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
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

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<td>Hereditary and epigenetic effects due to exposure of germ cell line (pre-conceptual exposure)</td>
<td>Effects arising from exposure of the embryo and fetus (post-conceptual exposure)</td>
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<td>Transgenerational effects in biota</td>
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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 extent 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
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Sara de Souza Zanotta Dumit, Liudmila Liutsko, Shayen Sreetharan)
Thank you for your attention