What radiation protection can request from radiation research

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R&D and Policy: a continuous loop

- **Research : production of new data**
- **Follow up and evaluation of the data**
- **Implications of new data: regulation, guidance, policy, other R&D**
- **Residual uncertainties, research needs and priorities**

Rad.Research and Rad.Protection

There are in practice **too few** interactions between those performing research, and even those planning and financing research,

and those interested in radiation protection (regulators, experts, practitioners, …).

The Art 31 RIHSS initiative

- Article 31 Group of Experts: Group of independent scientific experts referred to in Article 31 of the Euratom Treaty, that assist the European Commission in the preparation of the BSS
- RIHSS : Art 31 WP on Research Implications on the Health and Safety Standards
- ***Scientific RIHSS Seminars*** *(*yearly):
  - Leading experts summarize the **state -of- the -art**
  - Invited experts act as *peer reviewers*
  - **Discussion of the potential regulatory implications**

Bridge RP/Research

The RIHSS Seminars: often early warnings

- 1997: Radon
- 1998: Thyroid diseases and lessons from Chernobyl
- 1999: Genetic susceptibility
- 2000: Cancer risks at low dose
- **2001: In utero exposure in early phases of pregnancy**
- 2002: IR and breast cancer
- 2003: Medical overexposures
- 2004: Critical review ICRP draft 2005 recommendations
- 2005: Alpha-emitters: assessment of risk
- **2006: New insights in radiation risk and BSS *(incl: cataracts)***
- 2007: Tritium and low energy beta emitters
- **2008: Emerging evidence for radiation induced circulatory diseases**
- 2009: Childhood leukaemia – mechanisms and cause
- 2010: Issues with internal emitters
- 2011: Individual radiosensitivity

Proceedings of the EU RIHSS Seminars

Available on the web site of the EC:

http://ec.europa.eu/energy/nuclear/radiation_protection/publications_en.htm

Radiation Protection Serie

Include a chapter highlighting potential implications

Rad.Research and Society

There are even fewer interactions between the research community and the (stakeholders in the) society.

This is particularly so with regard to radiobiology, whose language and approach is often totally incomprehensible even for educated persons.

Societal requirements towards the research (and experts') community

Besides the obviously necessary competence, implicit assumption (and request) of:

- **neutrality**
- **objectivity**
- **priority concern about population's health and welfare**.

And, more recently,

- **participation**

This is far from being evident…

Neutrality?

Research depends on its financing and this financing – and the linked conditions- comes often from national or international institutions with obvious conflicts of interest.

Self-censorship is the easiest way for the researcher to avoid problems….

Scientific independence is a moral duty but also a difficult challenge.

« Purely scientific »?
Ethical issues within science

Science cannot avoid ethical issues, some of them being deeply imbricated (and often not seen) *within* the area of the scientific work.

Some examples are: selection of the sources (beliefs, hidden agendas, cognitive consonance with dominant paradigm), strive for conformity (club spirit, pressure of the peers), rightness of the assessments (value judgements, like on “importance” of the risk), management of uncertainties (more or less precaution) …

Precaution in Science: relevant!

Although frequently limited to the decision-making processes in situations of uncertainty, the precautionary approach is also relevant and appropriate in research.

As underlined in the COMEST report from UNESCO, the precaution approach in science includes:

- a systematic search for surprises ("**thinking the unthinkable**"), particularly for possible long term effects,
- a responsiveness to the first signals ("**early warnings**")
- and, last but not least, a **focus on risk plausibility rather than on hard evidence**.

« Scientific cautiousness » and precaution:

- The « cautiousness » for many scientists: their main concern is to avoid concluding that a causal relationship exists before it is firmly proved.

- The « cautiousness » expected from society in a rapidly moving world: the main concern should be to protect health; when there is scientific plausibility of the existence of a risk of serious harm (even if there is still uncertainty), the scientific community should alert/inform the policy-makers and stakeholders (precautionary approach).

Missed early warnings

Recent developments regarding the late recognized radiation effects of low to moderate doses on the lens of the eye and on the circulatory system are good illustrations of a lack of vigilance and responsiveness regarding early warnings that were described many years ago.

Radiation induced cardiovascular effects

Why were CV effects “recognized” **so late?**

- Too slow “digestion” of new scientific results by the existing assessment organizations?
- Resistance to change of paradigm?
- Mainly excessive focus on hard evidence and wrong comprehension of precautionary approaches

Precautionary measures were/are easy to take!

- Adaptation of radiotherapy protocols (breast cancer)
- Management of cumulative high diagnostic exposures
- Use of dose constraints to limit cumulative organ doses of workers (draft EU BSS)

Some current concerns

Irradiation in utero in early phases

(2001 RIHSS Scientific Seminar; 2011 SCK/FANC Symposium)

- Pre-implantation period: Current view: possible death of embryo above 0.1 Gy; if not killed the embryo develops normally; no congenital malformation
- New (not always!) data: Irradiation in animals during the pre-implantation period **can** induce congenital malformations (sometimes non lethal) or genomic instability, with or without genetic factors of predisposition; zygote stage more sensitive; thresholds uncertain; similar observations with chemicals
- Early organogenesis (incl. gastrulation): more congenital malformations in **genetically susceptible mice** (alteration of genes involved in DNA-damage response)
- Mechanism: persistence of **unrepaired or misrepaired DNA-damaged cells("teratogenically damaged cells")** (instead of the classical loss of cells)

Irradiation in utero: Thinking the unthinkable (1)

The same could exist in humans.

There could be for some inviduals a higher risk of radiation-induced malformations or lower thresholds and

the risk could also exist during the “safe” periods of pre- and

early post-implantation

Irradiation in utero: Thinking the unthinkable (2)

There are many genes implicated in the DNA-damage response and involved in the genetic susceptibility to cancer induction by irradiation ; if the mechanisms are similar (misrepair), it is plausible that a genetic susceptibility to the radiation-induction of congenital abnormalities or other non-cancer effects is associated with the human genotypes leading to cancer-proneness .

The use of a generally applicable threshold dose (like the 100 mSv figure) for the radiation induction of malformations or other non-cancer effects could then be an unjustified simplification.

Irradiation in utero

There are **still many other uncertainties**: radiation effects on gene expression, subtile effects or long term effects of NCS irradiation, internal (OBT ..,) and chronic exposures, ….

Unsuspected low dose effects from in utero exposure are currently somewhat out of concern, but could cause bad surprises in the future.

The potential implications are important.

More research is needed in this field.

Hereditary effects

Long term hereditary effects

are currently somewhat out of concern,

but could also cause bad surprises in the future.

Genetic risk **up to the 2d generation** (continuing exposure low dose-low LET) UNSCEAR 2001 / UNSCEAR 93

- Number of cases per Gray per million progeny: 6950-11400 (U93: 4640)
  - 2050-4000 dominant/X-linked diseases (U93:4300)
  - 500-2400 chronic multifactorial diseases (U93:ne)
  - 4400-5000 congenital abnormalities (~U93: 340 chromosomal diseases)
- Total = 0.7-1.1 % Sv^{-1} (U93: 0.46 % Sv^{-1})
- On comparable bases, the genetic risk is not diminished

Genetic risk at **equilibrium**
(continuous exposure low dose-low LET)
UNSCEAR 2001 / UNSCEAR 93

- U93: **1.2 %** per Gy (without multifactorial diseases and congenital abnormalities)
- U2001 (considered as pure assumption): in % per Gy
  - dominant/X-linked diseases : 0.25 - 0.5
  - recessive diseases: = 0.11 - 0.22
  - chronic multifactorial diseases = 1.3 - 5.8
  - congenital abnormalities: ?
  - Total: **1.65 - 6.5% per Gy**
- On comparable bases, the genetic risk is not diminished

Genetic risk:
Some radiobiological issues

- The complexity of the genome machinery: new data regarding epigenetic effects, transgenerational mutagenesis, ….
- The possible differences in genetic changes between external and (chronic) internal exposures
- The question of the minisatellite mutations:
  - Sometimes « associated » with genetic diseases (then possibly not pure markers without health significance)

« Lack of human (health) evidence does not mean evidence of lack of effect »

Dutrillaux views
(RIHSS seminar 2004)

- *According to him, the main problem is the radiation induction of small deletions leading to recessive mutations and diseases of which the phenotypes might frequently not be recognized by the physicians. Such cumulative small genetic disorders may propagate in the future generations with the risk of leading to more important pathological consequences.*
- Data on atomic bombing survivors and patient progeny have thus a major flaw: several generations are necessary for the passage to homozygoty of induced recessive mutations. There is not a sufficient delay to observed their expression today.

Hereditary effects: thinking the unthinkable

Considering the "*numerous uncertainties*" put forward by UNSCEAR/ICRP for not estimating the long term genetic risk, it seems paradoxical to recognize that considerable uncertainties still exist in this field, while concluding that enough is known as regards the mechanisms of radiation-induction of genetic effects to allow minimizing the possibility of significant long term risks.

Do we know enough to draw final conclusions?

Should we not be more “cautious”?

Working Party on Research Implications on Health and Safety Standards of the Article 31 Group of Experts

Recent scientific findings and publications on the health effects of Chernobyl

RADIATION PROTECTION NO 170

2011

Birth defects

- not dealt with in UNSCEAR 2011…..
  - Reason: prevalence at birth of the malformations recorded in the registry in Belarus: similar positive trend in areas of low and high contamination
- Brussels 2006 Symposium, Budapest 2007 Eurocat workhop :
  - From oblasts to districts
  - Clear excess of the congenital anomalies under study in the highly contaminated districts ***during the three first years*** (mainly polydactyly, reduction defects of limbs, multiple congenital malformations)

Birth defects: recent observations

- Wertelecki 2010 (University of South Alabama)
  - Ukraine oblast of Rivne: one of the populations most exposed to chronic low-dose radiation from Chernobyl
  - births between 2000 and 2006: overall rate of neural tube defects (including spina bifida) among the highest in Europe
  - limitations of this study: lack of data regarding levels of low-dose radiation, diet, possible folate deficiency, prenatal alcohol exposure.
- Dancause 2010: exposure routes in Rivne
  - Alcohol intake was low
  - Wild foods, especially mushrooms and berries, and locally produced foods, especially milk related, were major radiation exposure routes

Children's morbidity

- **Many claims** concerning the health of children in the contaminated territories around Chernobyl, which seem to suffer from multiple diseases and co-morbidities with repeated manifestations (compilation in Yablokov 2009)
- **Reports from international organizations did not give until now much interest: "psycho-social"**
- **But** most studies not available in English and not translated!

Although many studies do not meet the scientific and editorial criteria generally required in the Western peer reviewed literature, scientists cannot refuse to take the available information into account or at least to verify it !

Children's morbidity: recent initiatives

- Series of IRSN studies:
  - Rats exposed to ^{137}Caesium contamination during several months through drinking water (150 Bq/day/animal: comparable with a typical low intake in the contaminated territories (Handl's: 100 Bq/day but with variations from 20 up to 2000 as when excess consumption of mushrooms)
  - *Although the animals tested in theses studies did not show induced clinical diseases, a number of unexpected biological effects were observed on various systems*: increase of CK and CK-MG, decrease of mean blood pressure and disappearance of its circadian rhythm; EEG modifications, perturbations of the sleep-wake cycle, neuro-inflammatory response, particularly in the hippocampus, etc
  - currently IRSN clinical research (EPICE) on children in the area of Bryansk, particularly on cardiac rhythm and ECG perturbations. First results would be available in 2013

Children's morbidity: recent studies

- Series of longitudinal studies initiated recently in Ukraine in conjunction with the US University of South Carolina:
  - Stepanova 2008: 1993 to 1998: significant reduction in red and white blood cell counts, platelet counts and haemoglobin with increasing residential soil contamination (cfr Techa River)
  - Svendsen 2010 : 1993 to 1998: spirometry: statistically significant evidence of both airway obstruction and restriction with increasing soil contamination (immune mechanism?)

- **"The optimism of the UN reports may be based on too few studies published in English, conducted too soon after the event to be conclusive".**

Children's morbidity and internal exposures: thinking the unthinkable

We need further good quality research on morbidity in children living in contaminated territories (ARCH).

This may have major influence on our evaluation of the radiotoxicity, **particularly for children and infants**, of major radioisotopes susceptible to cause **chronic internal exposures** of the population.

A major underlying issue is

the **adequacy of the effective dose as risk indicator**.

Some related Art 31 MEDWP concerns and demands

- Epidemiological studies on non cancer effects in diagnostic and interventional imaging, particularly in children.

- Development of user-friendly indicators of dose and risk to support justification and optimization of medical exposures. (Brussels 2009 workshop on justification: AAA)

Objectivity and the club spirit

Science cannot escape from some intrinsic subjectivity. In an attempt to control this, one often appeals to consensus as a guarantee for objectivity.

Doing so, one forgets that scientists, coming from the same melting pot, spontaneously favour cognitive consonance and share the same interpretative language, the same paradigm (a whole of reference presuppositions, *which are often unconscious*).

On these grounds, interpretations of reality are not seen by them as subjective and have in their eyes an indisputable value

A broader approach is needed when risk problems are characterised by

complexity

uncertainties

value judgements

The stakeholder opening

Stakeholder involvement is the appropriate remedy for avoiding club thinking, allowing new views and perspectives to emerge and favouring creative thinking about mechanisms, scenarios or implications.

But…

Unfortunately stakeholder involvement is currently often just a façade. The invited stakeholders and experts are very few and their opinion often considered as irrelevant and hardly taken into account: the real experts and the others…

MELODI mission: a challenge!

1. **To impulse low dose risk research in Europe through an open and integrative SRA approach**

2. **To create a forum for dialogue with EU institutions and stakeholders,**

3. **To interface with international partners (WHO, IAEA, USA, Japan,…)**

Conclusion

There are implicit societal requirements towards the research (and RP!) community. Besides the obviously necessary competence, society asks for true independency, priority concern about population's health and welfare, responsiveness to "early warnings" (focusing on risk plausibility rather than on hard evidence) and systematic search for surprises particularly for possible long term effects ("thinking the unthinkable"). Last but not least, society requests real participation through stakeholder involvement processes, inviting scientists to more modesty and to look out of their box.