IRPA13 Forum F2.1.3

ICRU Report 86: A Consideration of Low-Dose Metrics

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ICRU REPORT 86

Quantification and Reporting of Low-Dose and other Heterogeneous Exposures

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INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS

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Background to the report

- Work on the report was stimulated by observations from laboratory studies that certain low-dose radiobiological responses were influenced by the proportions of hit and non-hit cells.
- Some low-dose effects involving cell signalling show appreciable non-linear dose-effect behaviour ("non-targeted effects").

See also at IRPA13:

- **TS1a.6** *Possible Consequences of Inhomogeneous Sub-organ Distribution of Dose and the Linear No-Threshold Dose-Effect Relationship,* Madas, BG*; Balásházy, I

- **TS11a.3** *Emerging Issues in Radiation Protection of Biota – The Impact of Non-Targeted Radiobiological Effects,* Mothersill, CE*; Smith, RW; Seymour, CB

Non-targeted effects of radiation

Photobiology: Wood & Hutchinson, 1984; Tyrrell, 1984. (Also “untargeted effects”)

Radiation biology: Ward, 2000

Responses that are not initiated by direct energy deposition in nuclear DNA, or by indirect attack on it by primary radicals, such as •OH

Classical (targeted) effects

DNA dsb → cell kill

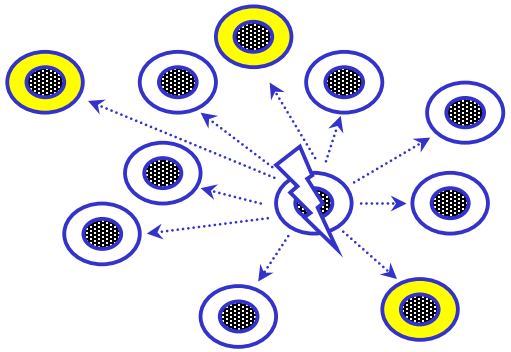
mutation
chromosomal damage
malignant transformation

Non-targeted effects

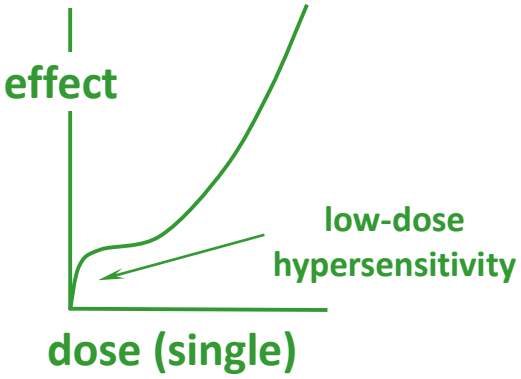
target/lesion? → bystander effects

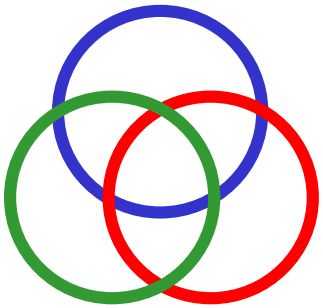
- cell kill
- mutation
- chromosomal damage
- malignant transformation

genomic instability
induced oxidative stress
gene induction
adaptive responses

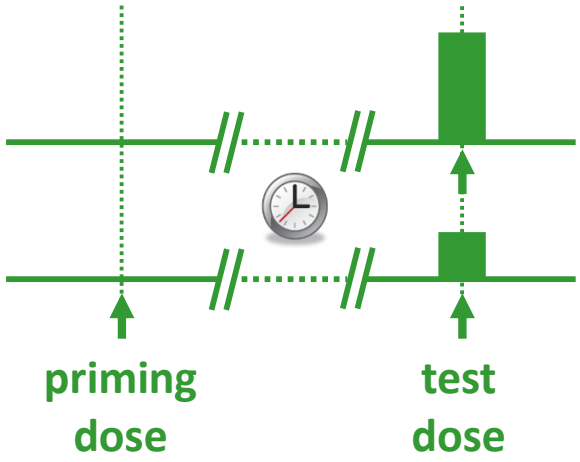


BYSTANDER EFFECT

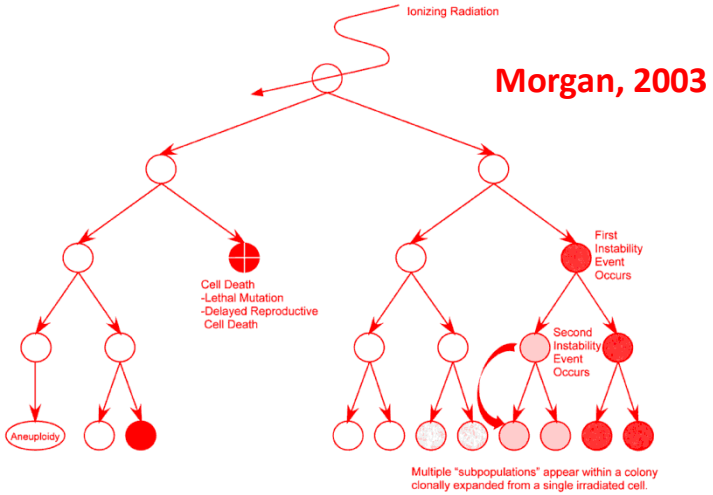




ADAPTIVE RESPONSE



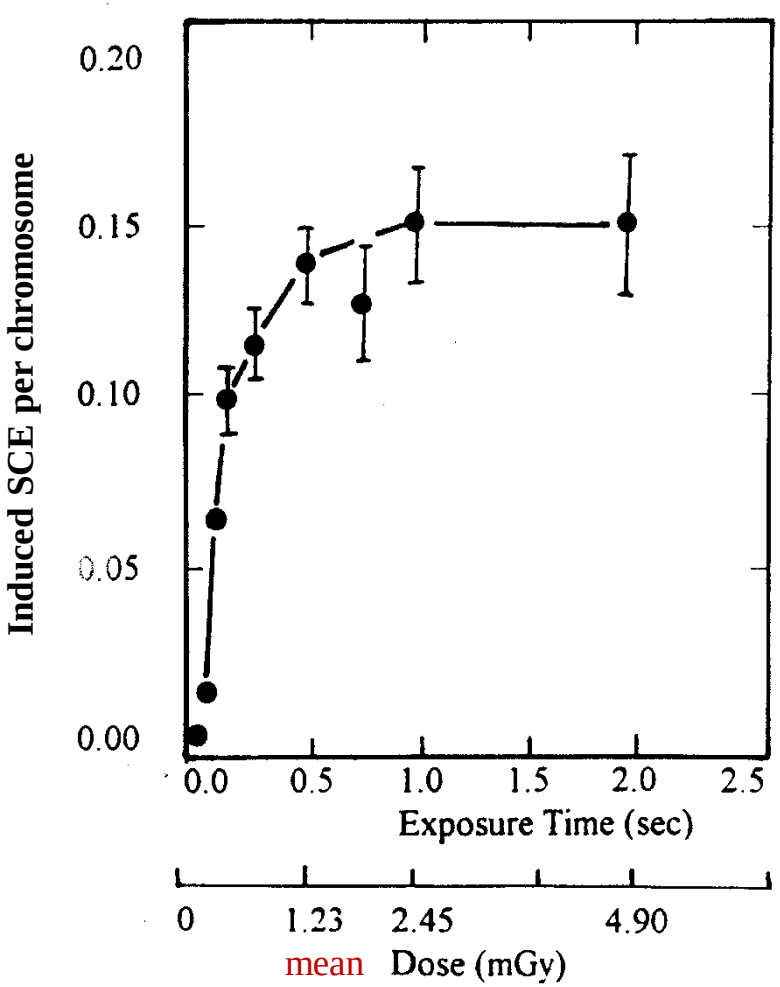
GENOMIC INSTABILITY

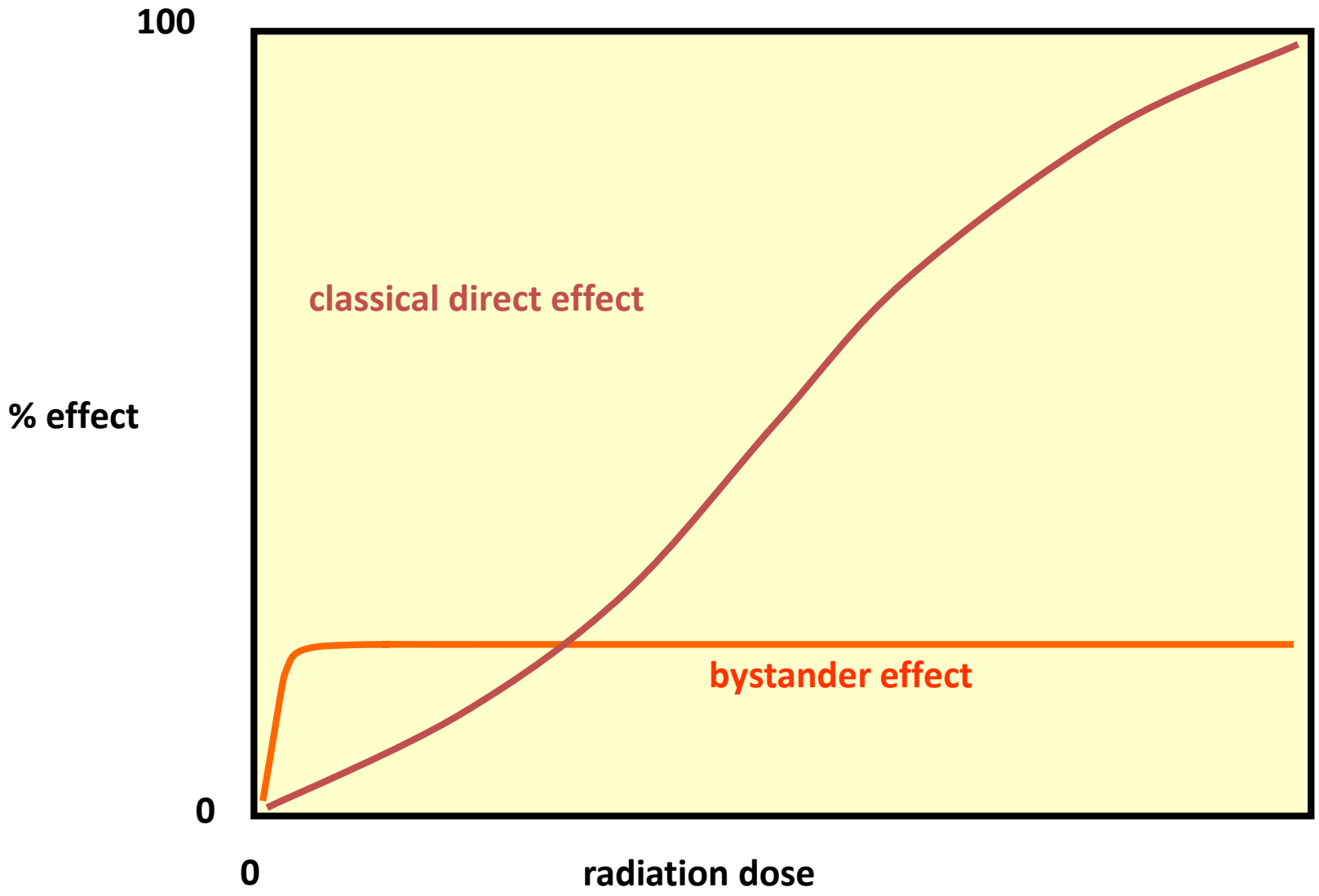


Morgan, 2003

Nagasawa and Little,
1992 *Cancer Res.* **52,** 6394-6396

- CHO cells irradiated with low doses of α-particles
- **≤40%** of the cells showed sister chromatid exchanges
- Less than **1%** were traversed by an α-particle
- With X-rays, 1-2 Gy required to give similar response (RBE>100)




100
% effect
0
0
radiation dose
classical direct effect
bystander effect

- Bystander effects include
  - cell kill
  - mutation
  - chromosomal damage
  - malignant transformation

- Other effects show a bystander-mediated component
  - genomic instability
  - adaptive responses
  - radiation-stimulated differentiation

RISK	
–	+
	+
–	+
	+
	+
–	
–	

Quantification and Reporting of Low-Dose and other Heterogeneous Exposures

1. Introduction
2. Heterogeneity: Physical, Chemical and Biological Considerations
3. Radiation Exposure from Internally Deposited Radionuclides
4. Heterogeneous Energy Deposition from External Radiations
5. Heterogeneity Induced for Mechanistic Studies
6. Options for Characterising Energy Deposition
7. Recommendations

Appendix: Examples of Recommended Approaches to Specifying and Reporting Irradiations

Heterogeneity: Physical, Chemical and Biological Considerations

- Heterogeneity of Energy Deposition by Particles
- Heterogeneity in Starting Points of Tracks
- Dimensions of Chemical and Biological Targets Relevant to Heterogeneity
- Heterogeneity Related to Low-Level Irradiation
- Biological and Physical Observations Suggesting a Need for Alternative Descriptions of Radiation Exposure

Radiation Exposure from Internally Deposited Radionuclides

- Sources of Incorporated Radionuclides
- Heterogeneity of Energy Deposition
- Radiobiological Use of Incorporated Radionuclides
- Heterogeneity from Internally Deposited Radionuclides Used for Clinical Diagnosis
- Internally Deposited Radionuclides for Therapy.

Heterogeneous Energy Deposition from External Radiations

- Tracks from High-Z, High-Energy Particles
- HZE Environment in Space
- Characteristics of Accelerator-Based HZE-Particle Irradiations
- Neutron-Capture Therapy
- Photon Microplanar Radiation Therapy Research
- Medical Applications of Ion Beams

Heterogeneity Induced for Mechanistic Studies

- Broad-Beam and Stripe-Filter Techniques
- Microbeam Exposures
- Incorporated Radionuclides
- Photon-Induced Auger Effect
- Summary of Irradiations with External Beams and Incorporated Radionuclides

Options for Characterising Energy Deposition

- Absorbed dose
- Energy imparted per event
- Radiometric quantities

Absorbed dose

Exposure: ionisation in air (ICRU, 1928)

"Energy units": a measure of the energy imparted (Zimmer, 1938; Gray and Read, 1939)

Absorbed dose: mean energy imparted per mass at a point (ICRU, 1954; 1962; Taylor, 1958)

$$D = \frac{\mathrm{d}\bar{\varepsilon}}{\mathrm{d}m}$$

Use in radiation protection requires a system of radiation quality and weighting factors
Use in radiotherapy requires a different system of factors to allow for fractionation, time, tissue type and radiation quality, generally based on L-Q formalism

+ Can be measured directly by calorimetry

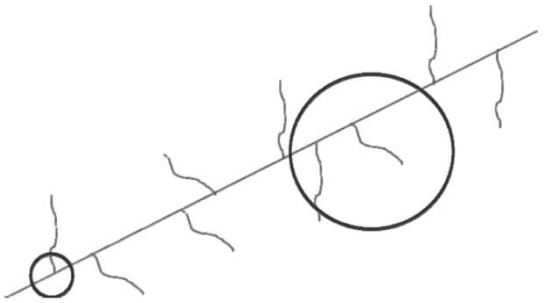
+ Wide selection of measurement techniques

+ Can be used for low-dose/low-dose-rate, also heterogeneous irradiations if extra information is provided

- Does not describe interactions; inadequate for mixed fields

- "Low" dose values suggest doses are low in all targets – this may be erroneous

Energy imparted per event



lineal energy $y = \frac{\varepsilon_s}{\bar{l}}$

specific energy $z = \frac{\varepsilon}{m}$

+ Ready-to-operate systems that measure probability density, *f*(*y*)
+ *y* and *n* can be measured in nearly any radiation field
+ Possible to determine proportions of sites with different *n*, also the event rate in sites with multiple hits
+ Useful for characterizing fields with two or more types of radiation present
- Requires the use of multiple site geometries to predict biological effect
- Limited range and number of site sizes that can be employed
- Not possible to unambiguously unfold particle ranges and velocities from the measured spectra

Radiometric quantities

Energy distribution of particle radiance $\dot{\Phi}_{\Omega,E} = \frac{\mathrm{d}\dot{\Phi}_{\Omega}}{\mathrm{d}E}$ $m^{-2}\ s^{-1}\ sr^{-1}\ J^{-1}$

Descriptor of field either at the source or at point in receptor
Transport and track structure calculations required to determine products in receptor
Must specify particle type(s) – different particles of same LET have different effects

+ Relates directly to proposal for risk cross section – e.g., in space

+ Fluence and fluence rate relate directly to dose and dose rate

- Problematic to calculate products from fluence

(a) use of analytic transport equations only suits simple products

(b) use of MC hampered by poor knowledge of cross sections , e.g., of ionisation and excitation in condensed media

Recommendations

The first priority is to describe the irradiation, the irradiated object and its environment so that the conditions can be reproduced exactly.

The most complete description of the radiation field is the energy distribution of particle radiance as a function of particle type and of time, $\dot{\Phi}_{\Omega,E,Z_\mathrm{p},m_\mathrm{p},t}$

Together with information about the geometry and composition of the target, this can in, principle, be used to calculate any interaction between the radiation and the target.

The radiation spectrum can be easily characterised in certain cases, e.g., orthovoltage x-ray sources and radioisotopes with well known emission spectra.

In microdosimetric measurements using a TEPC and in mixed fields it iss preferable to use a range of simulated site sizes. However, the measurements do not provide information on the angular distributions or the energies of the incident particles.

Recommendations

Table 7.1. Appropriate descriptive quantities for radiation exposure in different situations.

Situation	Example	Quantity	Additional specifications	Limitations
Heterogeneous radiation	Low-fluence particle beam	$\dot{\Phi}_{\Omega,E,Z_p,m_p,\ell}$	Reference position	None
Characterized (isotropic or parallel-beam) geometry	Charged particles from an accelerator	$\dot{\Phi}_{E,Z_p,m_p,\ell}$	Reference position	Isotropic field or parallel beam
Uncharacterized field	Secondary radiation around a high-energy accelerator	$f(y)$	Temporal distribution	Limited to measurement point
Homogeneous irradiation (high dose)	Radiation-therapy beam	$\dot{D}$	Temporal distribution	Limited to measurement point