How is STUK responding to emerging challenges?

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Activities and milestones in response to emerging challenges

- Lessons from Chernobyl - STUK as WHO Collaborating Centre
  - thyroid cancer in children - a sensitive subpopulation
  - WHO Guidelines on Stable Iodine Prophylaxis
- Scientific breakthroughs on non-targeted effects
  - delayed cell death (Seymour et al. 1986)
  - genomic instability (Kadhim et al. 1992)
- Organising international workshops and training courses
- STUK research priorities
- Coordination of international research projects
- Contribution to international research strategy
The classical paradigm in radiobiology - the basis of radiation-induced health effects

- Cancer
- Hereditary effects

DNA damage induced at the time of exposure

Mutation fixed in the first cell division (misrepair of damage)

Clonal proliferation

Health Effects
Genomic instability

The progeny of irradiated cells show

• occurrence of new aberrations and/or new mutations

• lethal mutations (delayed cell death)

These non-clonal effects occur in cells that have never been irradiated
International Workshop on Public Health Aspects of Radiation-Induced Genomic Instability

Helsinki 25-28 October 1995

STUK and WHO
Bystander effect

Mutation and cell killing seen in cells that were not directly hit by radiation but were nearby.

These effects occur in cells that have never been irradiated.
Minisatellite mutations and biodosimetry of population around the Semipalatinsk nuclear test site (SEMIPALATINSK)

- coordinated by STUK 1998-2000
- INCO COPERNICUS programme
- Kazakhstan, UK, Finland
- transgenerational effects after paternal exposure
- three-generation study
- minisatellites are non-coding DNA repeat sequences; mutations scored as changes in repeat number
Genomic instability and radiation-induced cancer (RADINSTAB) 2000-2003

- coordinated by STUK
- 5th Framework Programme, Euratom
- 9 European partners from Finland, UK, France, Germany, Sweden, Ireland
- induction and transmission of genomic instability
- relationship to radiation dose and quality
- delayed gene expression
- genotype differencies
RISC-RAD Training Course: Non-targeted effects of ionising radiation

14-16 February, 2005
Helsinki
Non-targeted effects of ionising radiation
Integrated Project, 2006-2010
General information

• Start date of the project: 1 September 2006
• Duration: 48 months
• 22 partner organisations
• Coordinating organisation: STUK - Radiation and Nuclear Safety Authority
• Project coordinator: Prof. Sisko Salomaa
• EURATOM Specific Programme for Research and Training on Nuclear Energy, 6th Framework Program
• Total eligible costs: 11.89 M€
• EC contribution: 6.33 M€
System of radiation protection

- Knowledge of radiation risk is based on direct epidemiological evidence, as well as scientific study of radiation biology
- The system is designed to protect against both deterministic and stochastic effects
- A linear, non-threshold (LNT) dose-response relationship is used for all long-term health effects (e.g. cancer, genetic effects)
- A dose and dose-rate correction factor is used to relate the effects of acute exposures to chronic exposures (DDREF)
- Radiation dose is used as a surrogate for risk
- The effects produced by different types of radiation are qualitatively the same
- Doses can be summed to predict overall risk
Concept of dose as surrogate of risk

LNT and radiation protection

• a linear dose response means that every increment of dose and the associated risk can be assessed separately, irrespective of prior or future doses, as long as doses are below deterministic effects
• a fixed dose increment is always associated with the same additional risk
• doses received by an individual at different time points can be summed up (cumulative dose)
• (collective dose can be used to predict risk at the population level)
Low-dose effects

- **targeted effects**: classical effects, dominant at high doses
- **non-targeted effects**: bystander genomic instability

Graph showing the relationship between dose and effects:
- Vertical axis: Effects
- Horizontal axis: Dose

Increasing dose leads to an increase in targeted effects and non-targeted effects. Non-targeted effects show a more gradual increase compared to targeted effects.
Non-targeted effects may be important modifiers of risk at the low dose region.
A new paradigm of Radiation Biology

Targeted effects • DNA damage occurs during or very shortly after irradiation of the nuclei in targeted cells • The potential for biological consequences can be expressed within one or two cell generations

Non-targeted effects

New evidence
• Bystander effect • Genomic instability • Adaptive response • Clastogenic factors • Delayed reproductive death • Induction of genes by radiation • Premature differentiation • Low dose hypersensitivity • Abscopal (out-of-field) effects

Classical paradigm of radiation biology

• DNA damage occurs during or very shortly after irradiation of the nuclei in targeted cells • The potential for biological consequences can be expressed within one or two cell generations
Paradigm shift

Classical paradigm

- DNA-targeted
- cells considered as isolated units
- clonal effects
- linear / linear quadratic dose response
- classical radiation biology (effects on DNA)
- physics, biophysics

New evidence

- non-targeted
- cells are communicating
- tissue responses
- non-clonal effects
- plateau-like dose response (on/off)
- need for new methodological approaches
- biology, biochemistry
General objectives of the NOTE IP …

• To investigate the mechanisms of non-targeted effects, in particular, bystander effects, genomic instability and adaptive response

• To investigate if and how non-targeted effects modulate the cancer risk in the low dose region

• To investigate if ionising radiation can cause non-cancer diseases or beneficial effects at low and intermediate doses

• To investigate individual susceptibility and other factors modifying non-targeted responses
General objectives of the NOTE IP

• To contribute to the conceptualisation of a new paradigm in radiation biology that would cover both the classical direct (DNA-targeted) and non-targeted effects.

• To assess the relevance of non-targeted effects for radiation protection and to set the scientific basis for a modern, more realistic, radiation safety system
NOTE website

http://www.note-ip.org

What is NOTE
The NOTE (Non-targeted effects of ionising radiation) project aims to expand the current understanding of health effects caused by low-level doses of ionising radiation. The key focus of the research programme is the possible health consequences of exposures to small radiation doses which have not been investigated sufficiently so far. Read more

What's new
Welcome to updated NOTE website.

NOTE Newsletters will consist of NOTE-related new materials intended for members of the general public, scientific community, radiobiologists and radiation protection specialists. You can join the newsletter mailing list.

1st NOTE newsletter was published on 31 May 2007.
Key questions from the radiation protection policy point of view

• For cancer risk: is there a deviation from LNT at low doses?
• Can ionising radiation cause non-cancer diseases or modify their risk at low / intermediate doses?
• Are there differences in the radiation sensitivity between individuals?

➢ International collaboration is essential to solve these issues (Europe, US, Japan, Canada...)


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