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Can and should radiological protection be individualised?

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UKHSA & ICRP Main Commission

Individual response to ionizing radiation workshop – Stockholm, September 2022

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Current system of protection

- Avoid tissue injury (deterministic effects)
- Minimise risk of stochastic effects (cancer/hereditary)
    - justification, optimisation, dose limitation
    - limits derived from notional average that does not exist

…a population-based system

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The reality

- Not everyone is identical
- Sex-specific differences in risk, especially in breast (ERR incidence per Gy, 0.58 in females vs 0.35 in males)
- Age dependency of risk

Categories requiring protection

Radiosensitivity syndromes

Rare recessive disorders leading to cellular and sometimes clinical radiosensitivity, include for example:

- Ataxia telangiectasia
- Fanconi anaemia
- Nijmegen breakage syndrome
- Cornelia de Lange syndrome
- Severe combined immuno-deficiency (SCID)

Radiation sensitive paediatric sub-populations

- Retinoblastoma (Rb)
  - soft tissue sarcomas in radiation fields
- Neurofibromatosis type 1 (NF1)
  - second cancers associated with R/T of gliomas
- Li Fraumeni Syndrome (LFS)
  - high RR of 2nd and 3rd cancers related to R/T
- Nevoid basal cell carcinoma syndrome (NBCCS)
  - multiple basal cell skin cancers in radiation fields

See Kleinerman RA (2009) Paediatr. Radiol. 39 Suppl 1: S27-S31

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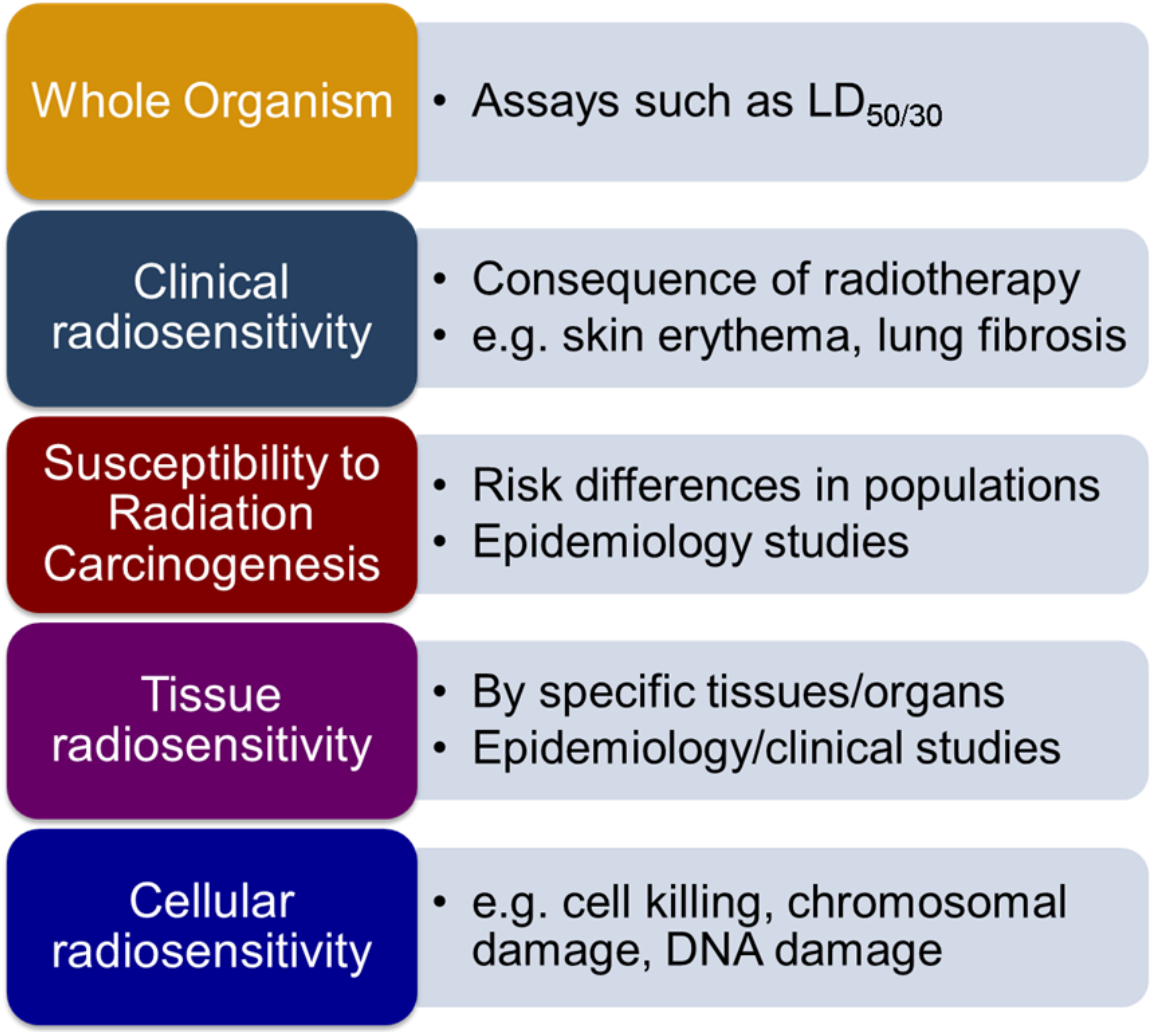
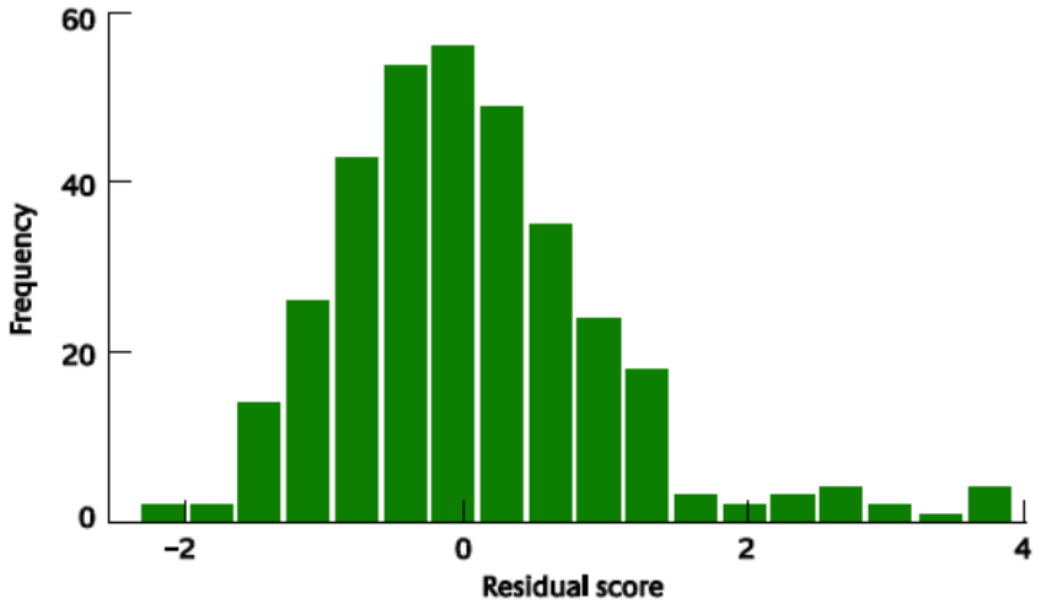
Measuring radiosensitivity



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

Modifiable risk factors - smoking

TABLE 2.2 Additional cumulative absolute risk of radon-induced lung cancer per 100,000 people (to age 75 years)

Long-term average radon exposure (Bq m^{-3})	Non-smokers *A*	Continuing smokers *B*	*B/A*
100	0.06	2.2	36.7
200	0.12	4.3	35.8
400	0.25	8.3	33.2
800	0.51	15.8	31.6

Modifiable risk factors - diet

- Dietary/calorie restriction known to extend life and reduce cancer burdens
- DR/CR found to modulate cancer incidence in irradiated animals – evidence from 1940s onwards
- Assumed to be due to epigenetic modification of gene expression

Reviewed by Karabulutoglu et al. Int J Radiat Biol. 2019, 95(4):452-479

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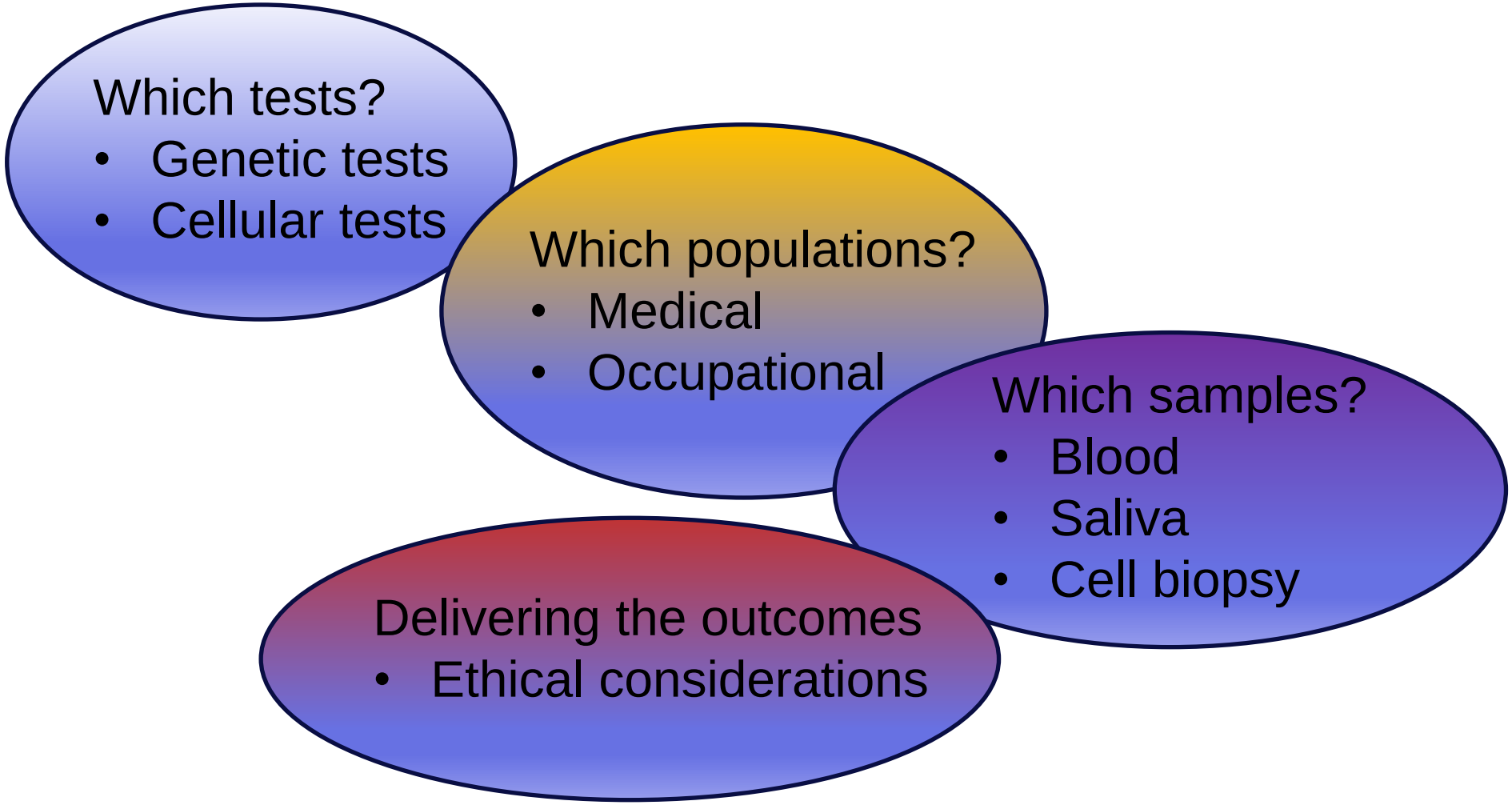
Measuring radiosensitivity



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What tests have been proposed?

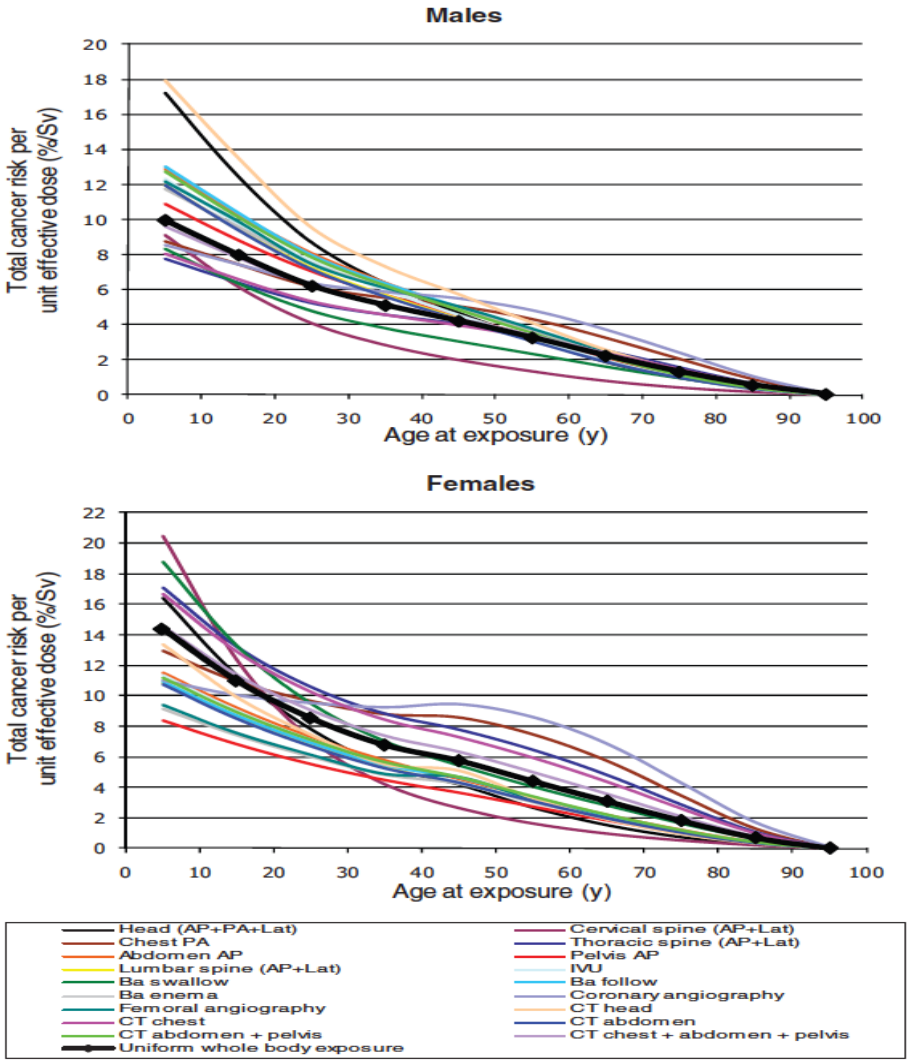
- Apoptosis in CD4/CD8 T-lymphocytes exposed to 8Gy found predictive of late normal tissue reactions in 399 patients (31% grade 2 toxicity, 7% grade 3). *Ozsahin et al 2005 Clin. Cancer Res. 11:7426-33.*

- ATM foci numbers in cultured skin biopsy fibroblasts at short times after exposure. *Vogin et al. Int J Radiat Oncol Biol Phys. 2018 101:690-693*. Also see http://www.neolysdiagnostics.com/en/

- Gene expression tests, eg using CDKN1 post-radiation upregulation. *Badie et al 2008 Br J Cancer. 98(11):1845-51*

Cancer risk variation by age at exposure – medical diagnostic exposures

The variation of lifetime Risk of Exposure-Induced Cancer incidence per unit effective dose (expressed as %/Sv) by sex and age-at-exposure for the ICRP Euro-American composite population, for 18 types of medical diagnostic X-ray examinations and a uniform whole-body dose of 10 mGy of reference low-LET radiation. Cancer incidence excludes non-melanoma skin and bone cancers, and no weighting by health detriment is included (Wall et al. 2011; Harrison et al. 2016).



Refined risk estimates for informed decision making?

- ICRP publication 147 suggests that in diagnostic medical settings, Effective doses could be adjusted for age and sex to provide a more accurate estimate of risk to individuals to inform decision making/consent for procedures
- Developments in medical dosimetry, notably due to the availability of a much larger and more representative range of phantoms for dose calculation have the potential to allow for a more refined estimate of dose to the body for individual medical diagnostic examinations
- While individualised dosimetry appears realistic, and computationally feasible, the uncertainties in risk remain considerable, most importantly at low doses in the range used in medical imaging

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Returning to ‘Can’ and ‘Should’

- The answers are inter-dependent and different for different categories of exposure

A. Medicine – radiotherapy

- There are indications that some assays can be predictive of normal tissue reactions, these are limited in use to just a few centres; there is no universally adopted assay.
- So, *can* protection against normal tissue injury in radiotherapy be indiviulaised?
- I think it *could* but we are not there yet
- Therefore, *should* individual protection be adopted
- I think yes, as and when rapid, robust, reliable and transferable assays are available
- Currently, patients can be provided with information on the ‘lifestyle’/modifyable factors that affect the severity of normal tissue reactions

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‘Can’and ‘Should’ II

B. Medicine – diagnostic exposures

- Age, sex and body form can provide improved dose information
- There is a reasonable understanding of how cancer risk varies with age and sex, but the uncertainties are considerable, particularly at the lowest diagnostic doses, and at younger ages
- So to a limited extent and with considerable uncertainty, a more individual approach *could* be adopted
- This latter point makes me somewhat uneasy in suggesting to patients that an individual risk estimate can be provided to them, at best they are age- and sex-adjusted
- Professionals might be concerned that patients could consider legal action if they did in fact develop a cancer after a procedure or set of procedures

‘Can’ and ‘Should’ III

C. Occupational exposure

- The ILO are clearly against the use of genetic testing in the workplace
- The age- and sex- dependence of cancer risk is of course present and could in principle be used to assign lower risk groups to higher risk tasks
- How would this fit with legislation regarding age- and sex- discrimination, and how would trades union groups view this?
- NB that in the special case of space flight crew, NASA adopted different dose limits for males and females – ICRP is developing a report in protection in space
- A case *could* be made for some sort of stratification, but I think it would be a very sensitive issue and unlikely to be adopted
- *Should* we individualise? Perhaps a case can be made in the case of high risk work in emergency recovery, but more generally, no

‘Can’ and ‘Should’ IV

D. Public protection

- The public dose limit is currently 1 mSv/y, ad so is already in the range where uncertainties are very high
- There is substantial variation in natural background radiation exposures around the world
- To me, these two factors alone make it clear that protection neither *can* nor *should* be individualised

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Thanks for your attention

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