TASK GROUP 111

Factors Governing the Individual Response of Humans to Ionising Radiation

Under Committee 1 & Committee 3

ICRP 2025
8TH INTERNATIONAL SYMPOSIUM ON THE SYSTEM OF RADIOLOGICAL PROTECTION

MANDATE

Tissue reactions and stochastic effects after exposure to ionising radiation are variable between individuals. Factors and mechanisms governing individual responses to ionising radiation are complex and not well understood. These responses can be measured at different levels of biological organization following varying doses of radiation by analysing different endpoints such as cancers, non-cancer diseases and mortality in the whole organism; normal tissue reactions after exposures; and cellular endpoints such as chromosomal damage and molecular alterations. There are many factors that, to different degrees, influence the responses of individual people to radiation. In addition to the obvious factors of radiation quality, dose, dose rate and the tissue (sub)volume irradiated, determining factors include, among others, age and sex, life style (e.g. smoking, diet, and possibly body mass index), environmental factors, genetics and epigenetics, stochastic distribution of cellular events and systemic comorbidities such as diabetes or viral infections. Genetic factors are commonly thought to be a substantial contributor to individual response to radiation. The inheritance of an abnormally responsive phenotype among a population of healthy individuals does not follow a classical Mendelian, monogenic heredity pattern. Rather it is considered to be a multi-factorial, complex trait.

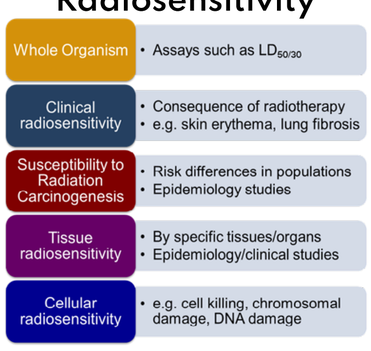
HUMAN HEALTH EFFECTS UNDER CONSIDERATION

- Clinical studies, including those concerning normal tissue reactions, cancers and non-cancer diseases such as circulatory diseases, cognitive dysfunction and cataract.
- Epidemiological studies.
- Animal experiments and cellular assays to mimic / model and explore the human situations.

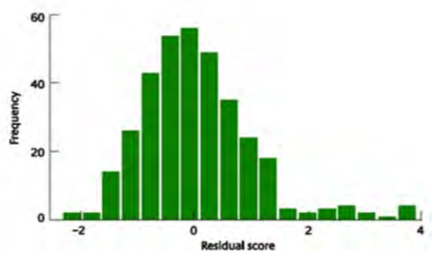
POTENTIAL CONTRIBUTORS TO VARIATION IN RESPONSE

- Age and sex
- Genetic factors
- Epigenetic modifications
- Abnormal DNA damage signaling and repair kinetics
- Lifestyle factors e.g., smoking
- Co-exposures e.g., chemicals
- Underlying health conditions e.g., diabetes
- Stochasticity of responses

Measuring Radiosensitivity



Clinical Radiosensitivity: Severity of Normal Tissue Reactions



1010 breast cancer patients: residual score standardized and accounts for patient and treatment related factors

Barnett et al 2011, Int. J. Radiat. Oncol. Biol. Phys. 82: 1065-1074

STATUS

The TG has now completed a full draft of its report that has undergone internal ICRP critical review by Committee 1, Committee 3 and Main Commission members. It will be considered at the October 2025 Main Commission for agreement to go to public consultation, which can be expected in 2026.

The draft also includes a section dedicated to uncertainties, and the level of confidence in the conclusions drawn.

DRAFT MAIN POINTS

- There is robust evidence for the severity of normal tissue reactions to radiotherapy being influenced by genetic factors (inherited monogenic disorders), concurrent chemotherapy, comorbidies (cardiovascular disease, diabetes, inflammatory bowel disease and hypertension) and age; additionally, some evidence supports a role of smaller genetic changes in some genes (single nucleotide polymorphisms); prediction of normal tissue reactions using cellular and other assays has been reported, but it remains unclear if prediction is possible.
- For circulatory diseases, concurrent chemotherapy with anthracyclins may influence risk, convincing evidence in relation to other factors is lacking, although age and sex may influence the liklihood of certain circulatory disease outcomes; investigation of the prediction of individual response has not been conducted.
- Only limited evidence is available in relation to cataract risk, some evidence suggests that concurrent diabetes increases risk; investigataion of the prediction of individual response has not been conducted.
- For cognitive effects, there is robust evidence for age at exposure influencing risk, with those exposed at younger age being at greater risk; investigation of the prediction of individual response has not been conducted.
- In terms of radiogenic cancers, robust evidence indicates that risk is influenced by age-at-exposure (younger ages at elevated risk, but with variation between cancer sites), biological sex (in terms of excess relative risk females are at greater risk, but with variation between cancer sites) and smoking (notably radon lung cancer risk higher in smokers); some evidence exists for genetic factors and female sex hormones influencing risk; prediction of radiation cancer risk by means of simple tests has not been convincingly demonstrated.
- Overall, only limited robust evidence is available on the influence of specific factors on responses to radiation exposure. The most secure evidence is in relation to age and biological sex, particularly with respect to radiation-related cancer. The ability to predict responses at the individual level remains a challenge.

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