Onkologisches Zentrum
Klinik für Strahlentherapie und Radioonkologie
Medizinische Strahlenphysik

The biological effectiveness of low-energy photons

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Methods for assessing biological effectiveness of ionizing radiation

- Linear-Quadratic (LQ) model for cell survival
- Microdosimetric quantities in combination with biological data
- Particle-track simulations of DNA damage

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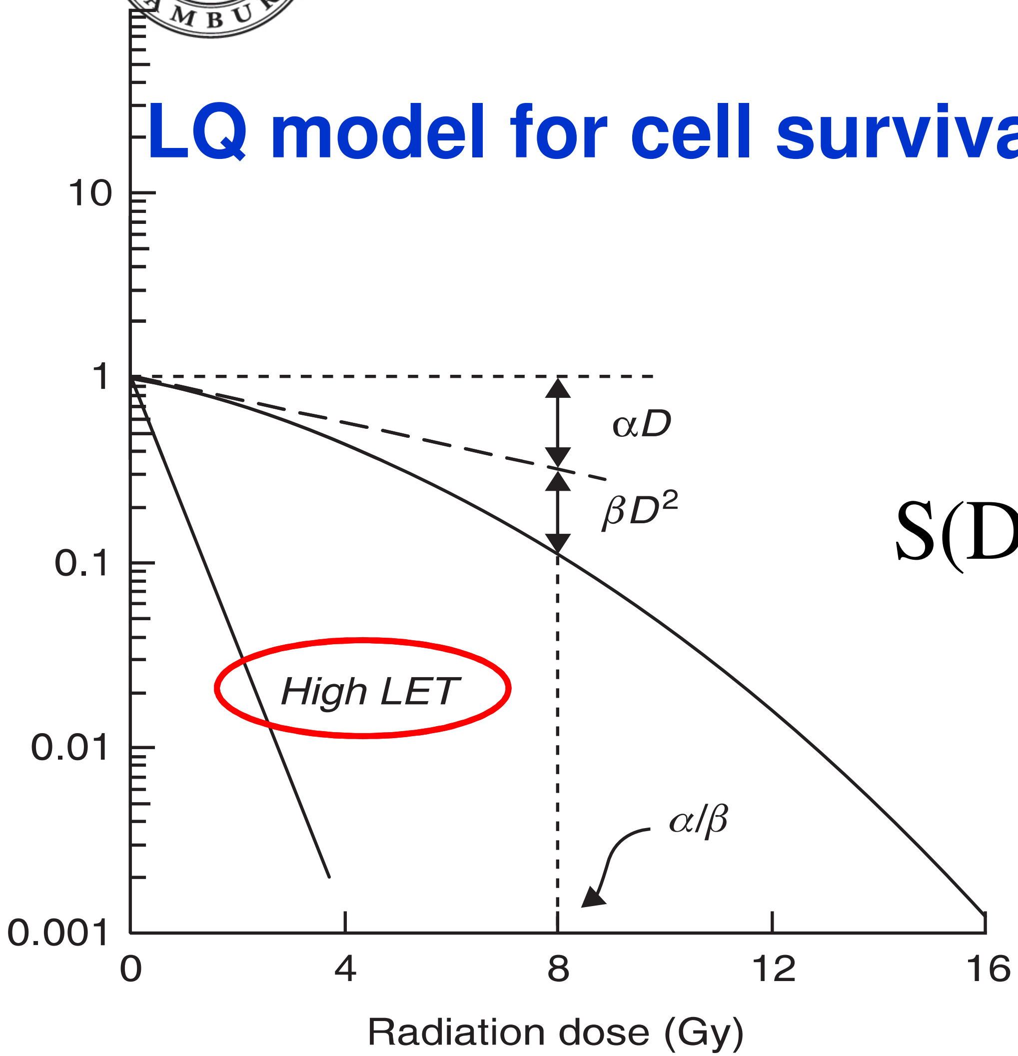
LQ model for cell survival



$$S(D) = S_{linear} \times F_{quadratic}$$

$$= e^{-\alpha D} \cdot e^{-\beta D^2} = e^{-(\alpha D + \beta D^2)}$$

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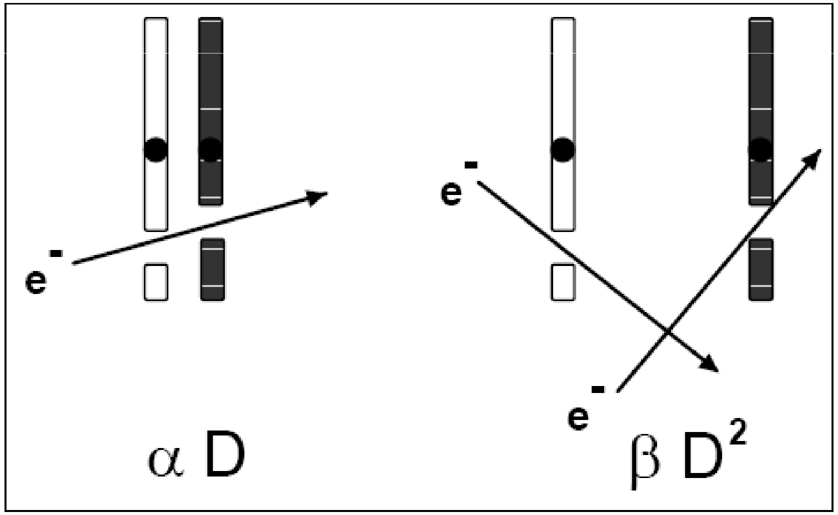
Estimate of biological effectiveness

- Linear or α-component:
  - One-particle events (DSB)
  - non-repairable damage: αD



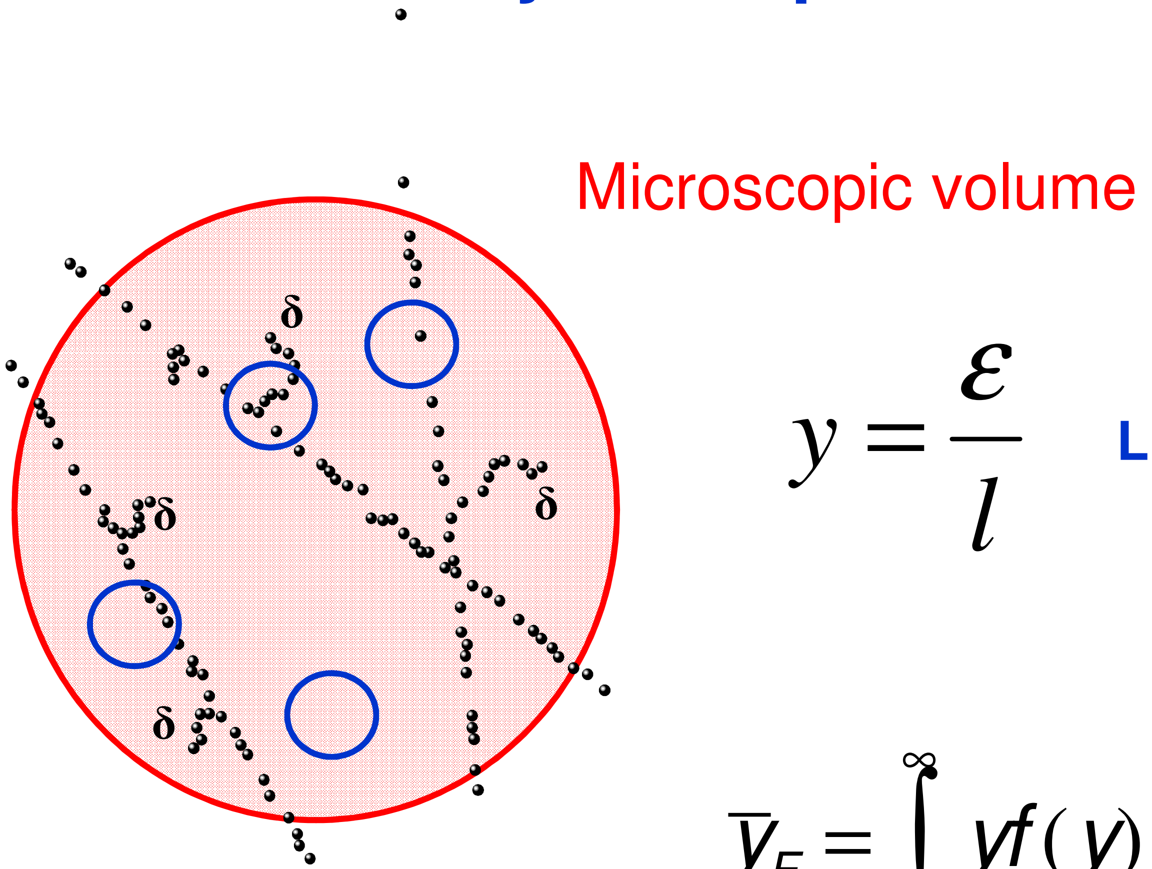
- Quadratic or β-component:
  - Two-particle events (DSB)
  - repairable damage: βD^2

Biological effectiveness from α-values

Group	Cell type	Photon energy	RBE $_{200kV}$	$RBE_{0.1, 200kV}$
Lehnert et al. (2008)	Human epith. cells	10 kV 25 kVp	1.39 1.46	1.21 ± 0.03 1.13 ± 0.03
Panteleeva et al. (2003)	Keratinocytes	25 kVp		1.33 ± 0.27
Panteleeva et al. (2003)	Mouse fibroblasts	25 kVp		1.25 ± 0.07
Frankerberg et al. (2002)	Human hybrid cell lines CGL1	29 kV 29 kVp	3.6 4.38±1.87	1.3
Frankenberg-Schwager et al. (2002)	Exponentially growing cells	30 kVp 29 kVp		1.0 1.2

Source: Nikjoo & Lindborg, Phys. Med. Biol. (2010), R65 and references therein

Microdosimetry concepts



$$y = \frac{\varepsilon}{l}$$

Lineal Energy

$$\bar{y}_F = \int_0^\infty y f(y)\, dy$$

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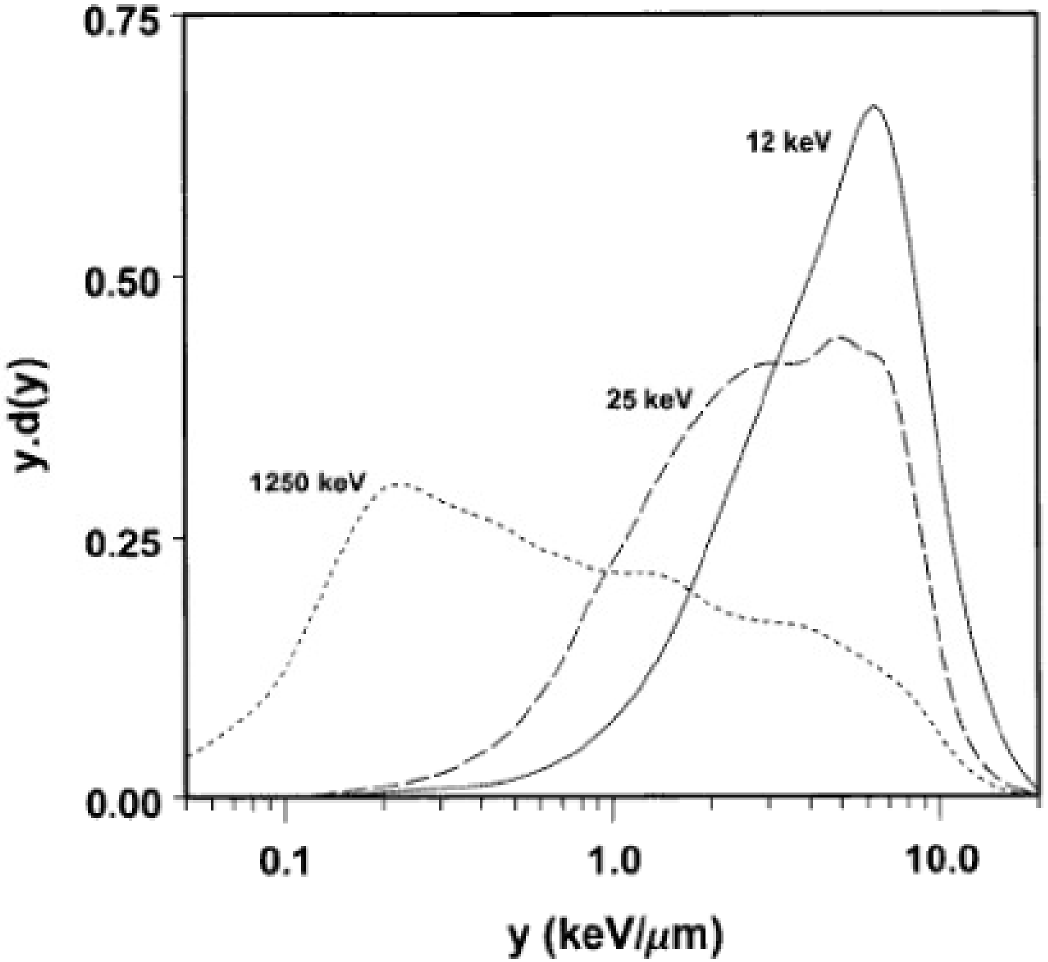
Microdosimetric spectra for different photon energies



(D = 1 μm)

$$d(y) = \frac{y}{\bar{y}_F} f(y)$$

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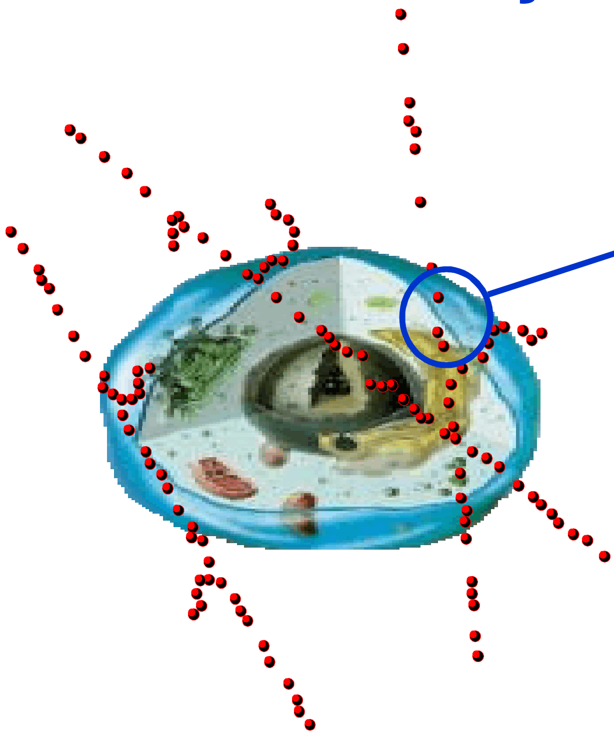
Microdosimetry and RBE



Ionizing radiation → energy deposition in the cell, typical for a given radiation quality but independent of end point → $d(y)$

Cells „react" with a biological response function, typical for a given end point ε, but independent of radiation quality → $q_\varepsilon(y)$

~RBE for low dose:

$$\alpha_\varepsilon = \sum_{i=1}^{N} q_{\varepsilon i}(y) d_i(y)$$

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Example of a biological response function

ZAIDER AND BRENNER

ussed above should need, on the account oi
verage.
ions which deposit most of their dose below
V electron beam), which deposit most of thei
protons), and which deposit most of their
V/amu iron ions) would be most desirable.

Dicentric chromosome aberration in human lymphocytes

Source: Zaider & Brenner, Radiat. Res. (1985), 302

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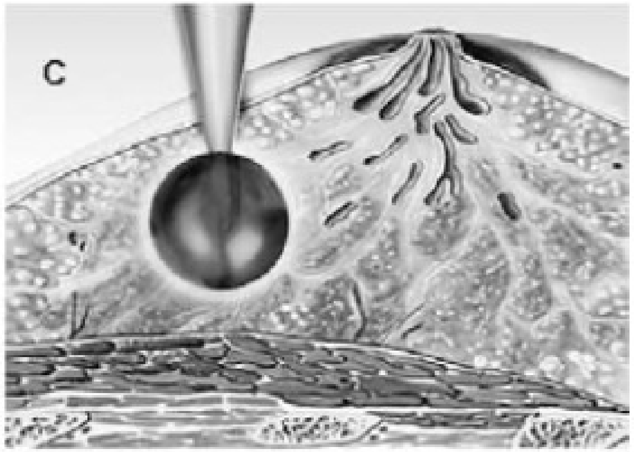
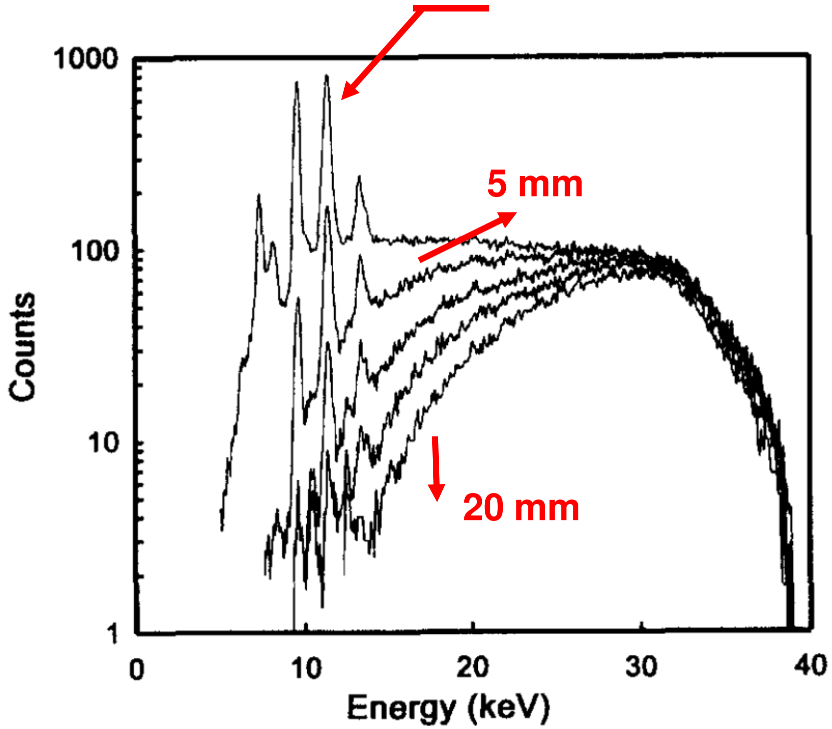
Example: RBE of IORT spectrum



Spectra in air and solid water



Source: Herskind et al., Int. J. Radiat. Onc. Biol. Phys. (2008), 1575

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RBE of IORT spectrum – Endpoint: dicentrics for human lymphocites

Table 1. Estimated low-dose RBEs (α_H / α_L; see equation (1)) and clinically relevant RBEs (23 min irradiation, 12.5 Gy) for low-energy x-rays as shown in figure 2, for a miniature photon radiosurgery system (Dinsmore *et al* 1996, Cosgrove *et al* 1997), operated at 40 kV.

	versus ^{60}Co		versus ^{192}Ir		versus ^{125}I	
Depth (mm)	Low dose	Clinical	Low dose	Clinical	Low dose	Clinical
0	3.05	1.53	2.11	1.38	1.23	1.12
5	2.67	1.44	1.85	1.29		
10	2.54	1.41	1.76	1.27		
15	2.48	1.40	1.72	1.25		
20	2.44	1.40	1.69	1.24		

Source: Brenner et al., Phys. Med. Biol. (1999), 323

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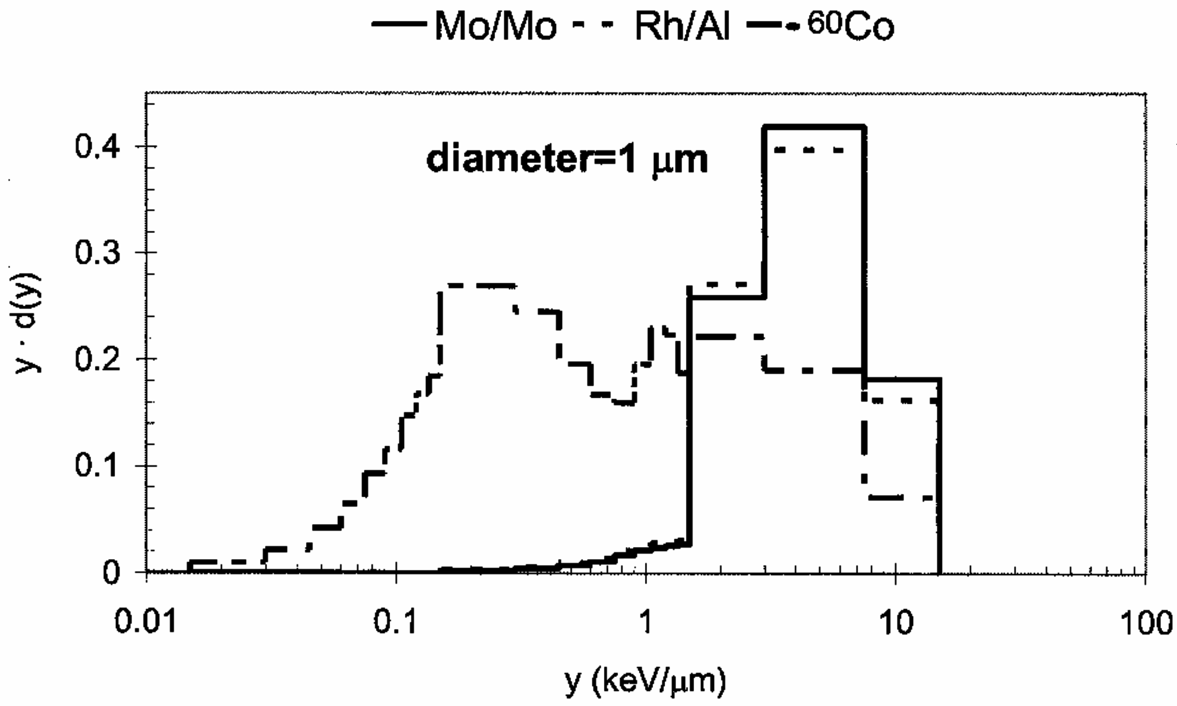
Example: microdosimetric spectra for mammography x rays



Average quality factor according to ICRU 40:

$$\bar{Q} = \frac{1}{D} \int D(y) Q(y) \, dy$$

Source: Verhaegen & Reniers, Radiat. Res. (2004), 592

Average quality factor for mammography x rays

TABLE 2
Average Quality Factors, *Q*, as a Function of Depth in 50/50 Breast Tissue for the Seven Radiation Qualities

Depth (cm)	Average quality factor, *Q*						
	Molybdenum/ molybdenum, 28 kVp	Rhodium/ rhodium,	Rhodium/ aluminum, 28 kVp	Gaseous water/ rhodium, 28 kVp	Molybdenum/ rhodium, 28 kVp	Molybdenum/ molybdenum, 25 kVp	Molybdenum/ rhodium, 32 kVp
0.1	1.41	[illegible]	1.33	1.34	1.38	1.42	1.37
1.5	1.38	[illegible]	1.31	1.33	1.36	1.39	1.35
2.5	1.36	[illegible]	1.29	1.31	1.34	1.38	1.33
3.5	1.35	[illegible]	1.28	1.30	1.33	1.37	1.32
5.0	1.33	[illegible]	1.27	1.28	1.31	1.36	1.30

Source: Verhaegen & Reniers, Radiat. Res. (2004), 592

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Other photon energies – Endpoint: chromosome aberration

Cell type	Endpoint	Energy	RBE as α-ratio
Lymphocytes	Dicentrics	^{60}Co 250 kVp 30 kVp	1.0 1.6 3.0
Peripheral blood	Dicentrics	^{60}Co 30 kV	1.0 1.79 ± 0.56
Mammary gland epithelial cells MCF-12A	Dicentrics & centric rings	200 kVp 25 kVp 10 kVp	1.0 1.08 ± 0.08 1.43 ± 0.12
Human peripheral lymphocytes	Dicentrics	^{60}Co 10 kVp 29 kVp 220 kVp	1.0 7.20 ± 2.98 6.12 ± 2.51 3.74 ± 1.46

Source: Nikjoo & Lindborg, Phys. Med. Biol. (2010), R65 and references therein

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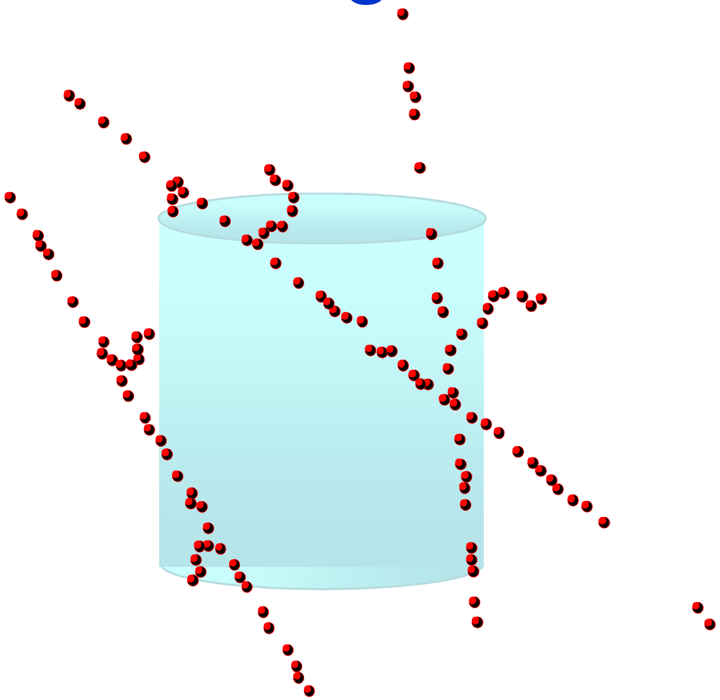
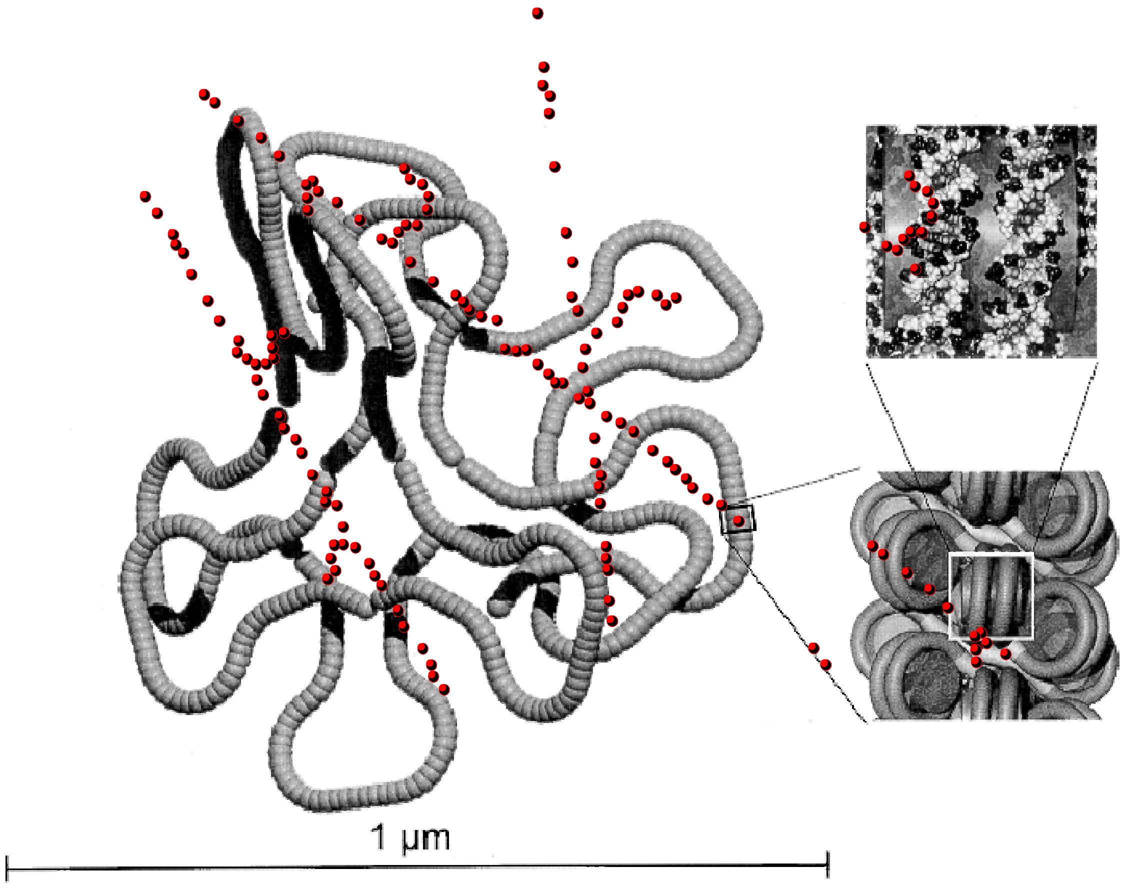
Particle-track simulation for modelling DNA damage: from simple....



DNA segment simulated as a water cylinder, 2 cm in diameter, 2 cm in height

Nucleosome simulated as a water cylinder, 10 cm in diameter, 5 nm in height

... to very complex geometries



Example: PARTRAC

Source: Friedland et al., Radiat. Environ. Biophys. (1999) 39-47)

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Information from particle track-structure simulation

Frequency distribution of energy deposition in a volume of interest →
microdosimetric quantities → relative quality factors (with respect to a reference radiation)

Ionization cluster-size distributions + chemical pathways → severity of initial damage to DNA

Example: RBE from DNA damage

Group	Photon energy	RBE (DSB)
Friedland et al (1999), calc	^{60}Co 220 kVp Al_K C_K	1.0 1.1 1.6 1.4
Hsiao &Stewart (2008), calc	^{60}Co 220 kVp (unf.) 29 kVp (Mo)	1.0 1.1 1.17
Nikjoo et al. (1997,1999,2002), calc (monoen. e-)	Al_K C_K	2.6 3.7
Kuhne et al. (2005), meas.	C_K	2.0
Frankenberg et al. (1981,1986), meas.	Al_K C_K	2.8 3.2

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Example: RBE for IORT spectra

Group	Spectrum	Cell type	Endpoint	RBE low dose	RBE high dose
Brenner et al (1999), computational microdosimetry	^{60}Co 40 kVp	Lympho-cytes	Dicentrics	1.0 3.05	1.0 1.53
Renier et al. (2008), Monte Carlo damage simulation	^{60}Co 40-50 kVp	Breast tissue	DSB in DNA		1.0 1.49
Marthinsen et al. (2010), measured	6 MV 50 kVp	Breast cancer cells: MCF-7 T47-D	Cell survival	1.0 1.9 3.1	1.0 1.4 1.4

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Discussion - I

Computational micro- and nanodosimetry is a useful tool to assess biological effectiveness of low-energy photons, comparing satisfactorily with experimental data

Physical particle-track quantities can be directly measured (with micro- or nanodosimeters) → they can be used to assess the “average quality” of ionizing radiation

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Discussion - II

However, they need to be combined with biological parameters (chemical pathways, free radical reaction probabilities, …) in order to compare results from calculations and radiobiological experiments

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Discussion - III

DNA initial damage is the underlying quantity, however..

It is necessary to specify the biological system (cell lines) and biological endpoint (cell survival, chromosome aberration, neoplastic tranformation).

Also: are we interested in radiation protection or in radiotherapy? Repair kinetics plays a role!

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Thank you!

FINAL MESSAGE: please be sure that you know how to use your calculated data!