Effects of radiation exposure on offspring and next generations:

Summary of a Workshop jointly organised by ICRP, MELODI and ALLIANCE

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Sixth IRPA European Congress on Radiation Protection, Budapest, 2022

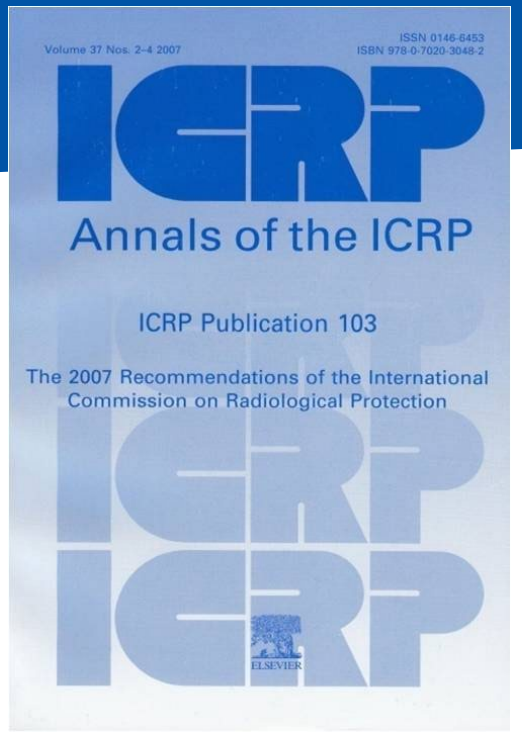
ICRP

Dominique Laurier

Workshop in Budapest

- **52 participants**
  (29 on site)
- **21 countries**
  (UK, France, Finland, USA, Singapore, Japan, Russian Federation, Canada, Sweden, Italy, Spain, Germany, Belgium, Australia, Ireland, Hungary, Romania, Portugal, Czechia, Ukraine, the Netherlands)
- **Budget ≈ 35k€**
- **1 Joint session with the IRPA congress**

Current situation



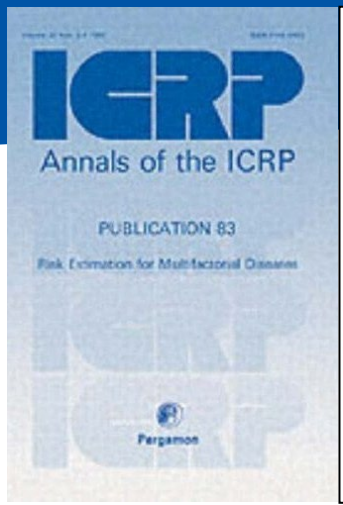
- Last recommendations in 2007: ICRP Publication 103

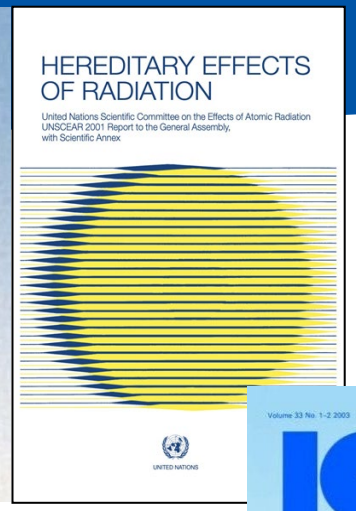
- Effects of in utero exposure to radiation
- Heritable effects of exposure to radiation
- Transgenerational effects on non-human biota not considered in the current Radiation Protection system

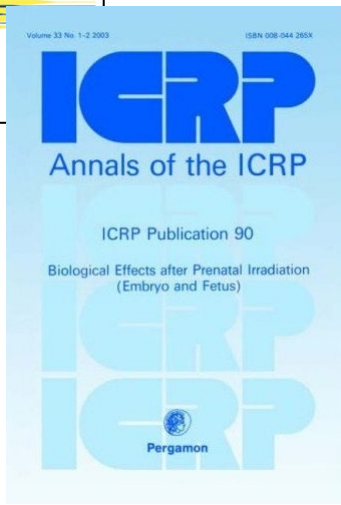
➡ **A revised assessment of the effects of ionising radiation in offspring and next generations is needed to inform the future revision of the system of radiological protection**

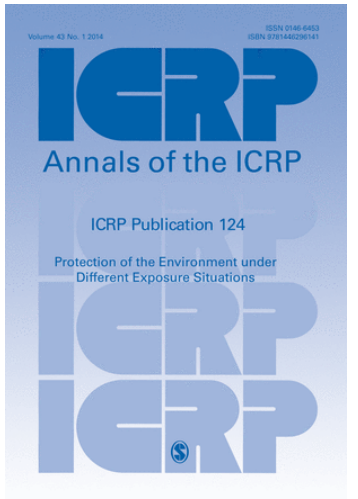
Objectives

- **Review of preconceptional effects due to the exposure of parents** (last update 1999-2001)
- **Review of postconceptional effects of radiation due to the exposure of the embryo and fetus** (last update 2003)
- **Review knowledge on transgenerational effects in wild species** (last update 2014)
- **Provide advice about the level of evidence and consideration of these effects in the system of radiological protection for humans and non-human biota**









Workshop in Budapest

Groups for Topical discussions

A Hereditary and epigenetic effects due to exposure of germ cell line (pre-conceptional exposure)

B Effects arising from exposure of the embryo and fetus (post-conceptional exposure)

C Transgenerational effects in biota

D Potential impact on the System of Radiological Protection

Chairs, Co-chairs and rapporteurs

A. Sisko Salomaa, Manoor Prakash Hande, Fieke Dekkers, Katalin Lumniczky
B. Richard Wakeford, Kimberly Applegate, Ämilie Louize Degenhardt Erbe, Liudmila Liutsko
C. Christelle Adam-Guillermin, Nele Horemans, Shayen Sreetharan
D. Dominique Laurier, Thierry Schneider, Friedo Zolzer, Aidana Amrenova

A. Preconceptional exposure of germ cells

New developments since 2007

Epidemiology:

- Re-analysis of A-bomb survivor studies: consistent indications for effects, on malformations, pregnancy outcomes but not significant
- Trio studies: No obvious effects on germ cells.

Epigenetics:

- Young and complex research area; uncertain contribution for future generations.
- Too early for risk estimates in future generations.
- Look beyond radiation science and study effects on somatic cells

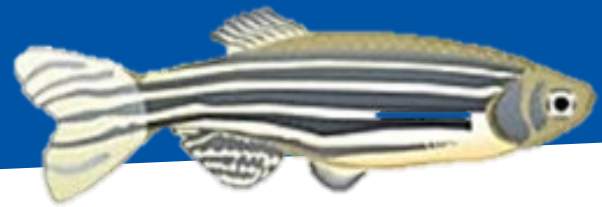
Knowledge gaps identified

- Whole genome studies: continue in trio studies, also in mice (use suitable methods to detect radiation effects: deletions!) (+ big data analysis)
- Dosimetry
- Variation in dose, dose rate (acute/chronic), internal/external, radiation quality, in trio studies and animal studies
- Consider paternal and maternal exposure, 3 generations in humans.
- In addition to occupational and environmental exposure, take into account cancer patients
- Address time gap between exposure and conception to identify sensitive stages in oogenesis, spermatogenesis.
- Confounders (including lifestyle) and background rates
- Consider all outcomes, also those with uncertain relevance for detriment
- Doubling dose: requires collection of evidence beyond current discussion
- For epigenetic effects: collaboration with non-radiation research to understand mechanisms
- Transferability from animals to humans, mathematical models
- Hypothesis/question driven studies to make results more interpretable

B. Effects of Exposure *in utero*

- **Antenatal exposure**
  - From the point of conception to the time of birth: for humans, about 40 weeks
- **Encompasses effects**
  - On the conceptus, embryo and through to the late fetus
- **Stochastic risks**
  - Risks of **cancer** and **hereditary effects** must be considered, as for postnatal exposure
  - But the magnitude of these risks may well vary with gestational age
- **Tissue reactions**
  - **Teratogenic** (developmental) effects, such as congenital malformations
  - Risk will vary with gestational age

C. Effects on non-human biota

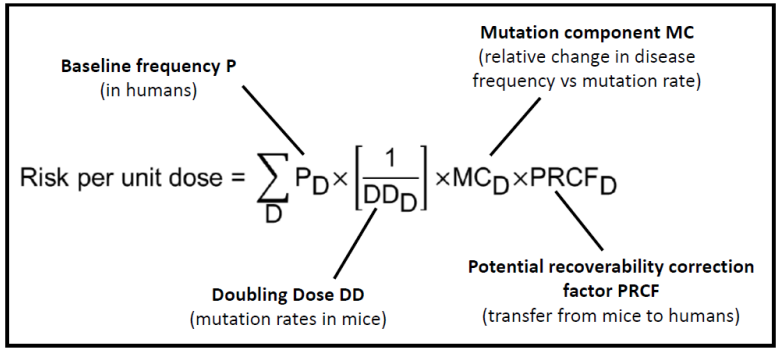


- **Consideration of radiation effects on biota:** reports (UNSCEAR 2008; ICRP Pub108 and 124) and Derived Consideration Reference levels for environmental radiological protection (TG99), but data on heritable effects is not included in the recommendations yet
- **Generation times** vary a lot in animal and plant species (life cycle of ~20 days for worms, vs > 1000 years for some trees) and exposure times of biota are long in contaminated areas
  - Multigenerational: same irradiation pattern (transient, seasonal or chronic) for each generation
  - Transgenerational: measuring an effect in an organism where no cell has been exposed to irradiation after parental exposure
- **Environmental perspective**
  - Are there ecologically relevant molecular effects impacting populations ?
  - How to take into account the historical dose ?
  - How many generations should be studied/monitored ?
  - Are these changes reversible ?
  - To what extend are these findings general for all biota or even for human ? (zebrafish and C. elegans have ~70% genetic similarity to humans)

D. Implications for the RP system

Impact on the assessment of harmful radiation-induced effects on human health

- Impact on the calculation of radiation detriment
- Impact on the characterization of tissue reactions associated with in utero exposure



Impact on operational radiological protection

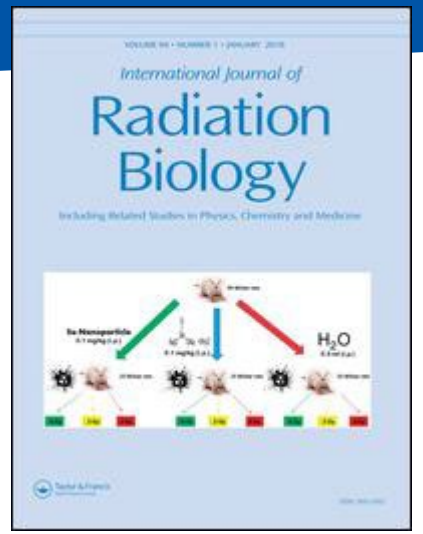
- Exponential rise in medical exposures pre-conception and post conception
- Concerns about potential effects from public, workers and patients
- Operational issues in medical radiological protection
- Ethical aspects

Consideration of effects on non-human biota in the system of radiological protection

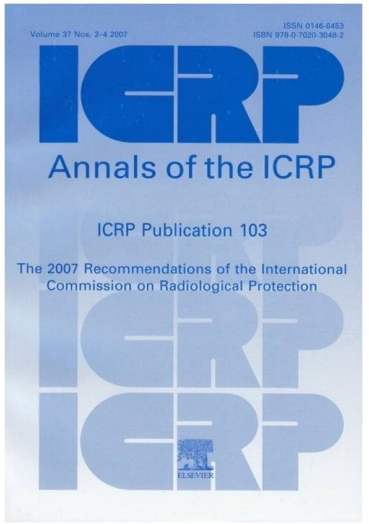
Perspectives

Special Issue in preparation

International Journal of Radiation Biology
Guest Editors: Manoor Prakash Hande, Ignacia Tanaka
About 15 articles expected



Contribution to the work of ICRP TG121, and *in fine* to the preparation of the next general recommendations of the ICRP



Acknowledgements

Warm thanks to

MELODI, ALLIANCE and ICRP for financial support,

the organiser of the IRPA Europe 2022 congress for hosting us as a satelitte workshop,

the Workshop participants,

the members of the ICRP TaskGroup 121,

all the persons involved in the organisation of the workshop
and in the preparation of these slides,

and the very active mentees (Aidana Amrenova, Ämilie Louize Degenhardt Erbe,
Sara de Souza Zanotta Dumit, Liudmila Liutsko, Shayen Sreetharan)

Thank you for your attention