further understand these issues.

Given the evidence, it is prudent to base the estimation and management of risks to the greatest extent possible on sound, scientific knowledge that is applicable to the specific situation, (e.g. internal exposures from long-lived radionuclides from such situations as waste disposal, site release, or effluent release). Where appropriate, stakeholder concerns (e.g. governmental, scientific, affected populations) could be addressed through relevant toxicological studies (either completed or newly proposed) in order to develop case-specific protection solutions.

The ICRP has already introduced such flexibility and is continuing with this line of thinking in defining its new approach to optimisation, taking into account stakeholder input.

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PART 2
POSSIBLE EMERGING CHALLENGES IN THE APPLICATION OF RADIOLOGICAL PROTECTION

Radiation Protection in medical exposures

Radiological protection of the environment: challenges to the current paradigm

Health impacts of accidents and malevolent radiological acts

RADIATION PROTECTION IN MEDICAL EXPOSURES

Medical exposures represent a clear benefit for the patients when these exposures are justified and optimised. However, medical exposures represent the largest man-made dose and are increasing rapidly. Individual doses can be high from some procedures, and stochastic risks can be particularly relevant for children and young adults. Patient doses need to be known by doctors (especially for the new techniques) to help in the justification and optimisation deliberations and to give the appropriate information to the patients. Industry should collaborate with researchers and practitioners in this effort.

New regulations and standards for medical exposures are being published and scientific data should be available to support their need and applicability. Development of "referral criteria for imaging" and "methodology to optimise medical procedures with ionising radiation" guides for new technology will be necessary. New technology in medicine requires periodic re-evaluation of the diagnostic reference levels (which indicate typical doses for a given procedure).

The aspects related to radiation doses (to the patients and to the staff) should be a substantial part of the clinical audit process for medical exposures. Industry should be advised of the need to implement dosimetric tools and electronic archives of the data, in new equipment for radiology. Physicians and practitioners should be assisted in understanding the risks associated with medical exposures and in optimising the use of new technologies.

Multidisciplinary, horizontal collaboration between the medical exposures and other areas of activity in radiation protection (e.g. dosimetry, epidemiology, radiobiology, radiation pathology, etc) should be promoted to take advantage of medical data for epidemiological studies.

1. What is the issue?

Patient exposure is increasing and will continue to increase in the domains of diagnosis and therapy for the following reasons:

- Diagnosis.
  - Medical imaging is decisive in making the diagnosis of many diseases.

  - Medical imaging brings critical information and thus contribute efficiently to the therapeutic strategy of diseases and especially of cancer treatment.
  - Technology has become so easily available that there is a real risk of unnecessary use of medical imaging results, resulting in an excessive exposure of the population.

- Therapy.
  - Radiation therapy is indicated in about 50% of cancers which are responsible for about 25-30% of all deaths.

- Diagnosis and therapy.
  - Interventional radiology contributes to both diagnosis and treatment, and in many circumstances is replacing surgery.

Thus it clearly appears that a medical exposure is closely connected to a clear benefit for the patients when these exposures are justified.

Diagnostic exposures on an average represent an effective annual dose to the population ranging from 0.3 to 1.5 mSv in the developed countries. Doses received by the individual patients are much higher. Therefore efforts on dose reduction in medical exposure are deemed to save much more population exposure than any other effort. But, it must be noticed that the different categories of population and the different organs are not identical regarding the risk due to exposure to ionising radiations. These efforts must mainly be focused on the protection of children and young adults who are still procreators, whereas exposure of older people is much less of concern for radiation protection. Thus it clearly appears that all justified exposures must be optimised, especially in the critical groups (children and young adults). Deterministic effects (skin and lens injuries) are also a matter of concern, especially during fluoroscopy guided procedures.

Since doctors, and especially general practitioners, may not have sufficient information to make decisions regarding the justification of the use of medical radiations in individuals, efforts should be made to develop practical guidelines regarding the prescription of the examinations, and adequate continuing education since new techniques develop rapidly. Indeed those guidelines must contain information about the doses delivered by the different examinations in order to help doctors selecting the most appropriate ones. On another hand, professionals of medical imaging should be supported in the process of optimisation of radiation protection; guidelines to optimise procedures should be made available to them and continuing training be offered as well.

Patients increasingly want information on doses and risks of medical exposures. It appears that doctors are in general not able to provide such

information. The guidelines suggested in the previous paragraph should contain that information needed to respond to patients' requests. The guidelines and the continuing training programmes should improve doctors' awareness of radiation risk issues and of the relevant results in radiation biology (for example, regarding the individual radiosensitivity, or epidemiologic studies).

In the process of optimisation, significant progress can be made by industry, either in the field of new technologies (for example with digital radiology, or with conformal radiation therapy) or in the domain of radiation protection itself (for example by the display of dosimetric parameters). Thus efforts should be made in collaboration with industry to ensure this progress is made and available at reasonable cost.

Radiation protection of staff in some medical practices (e.g. interventional radiology) is still a challenge. Sometimes the good protection of staff could entail an increase in patient dose (e.g. the use of some protection devices). Available dose values are not always represent the real dose due to the misuse or lack of use of personal dosimeters by some medical specialists. Training programmes should improve this situation.

2. Scientific evidence

The most important international organisations dealing with radiation protection are dedicating significant efforts to promote the best management of radiation doses in medical exposures. Digital radiology will be the main imaging technique in the next years for millions of patients. Doses can be increased in this way without the concurrent clinical benefit. Interventional techniques are increasing in number and complexity; the risks of radiation injuries need to be evaluated. Some diagnostic techniques (as computed tomography – CT) involve significant patient doses and the new protocols require detailed dosimetric studies before routine clinical use. The 2000 UNSCEAR report highlights these increases in patient doses derived from CT and interventional radiology. Also in the therapeutic area new techniques (such as intensity modulated radiation therapy – IMRT) and higher tumour doses are being used and efforts to improve planning and dosimetry will avoid the risk of secondary induced cancers.

ICRP has addressed some of these topics in the recent years: managing patient dose in digital radiology and in computed tomography, evaluation of doses to the embryo and foetus from intakes of radionuclides, prevention of accidents to patients undergoing radiation therapy, avoidance of radiation injuries from interventional radiology, pregnancy and medical radiation and patient doses from radiopharmaceuticals.

The ICRP also decided during its 2004 general meeting, to start with the preparation of some other reports on: RP for cardiologists performing fluoroscopically guided procedures, RP issues of modern radiotherapy techniques, protection of children, exposure of hands while preparing and handling radiopharmaceuticals, RP training for clinical personnel that uses ionizing radiation in medicine, medical-legal exposures using ionizing radiation without direct benefit to the exposed individual, medical examinations and follow-up of persons accidentally or occupationally exposed to ionizing radiation, medical screening of asymptomatic persons using ionising radiation and dose management in multi-detector computed tomography.

Voxel models are presently under process, for example at GSF – National Research Centre for Environment and Health (Germany), and their future use by the ICRP is planned. These advanced tools will help in the availability of more accurate dosimetric data for diagnostic and therapeutic applications.

The IAEA has launched the "International Action Plan of Radiological Protection of Patients" (resolution adopted on 20 September 2002 during the 10th plenary meeting of the General Conference), with the involvement of the main international medical societies, together with UNSCEAR, ICRU, ICRP, IEC, EC.

3. Possible research results

There is still a wide range of dose values reported by UNSCEAR for different countries, even when comparing developed countries. Procedures of measurement and refinement of data collection should be launched and evaluation of doses at the working place should be carried out especially for practices with high level of exposure, e.g., interventional radiology and brachytherapy. Some advances in the concept of dose (e.g. absorbed dose, effective dose) for practical use, especially for patients should also be obtained (effective dose is not a good quantity but it is still widely used for comparison purposes). The use of voxel phantom will help in the assessment of individual dose. It is necessary to continue developing dosimetry and voxel modelling.

Assessment and balance of risks and benefits

Dose and image quality management strategies (assessment of individual doses, relevance of ICRP risk models to estimate medical doses, use of new digital systems: multiple studies, multiplying doses, mammography, paediatric radiology, etc) are important for ensuring a balance between cost and benefit. It is possible to obtain more diagnostic information (especially with digital techniques and combined techniques such as PET-CT) by increasing radiation dose to patients. The challenge will be to have the capability to take this decision knowing the dosimetric information. Before new techniques are

introduced in the clinical practice the medical community should be trained to manage radiation dose and image quality to obtain the best benefit for the patients with a reasonably level of risk. In new digital systems the dose values should always be available and archived in electronic format, which is easy to do with modern technology.

It is also expected to improve the interdisciplinary communication (especially with epidemiologists and radiobiologists) of dose results, experience and knowledge, particularly with respect to effects of medical exposures (e.g.: X-rays of premature babies), accuracy of dosimetry for medical exposures, follow-up studies of medically-exposed patients, accumulation of medical and occupational doses, etc. Accuracy in dose values could be more precise for medical exposures than for some other occupational activities and this advantage could be beneficial for epidemiological studies. Some data from high dose procedures (e.g. interventional practices) could also be of interest in some radiobiology studies.

Emerging technologies and practices

Increasing use of CT and PET combined with CT as diagnostic techniques require a deep evaluation of risk versus benefit. Screening of disease with such techniques may be valuable. Because of the relatively high risk associated with this dosimetric technique the benefit of such an approach has to be demonstrated for the range of applications by powerful studies conducted based on an evidence-based medicine approach.

Non-ionising medical imaging techniques (magnetic resonance imaging and echography) should be favoured whenever possible. However, these techniques may not be available when needed and radiology or nuclear medicine examination remains justified when the diagnosis cannot be delayed. Furthermore, it should be noted that medical imaging techniques which are based on different physical principles may provide different types of information and therefore cannot always be used as a substitute for one another.

In radiation therapy, better dosimetry of the tumour in radionuclide therapy, conformal therapy and IMRT, and more accurate dosimetry of normal tissues will allow improvement in the clinical results while decreasing the risk of secondary cancers and or diseases, e.g. myocardial infarction or stroke. The potential for accidents should also be taken into account.

For all sources used in medicine, the precise quantification of their activity is the key for subsequent dosimetric evaluations. Thus efforts should be made to maintain reference laboratories for the precise calibration of all sources of ionising radiations

Strategies for risk communication to patients should also be explored (to avoid some tendency to self-referring).

4. Possible policy challenges

New regulations and standards for medical exposures are being published and scientific data should be available to support their need and applicability. Development of "Referral criteria for imaging" and "Criteria to optimise medical procedures with ionising radiation" guides for new technology will be necessary.

New technology in medicine requires periodic re-evaluation of the diagnostic reference levels to take into account developing good practice.

The aspects related with radiation doses (to the patients and to the staff) should be a substantial part of the clinical audit process for medical exposures. Industry should be advised on the need to implement dosimetric tools and electronic archive of the data, in the new equipment for radiology. Doctors should be assisted to establish and understand the risks and benefits associated with medical exposures and to optimise the use of new technologies.

5. Possible approaches to improve the situation

During the next years and with the support of information technology, patient doses should be available to the medical doctors and to the patients. Patient dose is a critical parameter to justify practices and to optimise medical procedures.

Multidisciplinary, horizontal collaboration between the medical exposures and other areas of activity in radiation protection (e.g. dosimetry, epidemiology, radiobiology, radiation pathology, etc) should be promoted to take advantage of medical data for epidemiological studies, for example in the fields of acute exposures, significant exposures (whole body) of premature babies, follow-up of patients treated with radiation (particularly young patients), exposures from interventional radiology and cardiology (patient and occupational exposures) and secondary cancers in radiotherapy.

Industry should be more involved in the radiological protection of patients and training in radiation protection should be substantially improved specially for the medical community.

There are ongoing studies that aim at reducing patient doses in diagnostic radiology without loss of image quality using various approaches. It is recommended to promote such research aimed at dose reduction, especially for imaging modalities involving relatively high patient doses.

Medical exposures represent the largest man-made dose, and are increasing rapidly. This is due largely to growing access to new and effective diagnostic and therapeutic technologies. Medical exposures are less a science issue than an issue of justification and optimisation of exposures.

As such, it is important to strongly encourage the search for new imagery systems, resulting in significantly less patient exposures or using technologies operating without ionising radiation.

However, medical practice will not remain isolated from the scientific debates raised in the preceding chapters. Indeed the controversies surrounding different medical screening programmes, such as for early identification of breast cancer, or of lung cancer among smokers, will be strongly affected by the result of the researches into effects at low doses.

Lastly, closer ties should be formed between researchers and medical practitioners. For example, collaboration on epidemiological studies (e.g. long-term effects of X-ray examination of premature babies, use of CT screening) should be more actively supported.

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RADIOLOGICAL PROTECTION OF THE ENVIRONMENT: CHALLENGES TO THE CURRENT PARADIGM

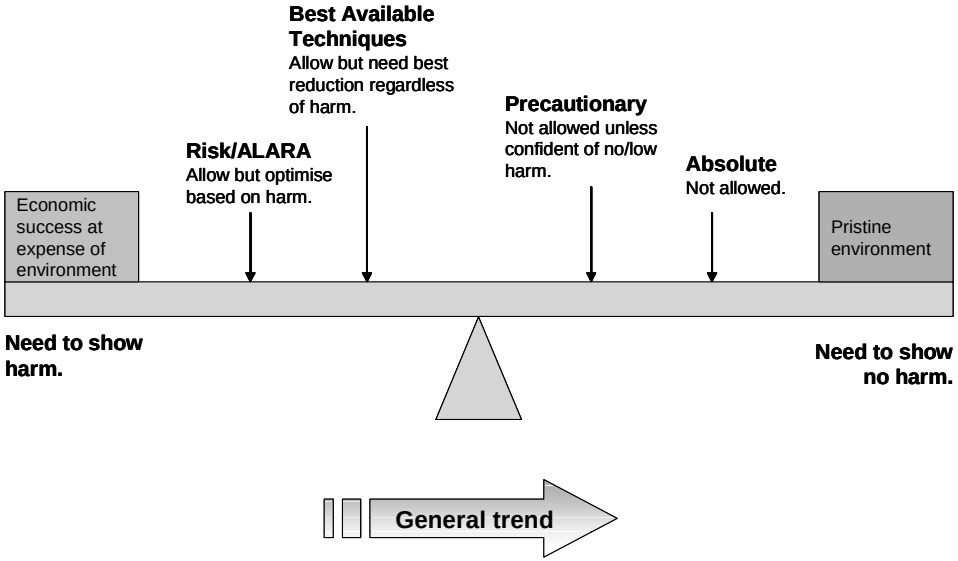
Due to pressures from society there is an increasing demand to adequately protect the environment. The precise nature of what is meant by protecting the environment is, however, still somewhat unclear at this point. As such, what to do, and how to interface radiological protection of the environment with other areas of environmental protection remain key questions in this important field. Nevertheless, radiological protection of the environment is increasingly an issue being discussed by governments and society in general.

1. What is the issue?

The current system of radiological protection, not having been designed for this purpose, is a weak tool to demonstrate the level of radiological protection afforded to the environment. Whilst the extent of the increase in societal concern can be questioned because it is difficult to gauge, what can certainly be seen is that there has been an increase in international agreements that refer to holistic protection of the environment. These agreements generally do not exclude ionising radiation; indeed at least one explicitly includes this physical property as a criterion (*per se*) for inclusion under the agreement.

Over time it can be seen that a number of principles have been used as a basis for deciding the level of control to exercise over dispersion of radionuclides which, it can be argued, have led to a shift in the burden of proof from a need to demonstrate harm in order to restrict an activity, towards a need to demonstrate that there is no harm in order to carry out an activity. This is illustrated schematically in Figure 1 and implies a need to demonstrate that releases of radioactivity to the environment have limited impact in order to continue them. Associated with this general trend, there is a view that humans should be cautious in interfering with the ecosystem on which they depend, since the ecosystem is a complex, highly non-linear system which is, in general, poorly understood.

Figure 1. **The trade-off in environmental protection, showing various principles used as its basis and the underlying burden of proof**



Although there is some evidence that points towards situations where the environment may suffer harm from radiation, most people involved with radiation protection and regulation of the nuclear industry feel that the current system gives an adequate level of protection to the environment. Nevertheless this is not the issue: rather, the issue is to demonstrate that this is so. The section following briefly discusses some possible situations of concern, so as to assist in choosing the appropriate options for further action in this area.

The interest of this report is the development of the science, in response to requests from society that will allow regulators (and other interested parties) to gauge the level of protection that is given and, where appropriate, tune the level of control. A key part of this challenge is not just collating data or carrying out experiments but also developing a means to apply this science; that is, devising a robust – perhaps very crude – model which will allow measurement data to be linked to protection of the environment.

This problem of linkage should not be underestimated, since it is in fact not clear what "protecting the environment" means in terms of policy objectives; it certainly applies beyond the field of radiological protection. Moreover, the ecosystem is complex and there is a possibility of significant synergistic (or indeed antagonistic) effects of radiation with other environmental factors. Both of these points suggest that any future system of

radiological protection for the environment should be developed in way that is consistent with approaches to handling other pollutants and stressors.

Thus the issue to be tackled has several major facets:

- Identification of pertinent endpoints.
- Construction of a robust – perhaps very simple – model to link measurement data to endpoints, including generating the necessary parameters for the model if appropriate.
- Identifying if action needs to be taken.
- Given the large number of issues requiring attention and wide belief that the current system is already largely effective.
- Initial efforts should emphasise a fit-for-purpose approach and not be resource intensive.

The first three bullet points will be discussed in the following sections through surveying available scientific evidence and discussing potential and proposed approaches to radiation protection of the environment whilst the final bullet is a general statement to be considered throughout this chapter.

2. Present scientific context

2.1 Scientific evidence

Today, under controlled practice and in normal operation of facilities, there does not seem to be any significant and visible harmful effect to the health of ecosystems that can be attributed to radiation. The last international review based on published data led to the finding that no significant harmful effects in animals and plants have been observed below 1 $mGy.d^{-1}$ (40 $\mu Gy.h^{-1}$) of radiation exposure that could put whole species at risk or promote irreversible imbalances between species. However, closer examination shows that these data mostly relate to external and acute exposure to gamma irradiation with observations made at the level of individuals. Updates of this initial effort are currently in progress with the aim of improving the database structure and relevance, and incorporating the recent scientific achievements from the last decade. Significant effects have indeed been observed at lower dose rates leading to recommend a predicted no effect dose rate for all ecosystems in chronic exposure situations of 10 $\mu Gy\ h^{-1}$ (0.24 $mGy\ d^{-1}$). In contrast, releases from normal operation of facilities are believed to usually be kept below 100 $\mu Gy\ h^{-1}$, but have also been reported to largely exceed this value, especially in mining areas promoting enhanced natural radioactivity levels. Furthermore, a key concern remains that there may still be ecosystem effects from long term

exposures, since the complexity and non-linearity of the ecosystem can lead to unexpected consequences from apparently innocuous activities, as was experienced from the release of CFCs into the atmosphere. Furthermore, the length of time for effects to manifest themselves can span several generations and so it is only now, after half a century of discharges, that we are approaching a suitable timescale for examining whether effects are occurring. Furthermore, recent compilations of continuous and low level irradiation effects have revealed the scarcity of data for a number of wildlife groups.

Overall, substantial knowledge gaps remain in understanding the biological effects 1) of long-term chronic exposures to low doses of radiation, 2) of long-term internal exposures to bio-accumulated α and β emitting radionuclides, 3) of radiation stress combined with other toxicants or stressors, 4) of the indirect effects driven by inter-species ecological interactions, 5) of their consequences at higher levels of biological organisation such as population, community and ecosystem. Altogether, these shortcomings lead to the requirement for the assessment methodology to rely on various extrapolations, the robustness of which need to demonstrated.

2.2 Current developments in application of the science: the "reference organism" approach

Current scientific developments in the field of radiological protection aim at designing an assessment methodology, as a first step, based on a bottom-up, individual-based approach, usually referred to as the "reference organism" approach. The approach tackles the high complexity of the ecosystem by selecting a small set of representative organisms; the radiation dose to individual members of these reference organisms is then calculated and from the effects at the individual level, the effects on higher levels of organisation (e.g. population, ecosystem) are extrapolated. The approach is pragmatic in that it reduces the complexity of the ecosystem to consideration of a few representative species, chosen so that they take into account a range of environments and taking into account the availability of appropriate scientific data. Among the criteria to support this selection, the radiosensitivity of species is not given an overdue importance as the most radiosensitive species may not be key in sustaining proper ecosystem balance. Nevertheless, knowledge gaps still exist and some current effort is directed at filling these. The approach also has the merit of being analogous to the system of human protection and therefore has many aspects that are straightforward for (human) radiological protection specialists. For example, reference organisms can be seen to correspond to reference man.

Despite these benefits, the approach does have some limitations. Mainly this is because of the way it simplifies the complexity of the ecosystem and there are several important aspects to this. Firstly, to understand how the environment as whole is protected, effects on individuals have to be extrapolated to higher levels of organisation and there is no generally applicable way of doing this that has been demonstrated to be accurate and robust. Secondly, it is not clear if the dose-response curves reflect the most sensitive stage in the life cycles of the biota. Thirdly, it is not certain if the reference organisms are adequate as 'indicators' for the status of the environment. Finally – and taking into account the previous points – it does not propose endpoints for assessment with respect to protecting the environment at large, being focussed on the endpoints for an individual plant or animal. Nevertheless, the approach does have strong merits, is better developed than other approaches and it should be noted that it is only proposed as a first step towards a more developed system.

3. Possible research strategy ahead

As indicated from the knowledge gaps identified above, the basic dimension of research that needs support in order to reach an efficient capability for assessing the radiological risk to the environment is novel data acquisition for non-human biota and model ecosystems especially focused on low-level effects in chronic exposure. But meanwhile, acquisition of this new understanding will gain in pertinence and consistency if further developed within several complementary perspectives, as described in the following.

3.1 Development of an "ecosystem health" approach

International agreements that deal with protection of the environment often refer to it in a general or holistic way. A holistic approach suggests one that considers ecosystem structure and functions. This has prompted the emergence of the "ecosystem health" concept which can be used as the final output of assessment to inform decisions as to their potential environmental impact. An approach based on this perspective emphasises consideration of the environment in an integrated manner that better reflects the actual complexity of nature. Thus such a top-down approach is to be favoured as it will address the limitations of the "reference organisms" approach whilst integrating its achievements.

The scientific challenge here is to produce assessment methodologies that can be demonstrated to broadly capture propagation from the individual to higher levels of biological organisation. This would also involve identification and integration of ecosystem-relevant endpoints. Experimental designs that can examine ecosystem processes such as microcosms, mesocosms and long term case studies need to be supported as they can, for example, assist in

identification of ecological endpoints, clarify the significance of biological markers and also identify species that could potentially be used as efficient sentinels for radiological stress. Such research would be complemented by a parallel effort to produce ecological models capable of giving an appreciation of potential long-term effects.

3.2 Chemical-radioactive synergies and integration

Another area of challenge is related to consideration of other environmental stressors, particularly chemicals, since only in limited cases (such as accidents) are there a singly dominant stressor-effect. Multiple stressors may have synergistic (or antagonistic) effects yet consideration of the combined effect of several stressors, such as radioactivity and chemical toxicants, is an area which is poorly developed. Moreover, communication difficulties could arise since currently radioactive materials are typically considered by the dose they can deliver whereas as chemicals are usually considered on the basis of their quantity or concentration.

3.3 Development of an international network or "Observatory"

At this stage, efforts in the areas described are generally fragmented and involve a range of disciplines, such as radiation biology, radioecology, environmental toxicology, ecotoxicology and ecology. Moreover, environmental data collected over the last half century by the nuclear industry for surveillance purposes has not been utilised in an efficient, co-ordinated manner. Therefore it is proposed that a useful development would be an international network that allowed researchers to co-ordinate and understand research in relevant fields. This "observatory" would be grounded on past and ongoing observations in the real environment and allow them to be linked with laboratory and theoretical developments.

4. Possible policy challenges

The issue is to develop understanding – meaning an approach as well as experimental data – that will allow regulators and others to demonstrate the level of environmental protection achieved. The current section examines particular challenges associated with further development in this area.

Firstly, radiation is only one of many environmental factors that are contributing to society's concerns over protecting the environment. Thus policy makers should make sure that any protection system they adopt is, at the very least, consistent with approaches and methodologies used elsewhere (particularly for chemicals) in order support assessment of the effects of several

factors. This applies both to ensuring comparability between systems and standards as well as capacity for considering multi-stressor effects.

Secondly, the most sophisticated approach to protecting the environment is expected to come from a holistic, ecosystem approach whereas the ICRP and much current research is to date focused on the "reference organism" approach. These two approaches need to be reconciled, explained and ultimately integrated.

Policy makers also need to consider difficulties surrounding identification of suitable endpoints for assessment and be prepared to consider recommendations that may be promulgated by the ICRP should the development of its system of environmental protection lead to this outcome.

Furthermore, policy makers need to consider that whilst thinking is still often rooted in the idea of demonstrating that protection of humans has resulted in protection of the environment, any approach they adopt should be able to withstand demands from wider society to protect the environment *per se*.

Finally, policy makers should be aware that on this topic science is responding to external demands and ensure that, where appropriate, science is given some guidance on what is needed, since policy makers may be better placed to understand the socio-political demands in this area.

5. Possible approaches to improve the situation

The scale of the problem to be tackled (in the sense of its difficulty and geographically wide nature), together with its holistic nature, point towards greater integration of research across the relevant fields. Such integration should lead to a more efficient approach to the issue. Several initiatives are already under way, for instance, the Worldwide Network of Radioecology Experimental Laboratories and the IAEA Action Plan on the environment with a useful "think tank" role being played by several organisations (e.g. IUR, NEA, WNA, and SETAC).

Recognising that improvements can still be made in the field of integration and co-ordination, it is suggested that a key action to improve the situation could be made through establishment of an international "Observatory", as described above. Development of an "Observatory" should lead to a strong and visible international research programme, which may give the further benefit of nurturing expertise in this area in some areas where it is under threat, for example, in USA and Europe where radioecological research groups and expertise have significantly diminished during the past decade.

Furthermore, a truly holistic approach, requiring integration of a wide range of scientific disciplines, is not encouraged by the programmatic structure that still prevails in many national and international organisations, which has separated the nuclear and non-nuclear field for historical and political reasons. Restructuring of these programmes could be carried out in order to abolish or reduce these barriers.

There is international consensus on the need to protect the environment. Contrary to the issues raised in the chapter on non-targeted and delayed effects, this consensus is not the results of scientific research that will have an effect on any radiation protection policy, regulation and application, but a social demand that has requested radiation protection science to study possible radiological harm to the environment.

Today, under controlled practice and in normal operation of facilities, there seems to be not indication of any significant or visible harmful effect on the health of ecosystems that can be attributed to radiation. But given the complexity of the situation (e.g. natural background, relationships between individual and ecosystems, many simultaneous stresses), the research necessary to scientifically answer questions regarding the well being of ecosystems must be well targeted and based upon the social choices at the international, national and local levels depending upon the situation being considered.

The maturity of the radiological protection system will be judged partly on how these questions are addressed, and on what paths forward are proposed.

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HEALTH IMPACTS OF ACCIDENTS AND MALEVOLENT RADIOLOGICAL ACTS

1. What is the issue?

As demonstrated by many situations in the past, in the aftermath of a nuclear or radiological accident there will be a significant ongoing issue of determining what dose was in fact received, and whether contamination continues to be present. This is of particular importance in situations in which the contamination of members of the population is *a priori* unknown, e.g. after the loss or the malevolent use of a radioactive source. As a consequence of the large variety of possible scenarios both internal and external exposures would have to be considered. There is a general consensus that most dispersion scenarios would not have significant public health affects and high-level irradiation would be the key health concern, probably only to a few individuals.

In situations of this kind it is most likely that significant public concern about potential radiological consequences would arise. If not properly handled, this could rapidly result in the disruption of the societal and economical situation.

Dose assessment

Authorities should expect a heavy demand for surveys and dose estimates. This is likely to include a great number of people who may not have received a significant exposure, but who are seeking some kind of confirmation or proof of their physical condition. For the purpose of dose assessment *Operational Intervention Levels* (OILs), which are expressed in quantities that are directly measurable, should be developed at the planning stage.

While OILs can provide helpful guidance for choosing between protection and treatment options, decisions on subsequent triage, monitoring or treatment should never be based on OILs alone. They should include medical expertise in the best possible way.

Triage and subsequent medical treatment

An important improvement of the present situation would be for local medical service personnel to be able to identify overexposed patients, who require subsequent medical surveillance or treatment ("triage"), even if they are not able to deal with their long-term medical care. For the purpose of on-site medical triage it is of vital interest to distinguish between exposures well below a level of the committed dose of several hundred MilliGray (no requirement of immediate medical treatment and surveillance) and one Gray (Gy) or above one Gy (urgent requirement of medical treatment). In general, with the exception of open wounds, the medical treatment of patients does not need to be hampered by the hazards of the contamination, provided that simple precautions not radically different from those normally employed in sterile work are taken to reduce the spread of contamination.

One characteristic that will affect medical planning is the fact that the number of potentially affected victims is unknown. Since radiological terrorist attacks may occur anywhere, planning should be part of national guidelines and standards for the preparedness of emergency medical services and hospitals, including smaller, general-care facilities. The guidelines should ensure that, throughout the country, medical personnel have a user-friendly, easy to understand reference guide on the basic measures required to deal with the urgent care of potentially overexposed and/or contaminated casualties. These guidelines should include information about useful equipment (dose meters) and practical advice that guarantees a minimum standard of radiation protection of members of emergency services. Provisions should be made throughout the country to help potential victims who did not or did not want to receive assistance and support by emergency medical services in the early phase of such an event.

2. Scientific evidence

There is a vast quantity of scientific evidence available in the areas of dose assessment and medical treatment of overexposed persons, which can be used for well-founded planning of the medical treatment of persons involved in a radiological attack. Recently these questions have become an issue of major concern of national and international security organisations and many studies have been initiated aiming at specific solutions. However, the results of many of these studies are not available in the open literature.

All patients should have their traumatic injuries, including so called "combined injuries", medically stabilised before radiation injuries are considered. Patients should then be evaluated for both *external radiation exposure* and radioactive *contamination.* State-of-the-art equipment is

commercially available. Dose assessment can be based upon various kinds of location and environmental measurements, on model estimates, on physical dose measurements, and on available methods for biological dosimetry. Recommendations for *Operational Intervention Levels (OILs)* are available. The OILs are expressed in quantities that are directly measurable for determining when exposure rates or contamination levels warrant taking urgent protective action. The unresolved challenge is the timeliness in which the results are required for decision-making (triage) and the high number of potentially exposed persons. For the purpose of on-site medical triage it is of vital interest to distinguish between exposures well below several hundred MilliGray (no requirement of immediate medical treatment and surveillance) and one Gray (Gy) or above one Gy (urgent requirement of medical treatment). Suitable methods for biological radiation dosimetry are available but their application is tedious and time-consuming with limited throughput.

Prodromal symptoms may be an indicator for high radiation overexposure. Nausea, vomiting, diarrhoea and skin erythema within a few hours may be the result of very high but treatable external radiation exposures. Such patients will show obvious lymphopoenia within 8 to 24 hours and evaluation for symptomatic patients includes a complete blood count every 6 to 12 hours for 2 to 3 days. Primary systems involved will be skin, intestinal tract and bone marrow. Part of the challenge comes from the fact that many prodromal symptoms of high radiation overexposure are the same as those of conventional illness, for example nausea and diarrhoea.

Medical treatment after high radiation overexposure should be supportive with fluids, antibiotics, and transfusions stimulating factors. If there are early CNS findings or unexplained hypotension, survival is unlikely.

Radioactive material may have been deposited on or in a person. More than 90% of surface radioactive contamination can be removed by removal of the clothing. Contamination on the skin can be effectively removed with soap, warm water, and a washcloth. Care should be taken not to damage the skin by scrubbing. Decontamination can usually be stopped once the contamination level is reduced to two times the background count rate of a radiation meter, or if repeated decontamination efforts are ineffective. Appropriate values of the acceptable residual contamination level need to be decided in conjunction with radiation protection experts at the planning stage. State of the art measurement systems are commercially available. In many contamination scenarios internal contamination is not a major health issue, except from the incorporation via open wounds. In such a case special treatment including de-corporation might be necessary. Treatment of this kind requires special skills available in dedicated treatment centres.

Despite huge previous efforts of scientific research aiming at the development of agents to prevent or treat adverse biomedical effects of an exposure, there is no evidence that new radio-protectors or therapeutic agents will be available for practical application in the near future.

International guidelines on the basic requirements and the organisation of medical treatment are available. They offer both advice about the needs of medical preparedness and the possibilities of support of international organisations in an actual situation.

3. Possible research results

Research in this area can build on a vast amount of scientific knowledge and experience. It can make use of a great number of highly specific technical equipment and detection methods.

Given the fact that there might be some urgency to resolve the key issues addressed in this section, the future research activities should be focussed, based on the following priorities: the development of strategies for fast and reliable dose assessment under real time conditions and for a large number of potentially exposed people can be based on a variety of available options and techniques. Strategies for initial dose assessment should address the specific needs for medical triage, i.e., they should aim at a distinction between total exposure level well below several hundred MilliGray and one Gray (Gy) or above one Gy. Both internal and external exposures should be considered. In subsequent steps a refinement of initial dose assessments should be achieved.

Available options and resources for treatment of external and internal exposures and their suitability under the given circumstances should be included in planning medical emergency response. The establishment of an information repository of pharmaceuticals and bioassays relevant for scenarios under consideration is an essential part of medical emergency management.

Guidelines should be developed which describe the specific needs and define minimum standards of national networks of organisations with various capabilities in the identification and treatment of overexposed individuals. Close co-operation between emergency response organisations and radiation experts is essential to set up a system of contamination monitoring for a large number of potentially contaminated people and mass triage procedures for potentially overexposed individuals and to avoid spreading of contamination in the affected territory. Pre-identification and use of existing national medical infrastructures and of international networks for medical response to nuclear accidents and radiological terrorist attacks will support the performance of medical emergency management.

The application of these guidelines must be a mandatory requirement of the emergency response organisations. Training programmes for radiation scientists, medical doctors, first responders and emergency personnel have to be established to regularly test the state of preparedness of the emergency response organisations. Important issues of emergency preparedness are provisions for the information and advice to the public to explain both the radiological risks and the available countermeasures in a rational and understandable fashion. Risk communication with the public has to specifically address the risks of special groups of the population, e.g. children, pregnant women, etc.

Strategies and practical guidance should be developed to provide support for all medical specialists to speak with a harmonised voice about the potential health impacts and to co-operate with media organisations to inform people on what to do and where to go so that the medical infrastructure is properly utilised. This will also contribute to maintaining or regaining public trust in the work of emergency organisations.

4. Possible policy challenges

Maintaining public confidence is a critical issue when dealing with the consequences of nuclear accidents or radiological terrorist attacks. It is generally recognised that this is an issue of outstanding importance in the very early stage of such an event. Malevolent actions may result in severe psychological reactions in the general public such as sadness, anger, fear, difficulty sleeping, impaired ability to concentrate, and disbelief.

People will likely seek information and guidance from healthcare providers who will most likely play a key role in determining how the general public will respond to a radiological malevolent event. Information provided by these organisations should not only address the consequences of high exposures but should also deal with the situation of the vast majority of people with low or no exposures. A well-organised, effective medical response system will instil hope and confidence, reduce fear and anxiety, and support the continuity of basic community functions.

Fortunately, nuclear accidents and radiological terrorist attacks are rare events. As a consequence, the resources allocated to respond to such events are limited. Key issues to be addressed in the planning stage of preparedness are:

- The information, training and protection of members of emergency services and health providers.
- The allocation of resources for dose assessment and for treatment of external and internal exposures.

- The establishment of an information repository of pharmaceuticals and bioassays relevant for scenarios under consideration.
- The development of strategies and practical guidance for all medical specialists to speak with a harmonised voice about the potential health impacts to the population (including pregnant women).
- The development of standards and procedures and of organisational structures for the psychological support for victims.

All resources available at national and at international level (e.g. WHO, IAEA) should be known and be included in a national strategic plan aiming at limiting the consequences of such an event. There should be regular updates of available strategic plans. Sharing experience and resources of nuclear weapon states with non nuclear weapon states would be a way to optimise resource allocation. Regular and realistic training of all organisations involved is a crucial element of medical preparedness in this field.

A common approach to addressing threats of this nature could be usefully and efficiently developed in a common, international framework. Governments need to decide whether such an approach meets their national needs, and to formulate and address the question to a competent international organisation such as the NEA.

5. Possible approaches to improve the situation

Research and planning should be organised in a transparent way both at national and at international level. International organisations should support national efforts on request by providing guidance and technical assistance. The efforts of WHO and IAEA to organise medical support through the REMPAN network should be supported and strengthened. Sharing experience and resources of nuclear weapon states with non nuclear weapon states would be a way of optimising resource allocation.

Key issues to be addressed in the planning stage of emergency preparedness are the training and protection of first-responders and of medical doctors. Emergency preparedness should include training of techniques of risk communication with the public and the media to maintain or quickly regain public confidence.

In the early phase of an accident or a radiological terrorist attack psychological support for victims can minimise major post traumatic stress disorders in the affected population. This could be achieved by networking of organisations which may be available in a country but which are normally not trained to deal with radiological events.

Pre-planning of medical follow-up of any health consequences in the affected population should be considered before hand both at national and international level including cross-border situations. In order to respond to likely political pressures, epidemiological studies should be initiated soon after such an event to acquire scientific evidence on possible long-term health effects of ionising radiation, especially cancer. Emergency planning should include the development and establishment of a strategy for retrospective dosimetry. For high exposures, individual dosimetry is required whereas group dose estimates will be sufficient for low-level exposures.

The long-term challenge in such a situation will be the rehabilitation of contaminated areas, including of course all concerns of the affected populations. To cope with this challenge requires special concepts and procedures, which go far beyond this document.

It is widely agreed that radiological events may occur.

There is a general consensus that most dispersion scenarios would not have significant public health affects, however, could cause wide-spread contamination and most likely significant public concern. More significant public health effects could, however, result from the use of large sources hidden in public places.

In preparation to address such events, it is important the have effective detection systems, and widely-applied training for early response teams. It would also be very useful to develop rapid triage techniques, as well as quick, large-scale biological dosimetry techniques for dose assessment.

It is also important to develop an international “standard” approach to post-accident health and epidemiological studies.

Finally, lessons learned from previous accidents, with respect to scientific issues, and the roles of RP professionals and their relationships with affected members of the public, should be applied to develop an effective rehabilitation strategy. Public confidence and effective provision of information will be key aspects of incident response.

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POSSIBLE AREAS OF NEW INTERNATIONAL COLLABORATIVE RESEARCH

Given important interfaces with other disciplines (for example, in medicine, the environment and malevolent acts) and shrinking radiological research communities, collaboration will be a key theme for radiological protection and its supporting science. Where appropriate, suitable collaborating organisations are suggested. However, for these initiatives to be truly successful, a useful starting point could be doing "catalogue" of existing RP research resources (principally animal study facilities, radio-biology / toxicology laboratories).

In view of the conclusions of this report, suggested collaboration is proposed in three forms: meetings, fora and discussions; establishment of information and experience exchange networks; and specific collaborative research projects.

Meetings/Fora/Discussions

1. International workshop on non-targeted effects: unified response or not – consequences for the current paradigm. In collaboration with the EC and the US DOE.

2. Individual sensitivity and risk in modern society: technical, ethical, legal issues.
   - Possible implications of individual sensitivity.
   - Individual risk assessment.
   - RP, chemical, biological, medical.
   - Genetic screening.

3. Forum on management of risks from radon isotopes.
   - Discussion of national approaches.
   - Discussion of how radon and smoking risks are addressed.
   - Include WHO programme.

4. Forum on sustainability of radioecology and radiological protection of the environment (with IUR).
   - RP and chemical aspects.
   - Waste issues (long-term).
   - Setting up international observatory of effects.

5. Forum on the limitations of the use of RP protection quantities for risk management with ICRU, ICRP (letter to recommend this discussion, offer to collaborate).
    - Use of quantities and units in radiological protection.
    - Dose response variations for internal exposures.

Establishment of information and experience exchange networks

1. An "ISOE system like" for medical exposure. Collaboration with WHO, UNSCEAR, EC work, Industry, IAEA.
    - Definition phase to begin.
    - Patient and occupational exposures.
    - Access to data/patient confidentiality.

2. An "ISOE system like" for NORM exposure? Collaboration with ILO, UNSCEAR, EC work, Industry, IAEA.

3. International data registry and assessment for environmental radiological protection, an international "Observatory" (with IUR).
    - Centralised data registry from contaminated areas, from areas of high background, from experimental investigations, also other contaminants.
    - Network of experimental facilities.
    - Network of existing research and experimental programmes (bio-geo-chemical cycles).
    - Network for database collection and assessment of environmental measurement data around nuclear installations.
    - Assess current data collection.
    - Identify additional measurements that could be added to better characterise environmental protection (as opposed to human protection).

4. Network for emergency-response for biological dosimetry in case of terrorist acts.

5. Network to integrate capabilities for collaborative animal research.
    - Standard approach to ethical approval of experiments.
    - Identification and co-ordination of capabilities.

6. Consolidation of the French-German initiative data bank on Chernobyl, for health effects, radio-ecology (and status of the sarcophagus), in collaboration with epidemiology and environmental protection programmes.
    - Discuss data collection and access rules and processes.
    - Tissue banks (follow biological example).

Collaborative research

1. Epidemiology of chronically exposed people, internal and external. Consolidation of EC programmes by cooperation with US and Japan (and others).

2. A specific sub-case of particular importance is that of paediatric exposures. These doses should be registered and made available for epidemiological studies, in that this population is at particularly elevated risk.

3. Research of links or not between molecular or cell modifications and observed pathologies. (Animal experiments and epidemiology).

4. The Ultra-Low Level Radiation Biology Laboratory, proposed by the US DOE, should be opened for international collaboration, including scientific and technical oversight, collaborative funding, and collaborative research.

5. Sound scientific evaluation of non cancer diseases by new mechanistic explanations.

6. Common definition of an international programme of Radiotoxicology linked to internal exposure.
   - Chronic exposure vs. acute exposure.
   - Biokinetics.
   - Late-effects.
   - Wider exploitation and exploration of the EC data bank (in collaboration with EC).

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CONCLUSIONS AND POSSIBLE POLICY CHALLENGES

Since its inception, radiological protection science has worked to quantify the risks of ionising radiation, and to identify the mechanisms leading to biological damage. Over the approximately 100-year history of RP science, this research work has been both proactive, addressing possible areas of new risk (e.g. early work on stochastic risks when limits were based on deterministic effects), and reactive, addressing emerging problems (e.g. work on radon).

The last 10 to 15 years of research has focused on understanding and quantifying the risks of low doses and dose rates, and on exploring mechanisms of damage. While these paths of research are far from completed, they suggest that our current models of damage may be incorrect, or at the very least not as generically applicable as we currently believe. Further, this research suggests that the tools that we are currently using to manage radiological risk, the Sievert and the LNT, may also not be supported by state-of-the-art science, or again at a minimum may not be as generically applicable is currently the case.

While there is a feeling that the current approach to radiological risk assessment and management is not under-protecting the public, workers or the environment, there is a growing view that some level of modification will be necessary. As such, it is suggested that the key challenges as outlined here should continue to be scientifically addressed, and their possible implications to radiological protection policy, regulation and application should be explored, beginning now, in order to be appropriately prepared for possible future changes.

In general, scientific evidence is questioning the universal application of a single risk assessment approach (currently the use of LNT). The report strongly supports the use of state-of-the-art scientific data and knowledge when it is applicable. This may be particularly significant for specific situations (such as site cleanup or long-term waste management) involving specific radionuclides (such as radium or plutonium) where specific risk data is available.

Non-targeted effects, adequacy of the concept of dose

While the evidence is not yet conclusive, current and further radiation biological research, in areas such as non-targeted effects, adaptive response, and dose response relationships, appears likely to lead to the formulation of a new radiation biology paradigm combining both the classical (targeted or direct) and the non-targeted (indirect) radiation effects. This could have significant implications in terms of how radiological risk is assessed. A new scientific approach, or a significant modification to the current approach, to coherent, holistic risk assessment (e.g. for all types of radiation, and all types of radiation exposure situations) may need to be developed. This could also have a significant effect on current approaches to risk management.

Radiosensitivity

Major advances in cellular and molecular biology are providing a basis for building a more complete understanding of variations in radiosensitivity within the population. Today, elevated radiosensitivity to ionizing radiation exposure is identifiable only for high levels of exposures. In the future, it is likely that individuals at increased risk for radiogenic cancer may be identified through simple, genetic screening. These developments may have important implications for the current system of dose limitation and radiation protection, particularly for workers and for medical patients.

These findings suggest:

- The need to define who is radiosensitive.
- The need to investigate whether protection would be better achieved through a single dose limit or dose limits customised to groups with differing radiosensitivity.
- The need to explore the ethical issues raised by genetic screening.

In light of the pace of these developments, it would be prudent and timely for the policy community to begin examining these implications in the near term. This issue is well suited to being addressed through broad stakeholder involvement, particularly at a formative stage. This will enable the concerns of those most affected by these developments (in particular, employers, employees and regulatory bodies) to be fully identified and accommodated within any new policy framework. Many of the issues to be addressed are common to genetic screening more generally (e.g., in other occupations, for insurance and employment purposes, etc) and benefit should be taken of developments elsewhere.

Epidemiology

Because radiation is only a weak carcinogen, large, long-term epidemiological studies are key elements in the assessment of risks. Funding of such studies (e.g. the Lifespan Study of Japanese A-bomb survivors, the study nuclear workers, radon studies, or studies of chronically exposed populations) should be long enough to allow the correct and complete collection of relevant data. Classical epidemiology will clearly not solve the issue of low-dose risks. Molecular epidemiology will be needed to address this issue.

Medical exposures

Studies of medical exposures of patients and medical workers indicate steady increases in doses. These increases support the need for better dose information (e.g. machines that are better equipped to measure and display patient exposures). This may also necessitate the implementation of a new approach, perhaps regulatory, to optimisation of exposures. Interface between medical practices and other areas should be encouraged in order to make best use of available knowledge and data.

Radiological protection of the environment

The development of radiological protection principles for the environment is a new challenge, and should not take place in isolation from other broader principles and related conceptual approaches which are either existing or under development.

Health impacts of an accident or a radiological terrorist attack

Maintaining public confidence is a critical issue when dealing with the consequences of nuclear accidents or radiological terrorist attacks. People will likely seek information and guidance from healthcare providers, who will most likely play a key role in determining how the general public will respond to a radiological malevolent event. Information provided by these organisations should not only address the consequences of high exposures but should also deal with the situation of the vast majority of people with low or no exposures. A well-organised, effective medical response system needs to be established and maintained, in order to instil hope and confidence, reduce fear and anxiety, and support the continuity of basic community functions.

Appendix 1

MEMBERSHIP OF THE EGIS EXPERT GROUP

Canada
R. Mitchel, AECL

Finland
S. Salomaa, STUK

France
M. Bourguignon, DGSNR
F. Bréchignac, IRSN
A. Flury-Hérard, CEA
H. Métivier, IRSN (Chairman)
F. Paquet, IRSN
M. Vrijheid, IARC

Germany
W. Weiss, BfS
M. Zankl, GSF

Japan
† M. Doi, NIRS

Spain
E. Vano, Madrid University

United Kingdom
N. Priest, Middlesex University

USA
A. Bouville, NRC
K. Mossman, Arizona State University

European Commission
G.N. Kelly

OECD/NEA Secretariat
B. Ahier
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T. Lazo

Appendix 2

GLOSSARY

AT: Ataxia telangiectasia; patients having ataxia-telangiectasia demonstrate increased chromosome breakage in lymphocytes and fibroblasts. The increase in risk dying of cancer is greater than that for a normal individual.

BCRA1, BCRA2:

CFC (chloroflurocarbons): a family of chemicals that was used for many years as propellants for aerosols and as refrigerant liquids. These compounds were originally regarded as essentially harmless, being largely inert and not demonstrating any (direct) toxicity towards humans, animals or plants. However, they were banned worldwide after realising that they indirectly caused harm to all life forms, through chemical interaction with the stratospheric ozone layer, resulting in its depletion and consequent loss of function as a shield from UV radiation for the earth's surface and lower atmosphere.

Conformal therapy: A modality of radiotherapy that delivers the required dose to a volume that closely conforms to the shape of the patient's tumour while sparing normal adjacent tissue. It requires to accurately identify both the shape and location of the tumour and to distribute the dose as close as possible to the target.

CT: Computer Tomography. A non-invasive medical imaging technique that takes cross-sectional images of the body using X-ray. Three-dimensional pictures can be reconstructed.

DDREF: Dose and Dose Rate Effectiveness Factor. A factor used to adjust for the different biologic effect with different doses and dose rate of low-LET radiation from those at which original data was obtained.

EC: the European Commission was created to represent the European interest common to all Member States of the Union. So that it can play its role as guardian of the Treaties and defender of the general interest, the Commission has been given a right of initiative in the legislative process, proposing the legislation on which the European Parliament and the Council decide (ec.europa.eu/index_en.htm)

ICRP: the International Commission on Radiological Protection is an independent Registered Charity, established to advance for the public benefit the science of radiological protection, in particular by providing recommendations and guidance on all aspects of protection against ionising radiation. (www.icrp.org/)

ICRU: International Commission on Radiation Units and Measurements,(ICRU) was established in 1925 by the International Congress of Radiology. Since its inception, it has had as its principal objective the development of internationally acceptable recommendations regarding (1) quantities and units of radiation and radioactivity; (2) procedures suitable for the measurement and application of these quantities in diagnostic radiology, radiation therapy, radiation biology, and industrial operations; and (3) physical data needed in the application of these procedures, the use of which tends to assure uniformity in reporting. The ICRU endeavours to collect and evaluate the latest data and information pertinent to the problems of radiation measurement and dosimetry, and to recommend in its publications the most acceptable values and techniques for current use (www.icru.org/)

IEC: International Electrotechnical Commission, founded in 1906 the IEC is the leading global organization that prepares and publishes international standards for all electrical, electronic and related technologies. These serve as a basis for national standardization and as references when drafting international tenders and contracts. Through its members, the IEC promotes international cooperation on all questions of electrotechnical standardization and related matters, such as the assessment of conformity to standards, in the fields of electricity, electronics and related technologies. The IEC charter embraces all electrotechnologies including electronics, magnetics and electromagnetics, electroacoustics, multimedia, telecommunication, and energy production and distribution, as well as associated general disciplines such as terminology and symbols, electromagnetic compatibility, measurement and performance, dependability, design and development, safety and the environment. www.iec.ch/

ILO: International Labour Organisation, The International Labour Organization is the UN specialized agency which seeks the promotion of social justice and internationally recognized human and labour rights. It was founded in 1919 and is the only surviving major creation of the Treaty of Versailles which brought the League of Nations into being and it became the first specialized agency of the UN in 1946. The ILO formulates international labour standards in the form of Conventions and Recommendations setting minimum standards of basic labour rights: freedom of association, the right to organize, collective bargaining, abolition of forced labour, equality of opportunity and treatment, and other standards regulating conditions across the entire spectrum of work related issues. www.ilo.org/

IMRT: Intensity Modulated Radiation Therapy. A type of radiation therapy that uses computer-generated images to match radiation to the size and shape of a tumour by varying the beam intensity across each treatment field to deliver a higher radiation dose to a tumour with less dose to nearby healthy tissue.

ISOE: The Information System on Occupational Exposure, organised jointly by the NEA and the IAEA, is a network of RP experts from nuclear power stations and national regulatory organisations that focuses on the collection and assessment of occupational exposure data, and the exchange of experience and information relating to occupational exposure management. www.isoe-network.net/

IUR: International Union of Radioecology, a non-political and non-profit scientific organisation for professional radioecologists seeking to promote interdisciplinary information exchanges and research advancements in areas that involve radioactivity and the environment with a special dedication to risk assessment. www.iur-uir.org/

LET: linear energy transfer of charged particles in a medium, the quotient of dE by dl, where dE is the energy lost by a charged particle in traversing a distance dl (or: *Amount of energy lost by ionising radiation by way of interaction with matter for each unit of path length through the absorbing material).* X-rays, γ radiations are called low LET radiations, α particles height LET radiation.

LNT: Linear No-threshold; assumption selected to only built the radiological protection system, according to which any amount of radiation causes a biological effect, its frequency depends on the amount.

Mayak workers: The “Mayak” Production Association (MPA) is the first nuclear plant constructed in Russia for the production of plutonium for military purposes. This plant is now reprocessing irradiated fuel of research reactors and transportation facilities. Radiation accident occurred the 29 September 1957, It referred as index 6 or 7 on the International INES scale.

NORM: Naturally Occurring Radioactive Material, referring generally to uranium and thorium chain radionuclides found in nature (e.g. radon in soils), or found in materials or products that have been processed for uses not related to the radioactivity they contain (e.g. non-uranium mining tailings, gypsum containing thorium and its decay products, etc.). These processed materials are sometimes referred to as TENORM (Technically Enhanced NORM).

PET: Positron emission tomography. A medical imaging technique that gives a three-dimensional picture or sectional view of the body, reconstructed using the radiation emitted by a positron-emission radioactive material previously administered to the patient.

RBE: Relative biological effectiveness, ratio of the absorbed dose of a radiation of reference, generally that of the ^{60}Co or that of X-rays of high energy (> 1 MeV), with that of the radiation studied, necessary to obtain the same biological effect.

REMPAN: the Radiation Emergency Medical Preparedness and Assistance Network of the United Nations World Health Organisation. The network has 27 institutes worldwide and promotes medical preparedness for radiation accidents and radionuclear threats worldwide; in the event of such an incident, the network can provide assistance and advice, and assist in follow-up studies and rehabilitation.

SETAC: Society of Environmental Toxicology and Chemistry, a non-profit, worldwide professional society which promotes the advancement and application of scientific research related to contaminants and other stressors in the environment, education in the environmental sciences, and the use of science in environmental policy and decision making.

SNP: Single nucleotide polymorphisms

Techa River Basin: Disposals of liquid radwastes into the Techa River during the Mayak plant commissioning were a forced measure

inspired, first of all, by the need to start-up as soon as possible the first in the USSR plutonium plant in 1948. Radioactivity was beginning to arrive in the Techa River in June 1948. Owing to the control of the lake runoff, water containing radioactivity periodically entered the Techa River. It is estimated that during the 1949-1956 period 2.10^{-3} PBq of α-emitters and 110 PBq of β-emitters was released to the Techa River.

UNSCEAR: United Nations Scientific Committee on the Effects of Atomic Radiation. was established by the General Assembly of the United Nations in 1955. Its mandate in the United Nations system is to assess and report levels and effects of exposure to ionizing radiation. Governments and organizations throughout the world rely on the Committee's estimates as the scientific basis for evaluating radiation risk and for establishing protective measures.
www.unscear.org/unscear/index.html

WIPP: Waste Isolation Pilot Plant in Carlsbad, New Mexico, USA; a deep geological repository for disposal of transuranic (long-lived, alpha-emitting) radioactive waste left from the research and production of nuclear weapons. Located in a remote desert of the southwestern U.S., project facilities include disposal rooms mined 2 150 feet (655 meters) underground in a 2 000-foot (610 meters) thick stable salt formation. WIPP began operations in March 1999.

WNA: World Nuclear Association, The World Nuclear Association is the global organisation that seeks to promote the peaceful worldwide use of nuclear power as a sustainable energy resource for the coming centuries. Specifically, the WNA is concerned with nuclear power generation and all aspects of the nuclear fuel cycle, including mining, conversion, enrichment, fuel fabrication, plant manufacture, transport, and the safe disposition of spent fuel. www.world-nuclear.org/

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Scientific Issues and Emerging Challenges for Radiological Protection

Scientific knowledge is constantly evolving as more advanced technologies become available and more in-depth research is carried out. Given the potential implications that new findings could have on policy decisions, in 1998 the NEA Committee on Radiation Protection and Public Health (CRPPH) performed a survey of state-of-the-art research in radiological protection science. This study suggested that, while the current system of radiological protection was well-underpinned by scientific understanding, growing knowledge in several areas could seriously impact policy and regulation. Ten years later, the CRPPH has again performed a survey of state-of-the-art research which reiterates and clarifies its earlier conclusions.

This report summarises the results of this latest CRPPH assessment of radiological protection science. Specifically, it explains that knowledge of non-targeted and delayed effects, as well as of individual sensitivity, have been significantly refined over the past ten years. Although at this point there is still no scientific certainty in these areas, based on the most recent studies and results, the report strongly suggests that policy makers and regulatory authorities should consider possible impacts that could arise from research in the next few years. Further, the report identifies research areas that should be supported to more definitively answer scientific questions having the most direct impacts on policy choices.

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