What is 'radiation quality' ?

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radiation quality ?

Try the web:

radiation quality,

a descriptive specification of the **penetrating nature** of an x-ray beam. It is influenced by kilovoltage and **filtration**: a higher kilovoltage produces more penetration, and filtration removes selected wavelengths and "hardens" the beam. medical-dictionary.thefreedictionary.com

The ability of a beam of x-rays to allow the production of **diagnostically useful radiographs**. Usually measured in **half-value layers** of aluminum and controlled by the kilovolt peak.

Mosby's Dental Dictionary

The spectrum of radiant energy produced by a given radiation source with respect to its **penetration** or its **suitability** for a specific application.

McGraw-Hill Science & Technology Dictionary

Such 'definitions' depend on the application of interest ??

Mostly regarding radiography/imaging rather than biology/health effects

Try: International Commission on Radiological Protection (**ICRP**)
International Commission on Radiation Units and Measurements (**ICRU**)

ICRP Publication 92 (2003): Relative Biological Effectiveness (RBE), Quality Factor (Q), and Radiation Weighting Factor (w_R)

ICRP Publication 103 (2007): The 2007 Recommendations of the ICRP.

ICRU Report 16 (1970): Linear Energy Transfer.
ICRU Report 36 (1983): Microdosimetry.
ICRU Report 40 (1986): The Quality Factor in Radiation Protection.
ICRU Report ICRU 60 & 85 (1998 & 2011). Fundamental Quantities and Units for Ionizing Radiation.

ICRP Publication 60 (1991): 1990 Recommendations of the ICRP

"The probability of stochastic effects is found to depend, not only on the absorbed dose, but also on the type and energy of the radiation causing the dose. This is taken into account by weighting the absorbed dose by a factor related to the quality of the radiation."

But, what is "quality of the radiation"?

When x rays and γ rays were the only types of ionizing radiation available to the therapist, the term "quality" was used to describe the penetrating power of the radiation. Quality was usually expressed in terms of the half-value layer in copper or aluminium (i.e., the thickness of material required to reduce the intensity to half). With the extension of radiotherapy and radiobiology to other types of radiation it was realized that the biological effect per unit absorbed dose depended on the radiation used. The term "quality" became a description of the radiation as it affects the biological response;

(Bewley 1973)

From "Radiation Quality and its Influence on Biological Response"

"The pioneering experiments by Zirkle (1935) and a multitude of succeeding studies have established that the **biological effectiveness of ionizing radiation depends** not only on the amount of energy absorbed but **also on the spatial distribution of energy deposition.** Since the **energy is imparted in or near the tracks of charged particles**, it has been considered convenient to express the **heterogeneity of energy deposition** in terms of the linear density of energy loss in these tracks. The term linear energy transfer (LET) has been coined by Zirkle et al. (1952) for this purpose. Using this concept one may express **radiation quality** as a distribution of dose in LET, specifying the **fraction of the dose deposited in each LET interval**."

From "Specification of Radiation Quality" (Rossi 1959)

- **We now know, of course, that LET is far from adequate to specify radiation quality.**

(LET = Linear Energy Transfer)

To describe radiation effects or mechanisms, need physical specification of:

1. **Measure of <u>quantity</u> of radiation:** **-- Use absorbed dose, or fluence**

2. **Variations of dose on scale of interest** e.g. isodose plots; tissue compartments; doses on more microscopic scale from internal radionuclides;

3. **<u>Time</u> course of delivery:** **e.g. Dose rate, fractionation or fluence rate, etc**

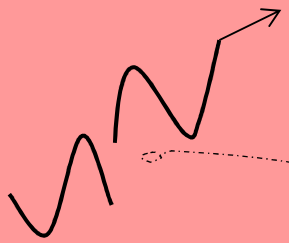
4. **Specification of '<u>quality</u>' of the radiation:**

   LET as 1st approximation.
   Better options?

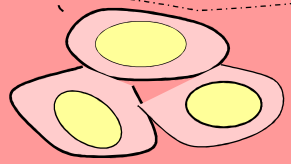
Of course, effects depend also on the particular biological system itself and its environment.

The insult to DNA, cells and tissue from ionizing radiation is always in the form of structured tracks from charged particles

X-,γ-ray



electron track **(Low LET)**



neutron

recoil proton track **(High LET)**

Radio-nuclides

Alpha-emitter

❷+

α-track **(High LET)**

Beta-emitter

❶-

electron track **(Low LET)**

Accelerated ion
Cosmic ray ion

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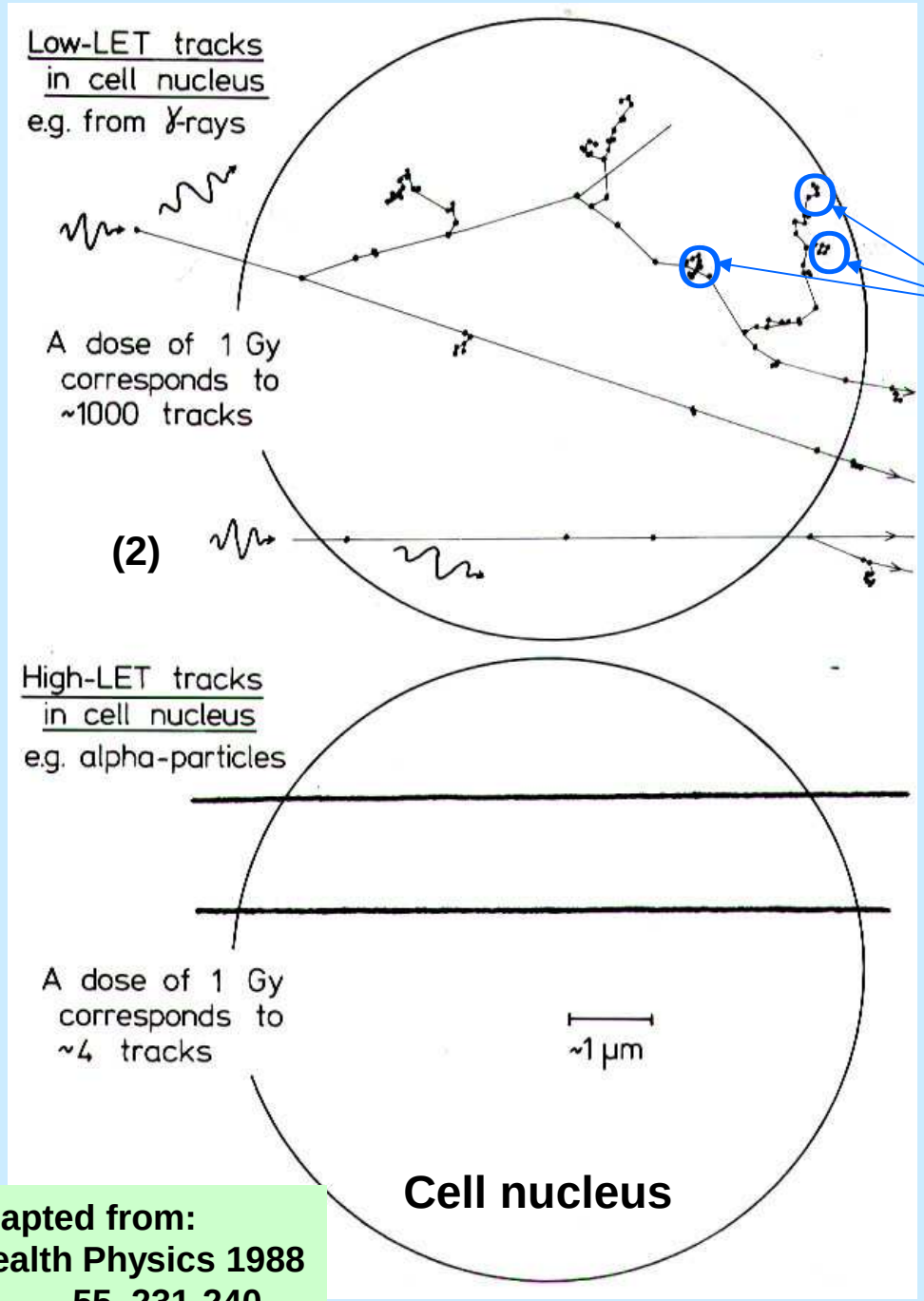


Adapted from:
Health Physics 1988
55, 231-240

Low-LET radiation:

Sparsely ionizing on average, but ~ 1/4 of energy deposited via denser clusters of ionizations from low-energy secondary electrons (on scale of nanometres)
(Magnified in diagram)

Very low dose from a single track
(~ 0.001 Gy to cell nucleus)

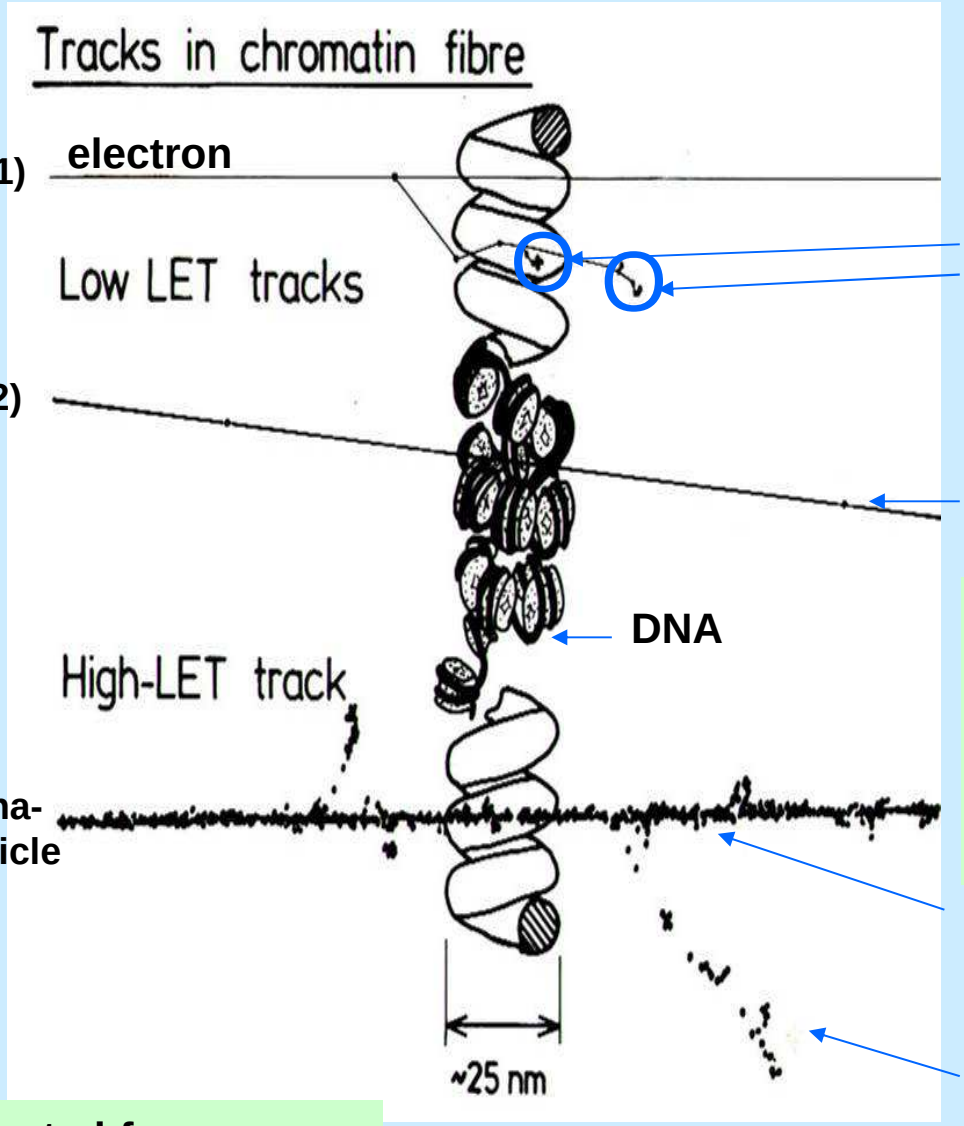
High-LET radiation:

Densely ionizing on average
(especially for low-velocity ions, natural alpha-particles, etc)

High dose from a single track
(~ 0.2 - 0.5 Gy from single α-track)

LET = Linear Energy Transfer

All radiation tracks are highly structured on the scale of DNA



Clustered ionizations from low-energy electron

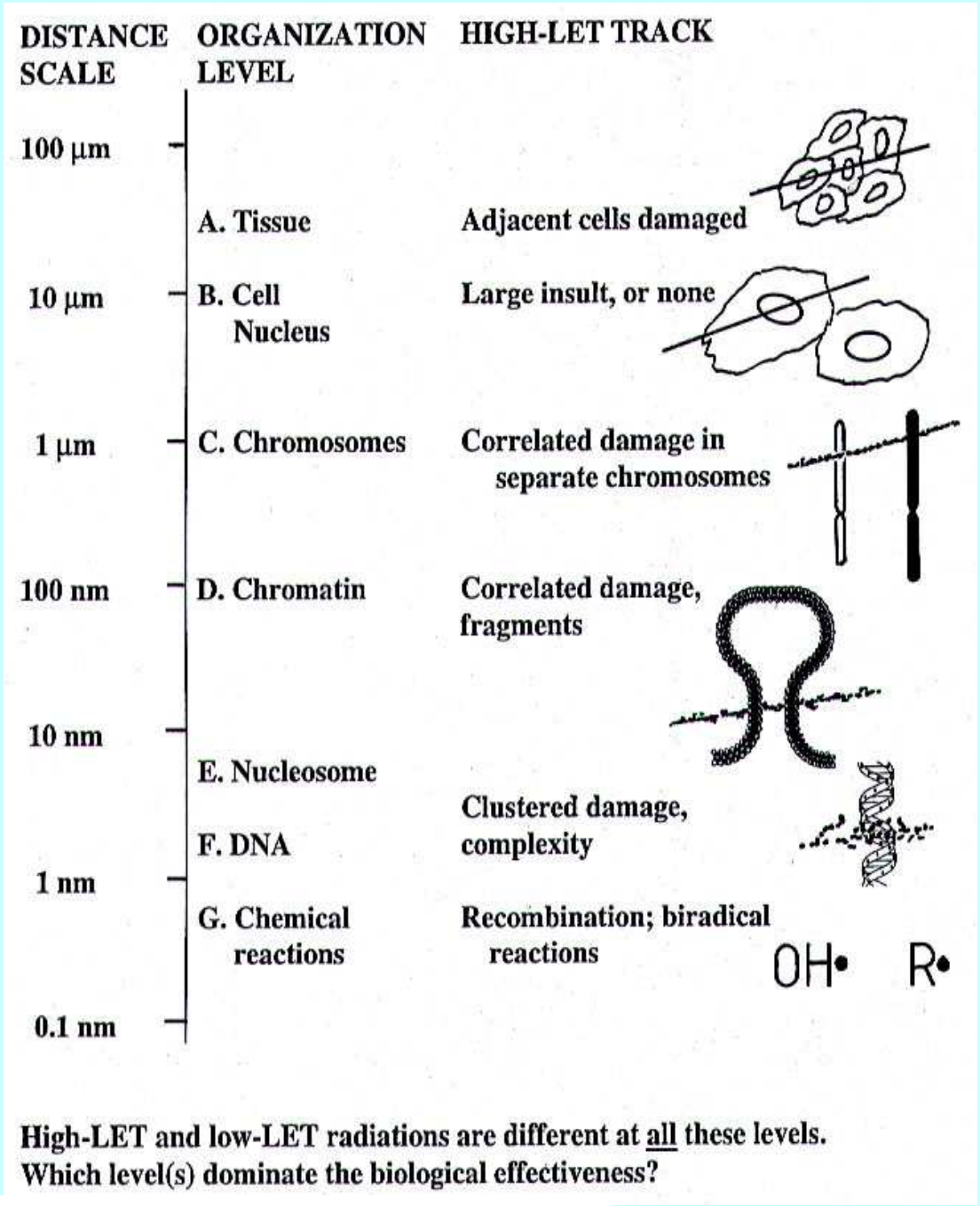
Single ionization

Opposing trends: Alpha-particle has
-- low probability of hitting DNA (few tracks per Gy)
-- high probability of damage when it does hit.

Dense ionization clustering along path of alpha particle

Delta-ray electron

Adapted from:
Health Physics 1988
55, 231-240



J. Radiat. Res. (Japan) 40, Suppl. 1-13 (1999)

Radiation track structure is important at all levels of organisation,
from molecules to tissue, from sub-nanometres to 100s of micrometres

The DNA level (nanometres) is particularly important.

Absorbed dose of ionizing radiation is:

- the amount of energy imparted per unit mass of tissue.
- measured in units of joules per kilogramme, given the special name gray.

$$1\ \text{Gy} = 1\ \text{J/kg}$$

ICRU Definition:

4.2.5 Absorbed Dose

The **absorbed dose**, D, is the quotient of $d\bar{\epsilon}$ by dm, where $d\bar{\epsilon}$ is the mean energy imparted to matter of mass dm, thus

$$D = \frac{d\bar{\epsilon}}{dm}.$$

Unit: $J\,kg^{-1}$

The special name for the unit of absorbed dose is gray (Gy).

Usually applied as an <u>average</u> in a <u>macroscopic</u> mass (volume) of tissue

- **Ignores microscopic variations and stochastics**

Radiation Quality is defined by the fluence spectrum of radiation particles at the locations of interest in the target material.
(biological system)

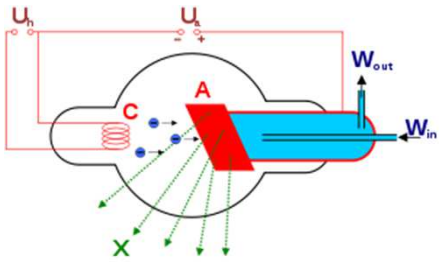
- Depends on characteristics of the radiation source and the intervening material

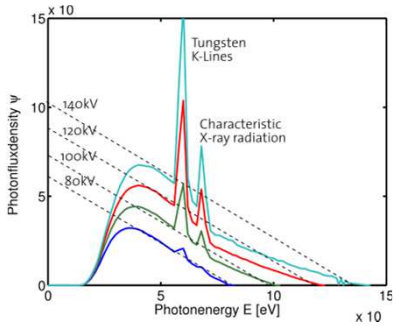
Fluence spectrum:

- specifies the relative numbers of particles according to type and energy
- includes:
  - charged particles ---- of particular importance for most biological effects (e.g. electrons, protons, alpha-particles, heavier ions)
  - (neutral particles also, such as X- & γ-ray photons and neutrons)

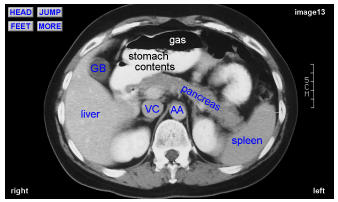
RADIATION QUALITY

Radiation source characteristics

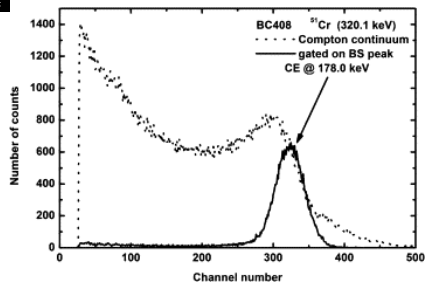


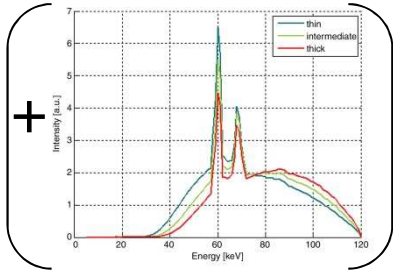


Intervening material

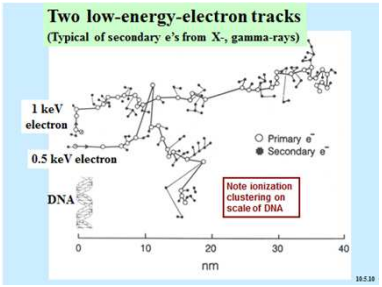


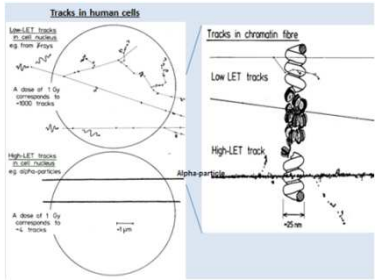
Fluence spectrum of <u>charged</u> and neutral particles (particle types and energies)



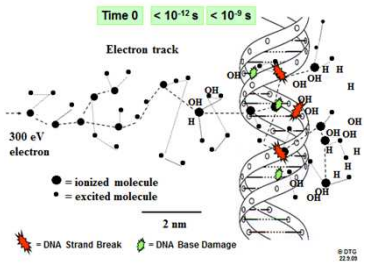


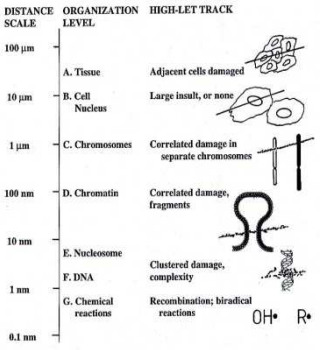
Track structures

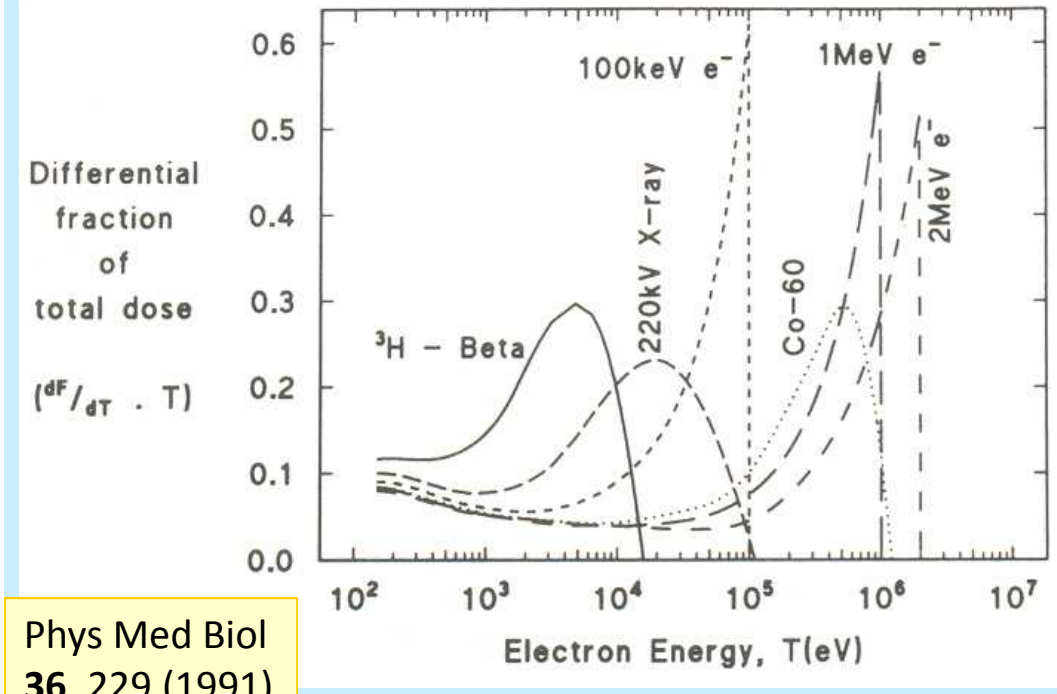




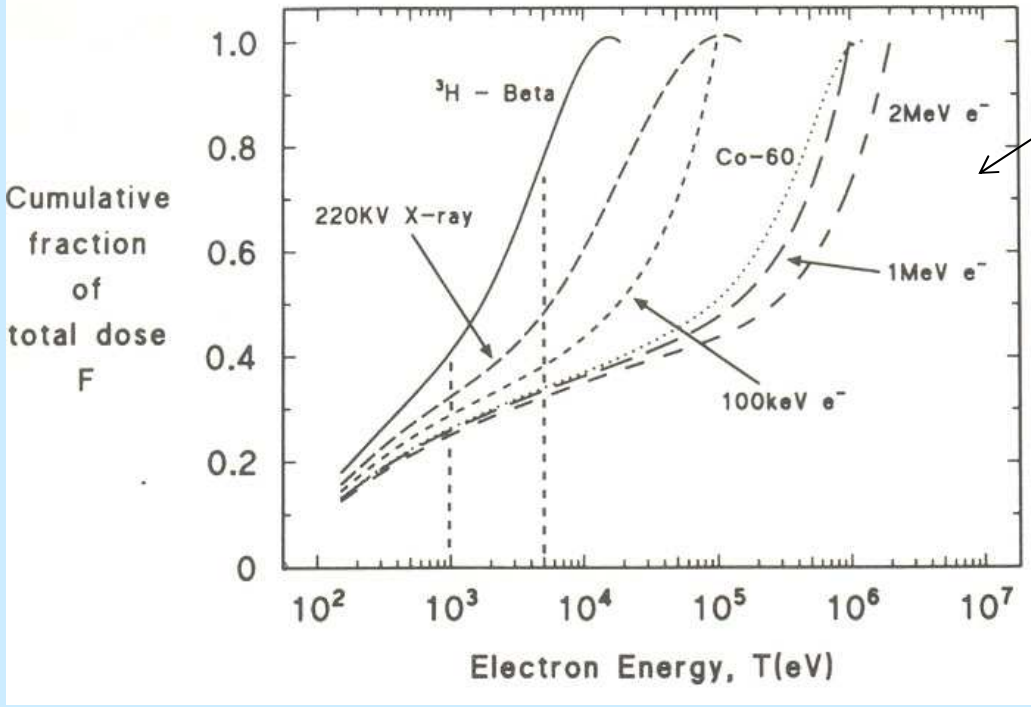
Biological damage and health effects







Phys Med Biol **36**, 229 (1991)



Differences in quality between some low-LET radiations

Low-energy electrons are an important component for dose deposition by all low-LET radiations (X-, γ-rays, beta-emitters)

Such differences in radiation quality can be significant for biological effects

COMPARING LOW-LET RADIATIONS:

Dose fraction deposited by electrons of energies 0.1 to

	5 keV	1 keV
Tritium β	77 %	42%
220 kV X-rays	48 %	33%
Co γ-rays	34 %	27%

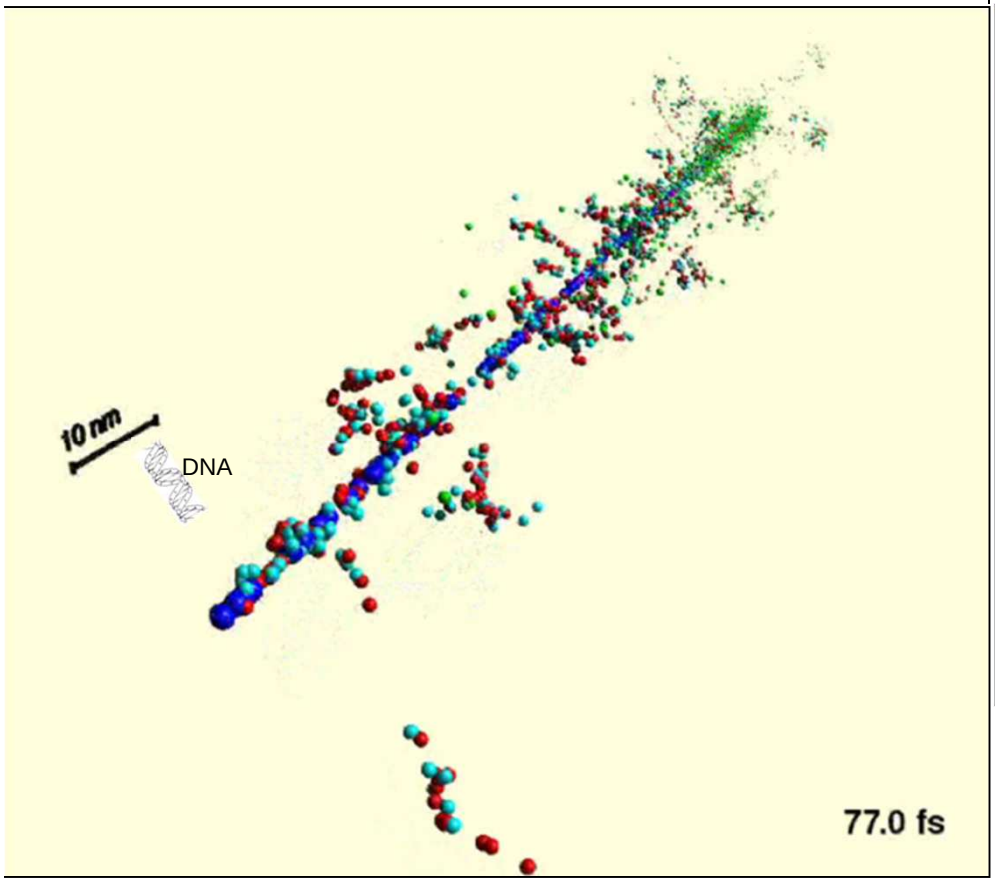
NOTE: Low energy electrons are more efficient at producing:

- **DNA double-strand breaks (DSB)**
- **a higher proportion of complex DSB (and other clustered damage)**
- **a wide variety of biological effects in cells (mutations, chromosome aberrations, malignant transformation, killing, etc)**

5.3 MeV alpha particle

1.3 MeV/u

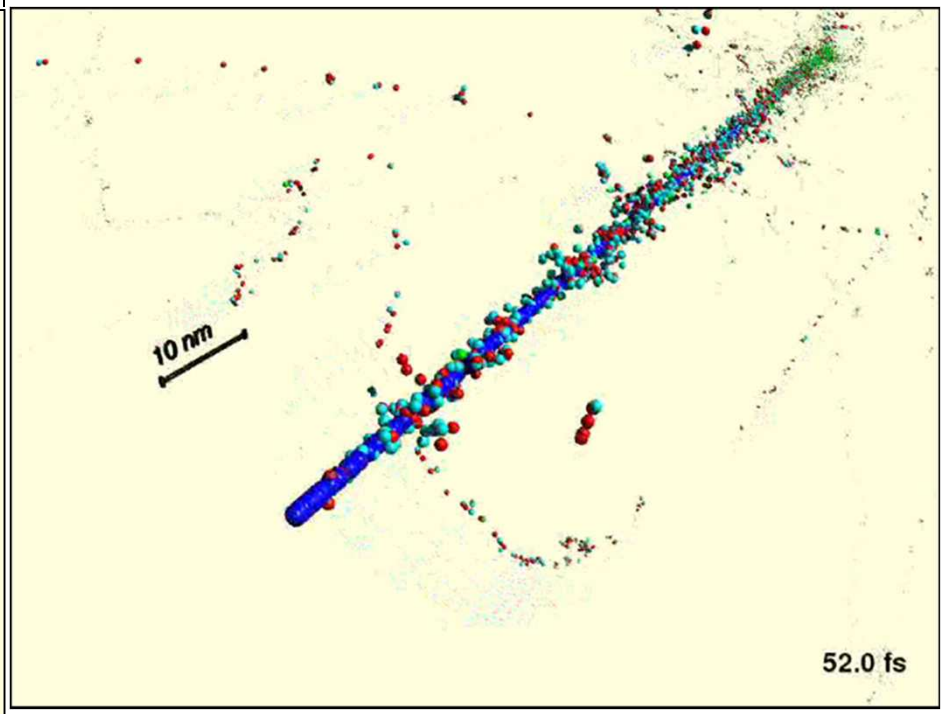
LET ~ 88 keV/µm



200 MeV Oxygen ion

12.5 MeV/u

LET ~ 250 keV/µm



NOTE: Each symbol represents a point interaction.

These diagrams use finite spheres to provide a perspective of distance.

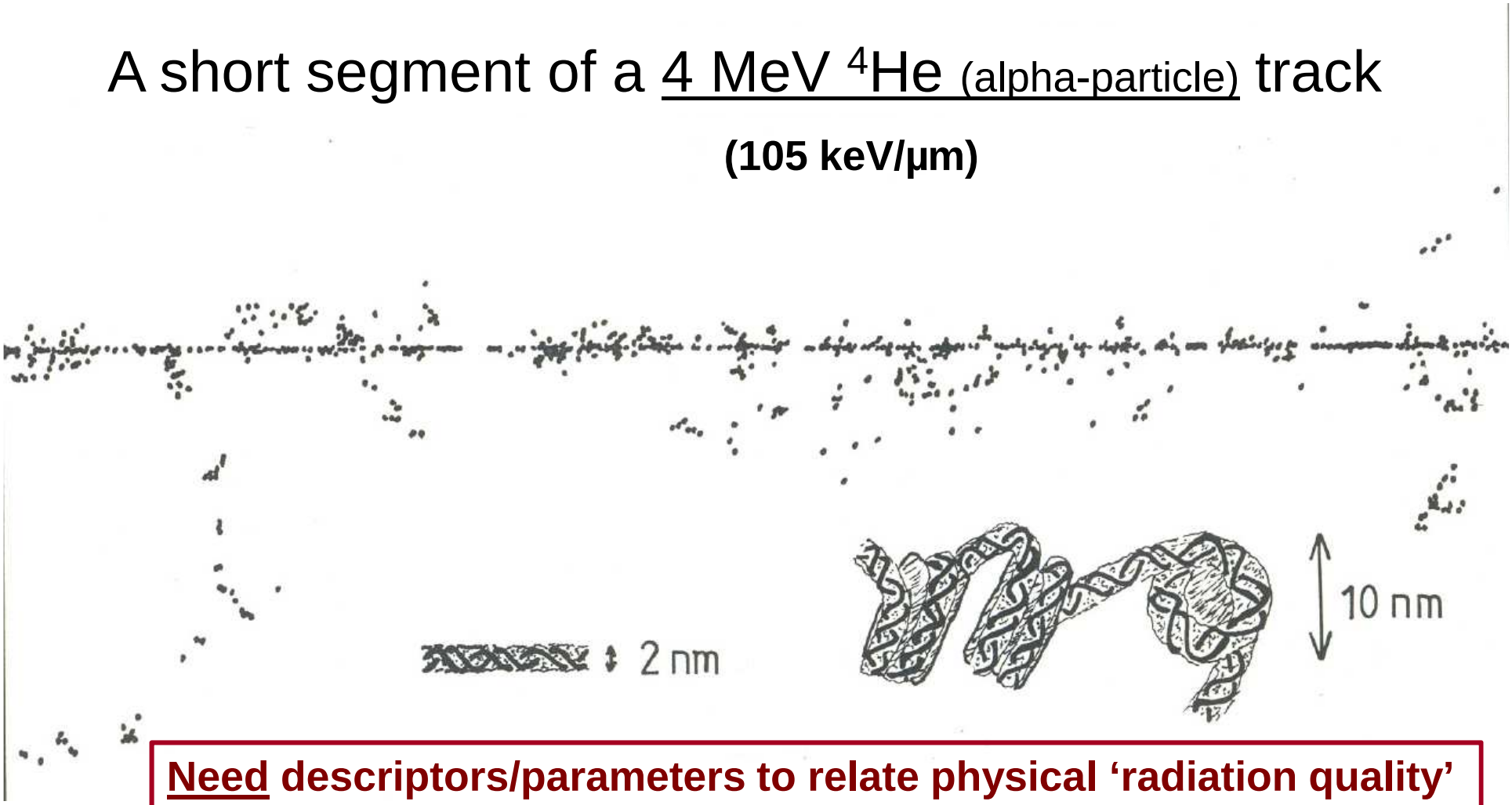
Shown are frozen sample screens from live simulations run for visual appreciation of track structure.

By courtesy of Herwig Paretzke, Werner Friedland and Maximillian Kreipl

Track simulation methods in: Kreipl et al, Radiat Environm Biophys 48, 349-359 (2009).

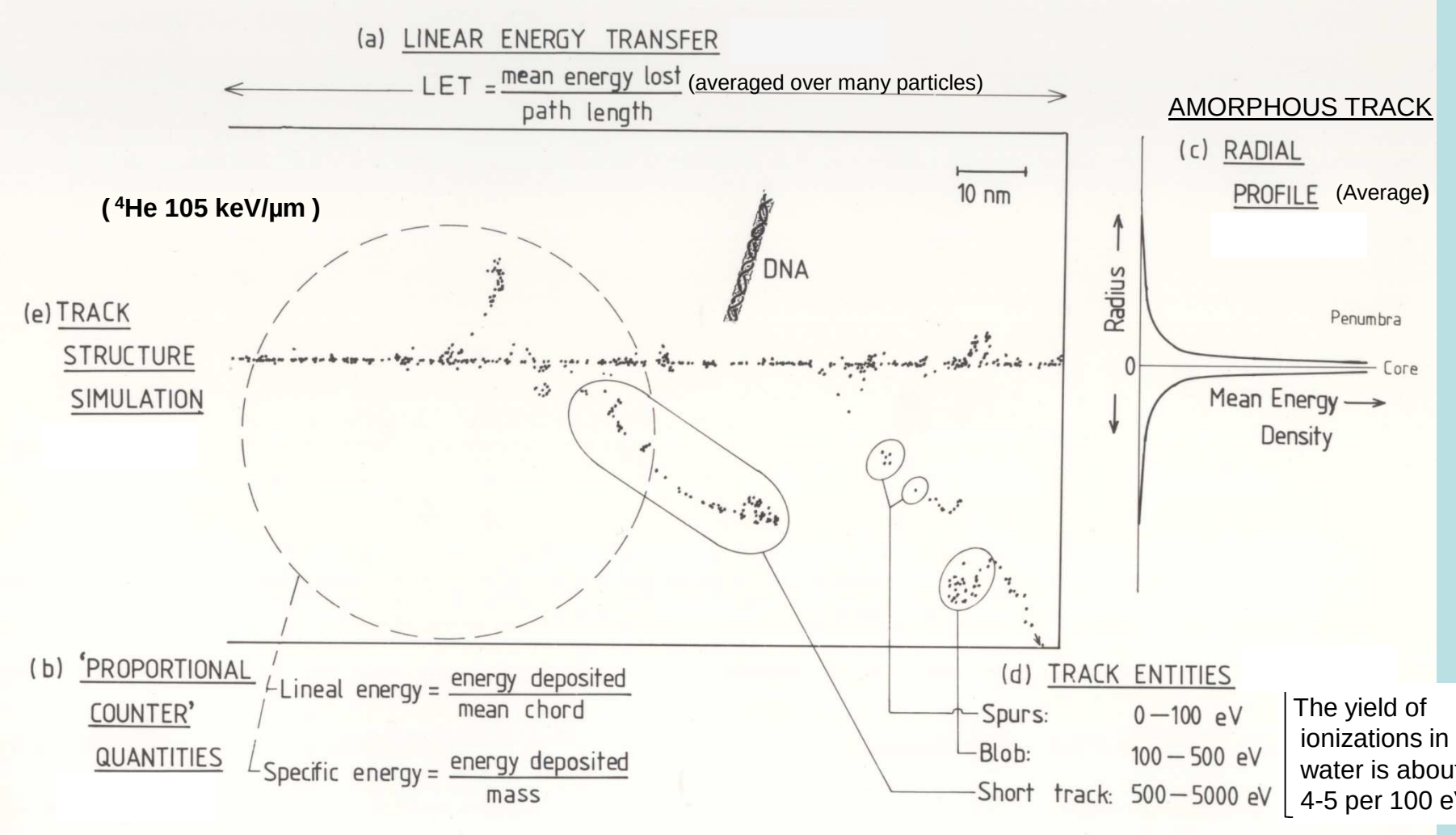
A short segment of a 4 MeV ^{4}He (alpha-particle) track

(105 keV/µm)



Need descriptors/parameters to relate physical 'radiation quality' to biological effectiveness

Descriptions of radiation quality:

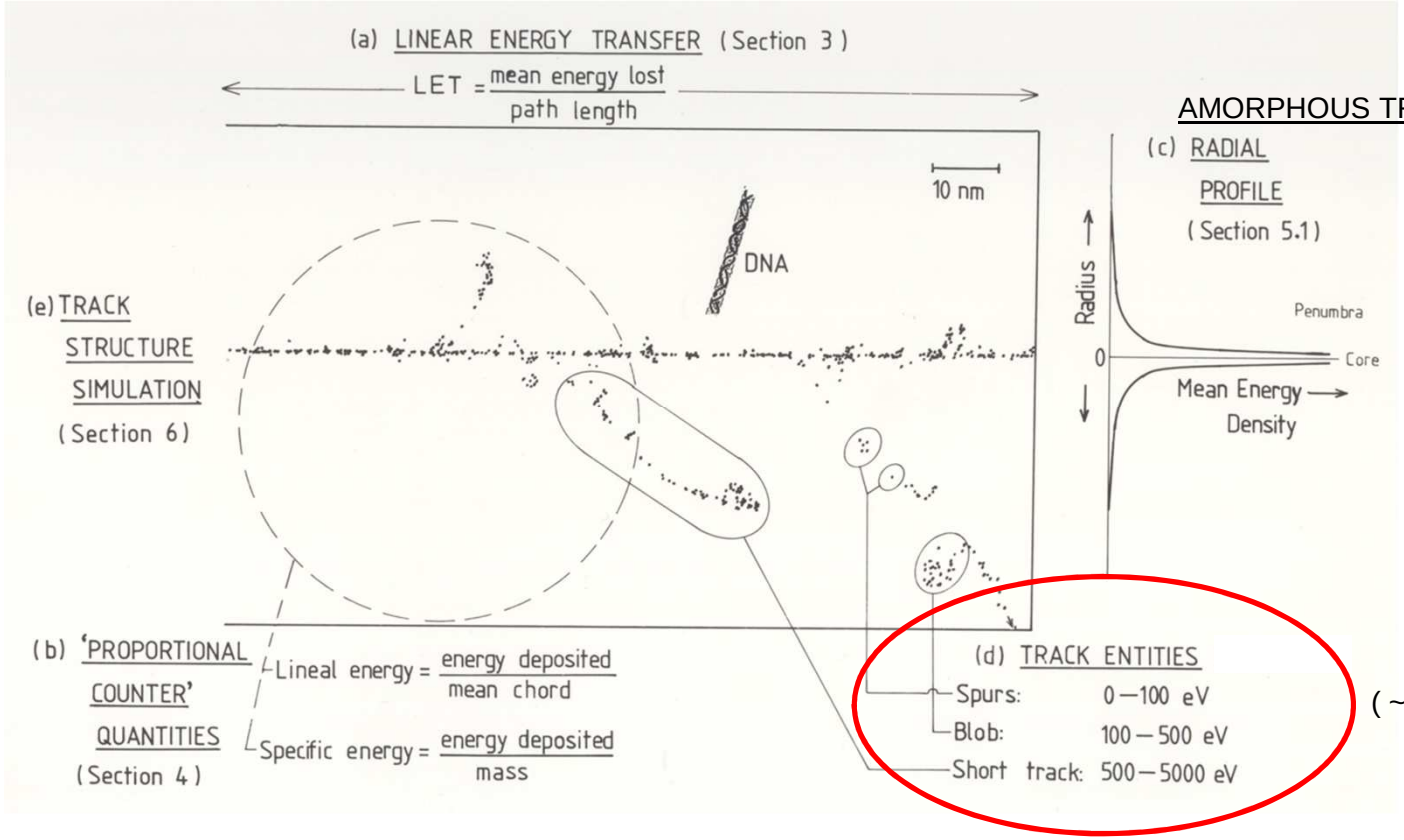


[Adapted from Int J Radiat Biol 56, 623 (1989)]

No single description is adequate or sufficient

Track simulations give ~ complete description, but info must be distilled/reduced

Track entities:

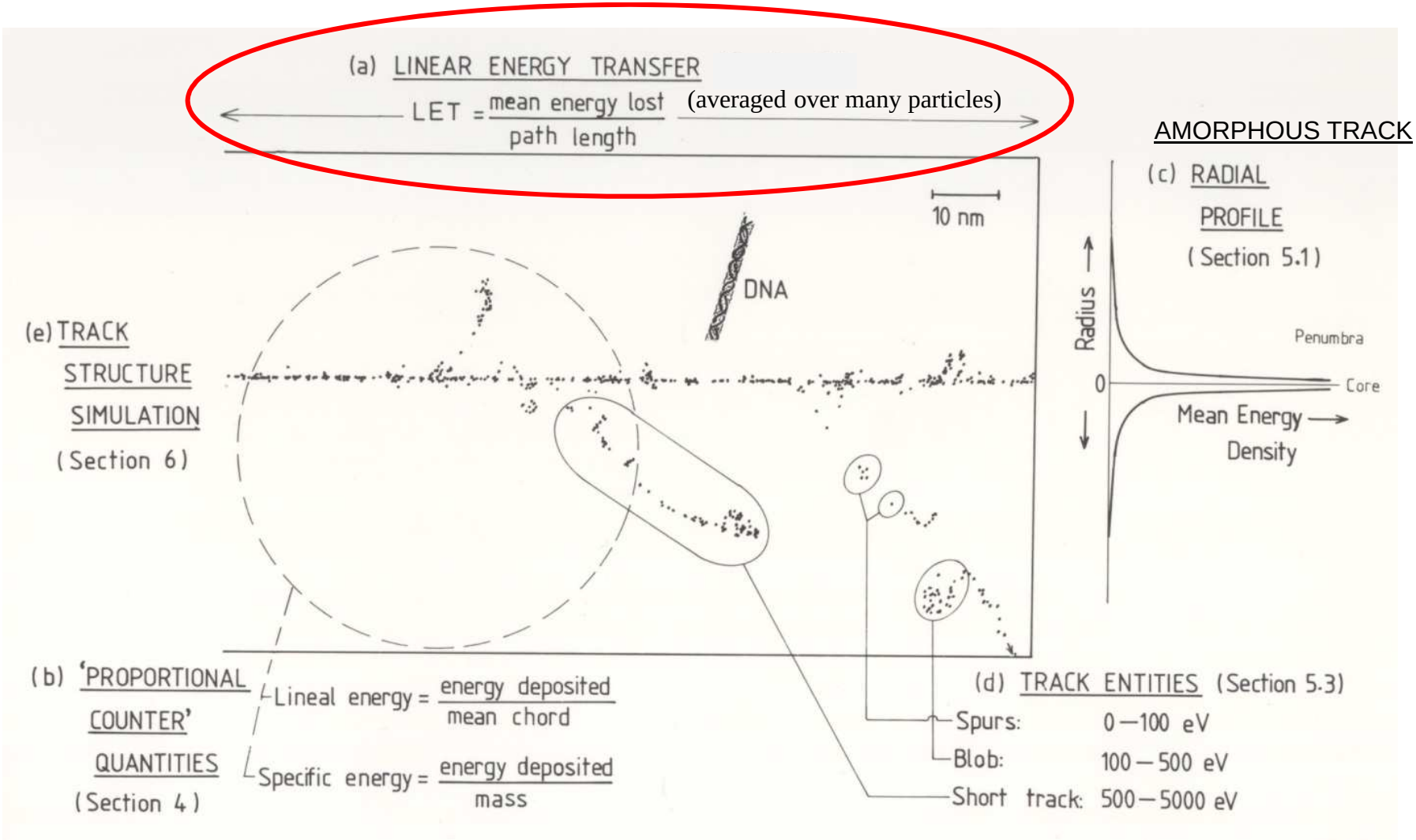


AMORPHOUS TRACK

(~ 4-5 ionizations per 100eV)

- **Developed and used by radiation chemists** (Mozumder & Magee1966: Radiat Res **28**, 203-214)
- **Little application in radiation biology** (e.g. Ward 1981: Radiat Res **86**, 185-195)
- **~ No application in radiation protection or medicine.**

Linear Energy Transfer (LET):



Consider LET

- **Describes energy transfer (loss) along the path of the particle** (Averaged over many particles of same Z, E)

- **BUT gives NO information on:**
  - -- Fluctuations in energy loss (stochastics)
  - -- Lateral spread of the track

- **LET depends on particle charge (Z) and velocity (V)**

$$\sim Z^2/V^2$$

$$-\frac{dE}{dx} \approx \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0}\right)^2 \cdot \left[\ln\left(\frac{2m_e c^2\beta^2}{I\cdot(1-\beta^2)}\right) - \beta^2\right]$$

Linear electronic Stopping Power

Hence

⇨ **Particles of same LET can have grossly different track structures**

Note: An alternative is to use z^2/β^2 instead of LET, but generally similar limitations.

The **linear energy transfer** or **restricted linear electronic stopping power**, L_Δ, of a material, for charged particles, is the quotient of dE_Δ by dl, where dE_Δ is the energy lost by a charged particle due to electronic collisions in traversing a distance dl, minus the sum of the kinetic energies of all the electrons released with kinetic energies in excess of Δ, thus

$$L_\Delta = \frac{dE_\Delta}{dl}.$$

Unit: $J\,m^{-1}$

The cut-off value (Δ) is usually in electron-volts (eV)

Most commonly used are:

L_∞ i.e. no cut-off (unrestricted), simply written as L

L_{100} i.e. 100 eV cut-off, includes only electrons of range ~nms (ie very local)

Hence, can define mean LET of a radiation field as:

Track-average LET:

$$\bar{L}_T = \int_0^\infty Lt(L)\,dL \Big/ \int_0^\infty t(L)\,dL$$

Use if effect of interest is ≈ proportional to L .

Dose average LET:

$$\bar{L}_D = \int_0^\infty L^2 t(L)\,dL \Big/ \int_0^\infty Lt(L)\,dL$$

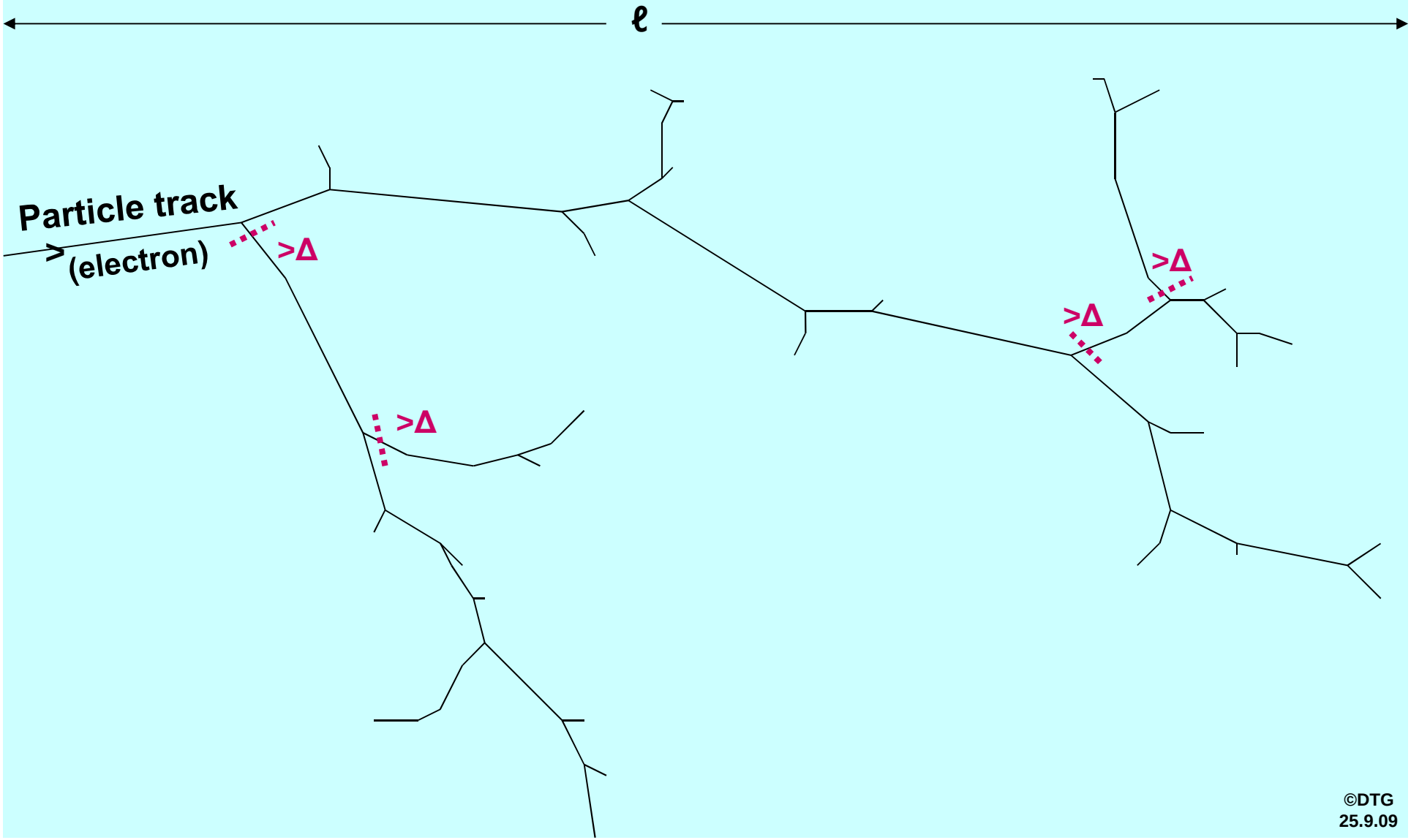
Use if effect of interest is ≈ proportional to L^2 .

where t(L) is the frequency distribution of L in the field

Linear Energy Transfer (LET), $L = \frac{\overline{\Sigma \varepsilon}}{\bar{\ell}}$ (Averaged over many tracks of this energy)

Restricted LET, $L_\Delta = \frac{\overline{\Sigma(\varepsilon<\Delta)}}{\bar{\ell}_{total}}$

If ε>Δ Cut off and treat as separate track



Linear Energy Transfer (LET), $L = \frac{\overline{\Sigma \varepsilon}}{\bar{\ell}}$ (Averaged over many tracks of this energy)

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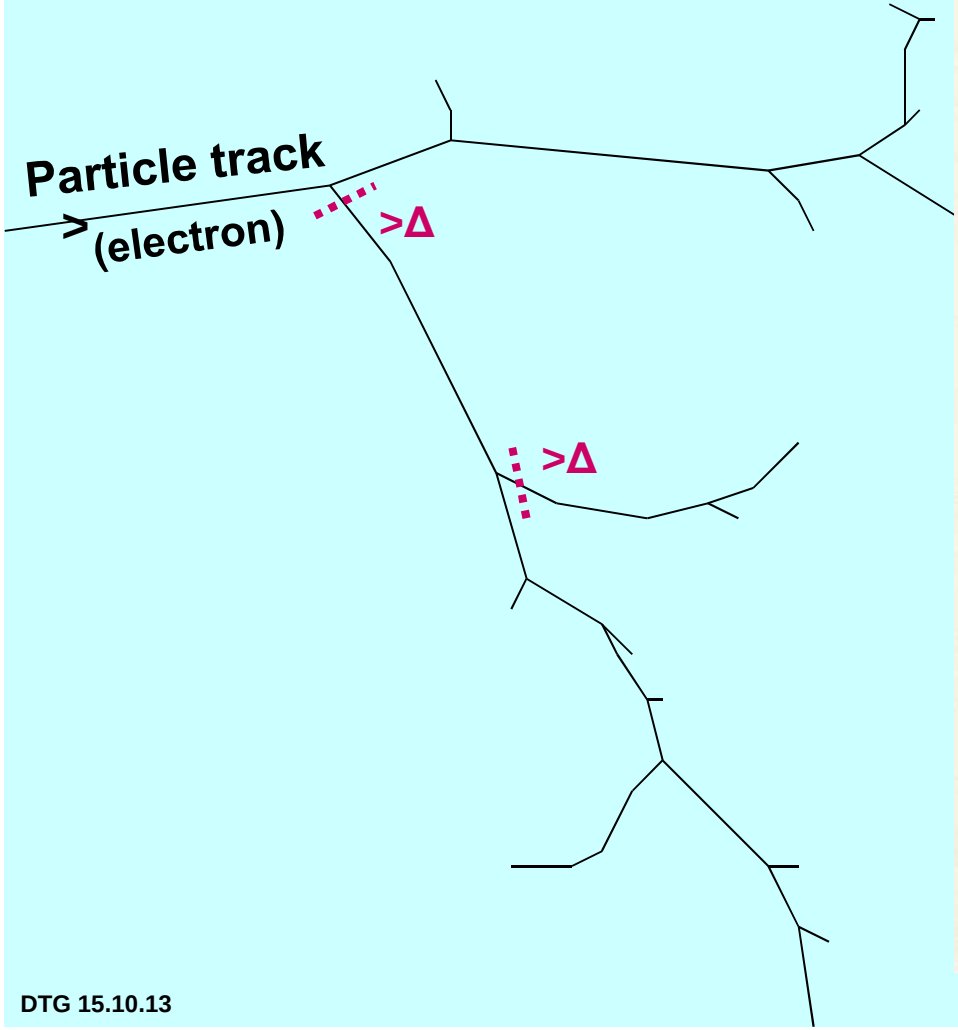
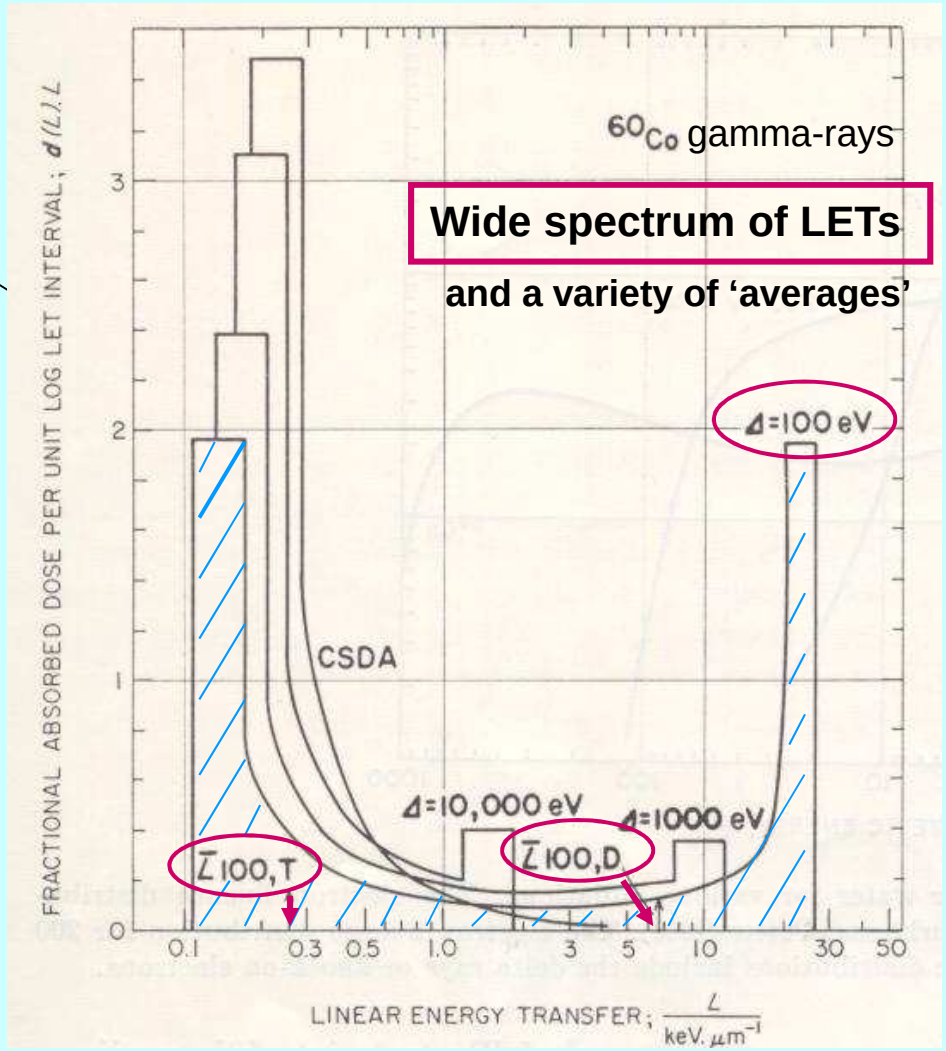
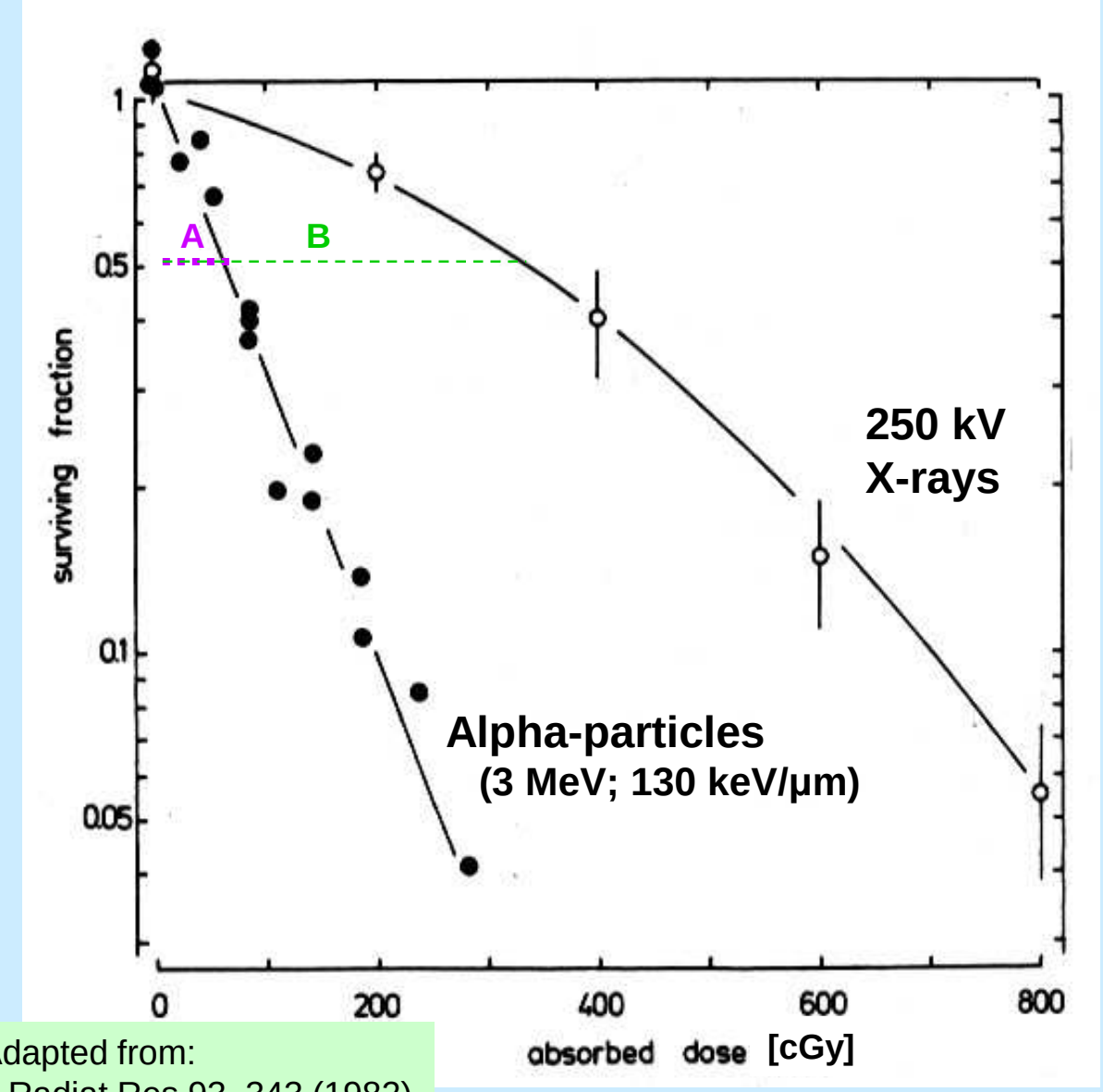




ICRU Report 16 (1970)

Ionizing radiations can kill cells:

e.g. Cell survival after alpha-particle irradiation compared to X-rays (in V79 cells)



Adapted from:
Radiat Res 93, 343 (1982)

For 50% survival of these cells the RBE* of alpha-particles relative to X-rays is

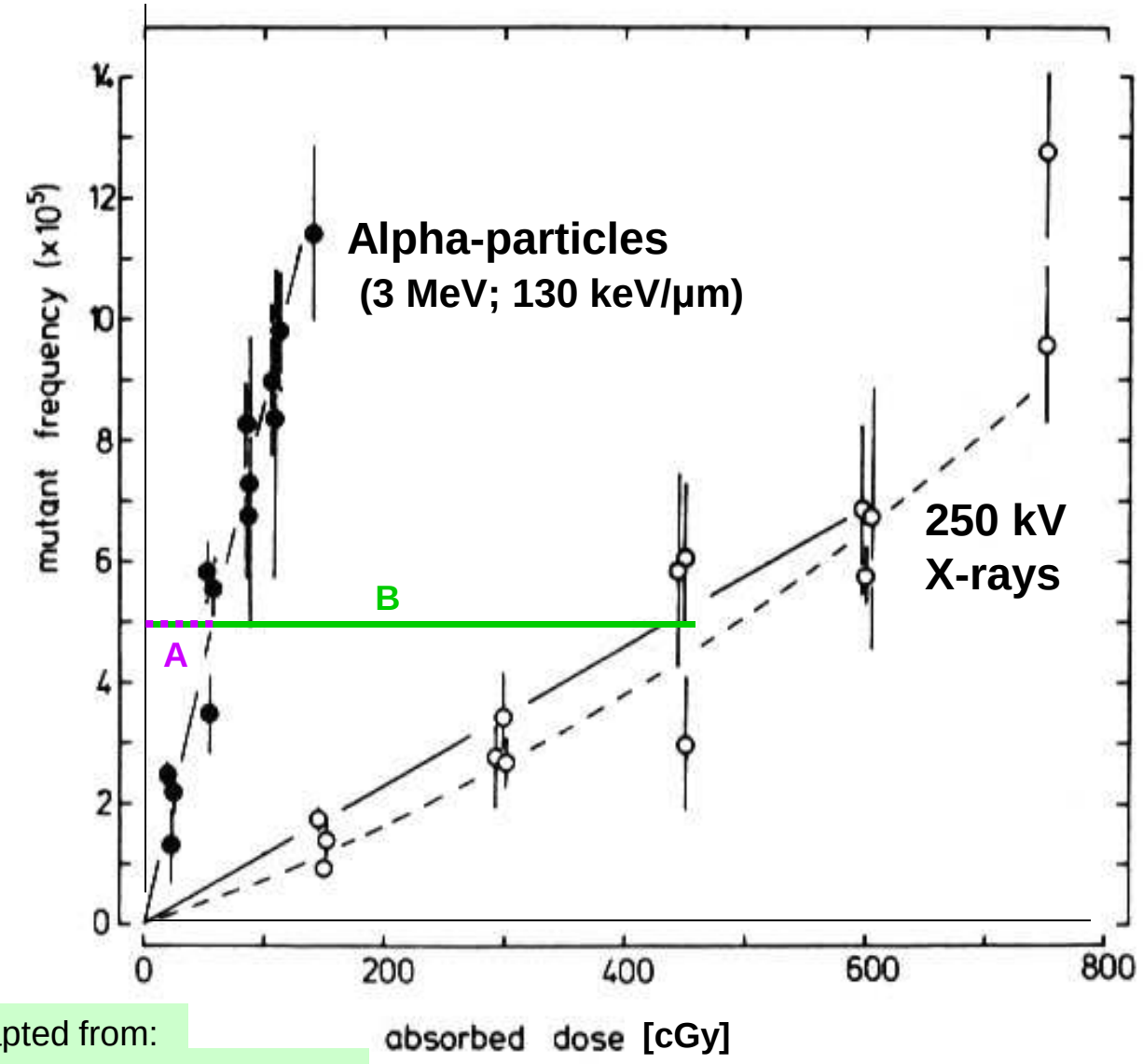
$$\frac{\text{Dose B}}{\text{Dose A}} \sim 5$$

This RBE is dose-dependent
-- larger at lower doses

*** RBE = Relative Biological Effectiveness**
= Ratio of doses for identical level of biological effect

Ionizing radiations mutate genes in cells:

e.g. hprt mutation-induction by alpha-particles compared to X-rays (in V79 cells)



Adapted from:
Radiat Res 93, 343 (1982)

In general, biological effectiveness depends on:

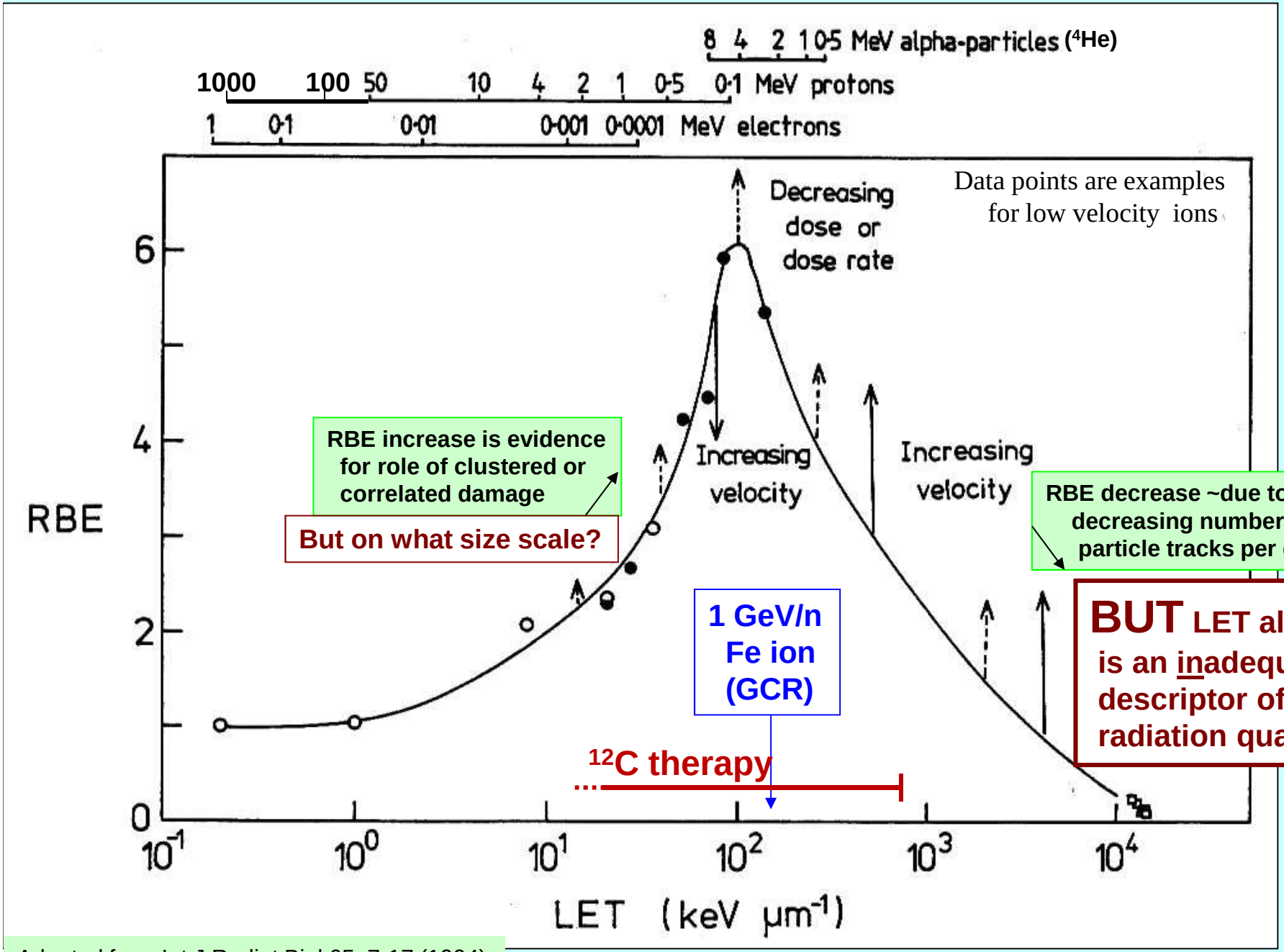
- --- radiation quality
- --- dose
- --- dose-rate
- --- biological system

Here:

Relative Biological Effectiveness (RBE) of alpha-particles in this system is

$$\frac{\text{Dose B}}{\text{Dose A}} \sim 8$$

Relative Biological Effectiveness for Cell Inactivation by Ionizing Radiations



Adapted from Int J Radiat Biol 65, 7-17 (1994)

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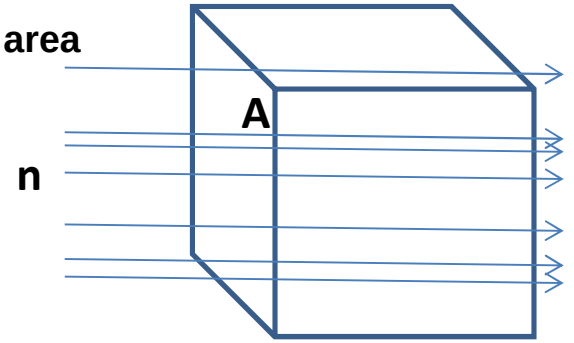
Some applications of LET

- Absorbed Dose ⟷ Fluence relationship

For fluence F of particles of LET L, the absorbed dose D is

D = kFL **where F = n/A = number of particles/unit area**

= 0.16FL **for A (μm), D (Gy), L (keV/μm**



- Organise radiation-quality data

e.g. RBE versus LET plots

Basic studies:

- Early analyses of radiation action for cell killing , mutation, aberrations , etc

e.g. Brustad (1962), Howard-Flanders (1958), Barendsen (1966), Goodhead (1980)

Radiation protection:

- Quality factor, Q(L), to convert absorbed dose to dose equivalent, in current operational radiation protection (monitoring)

Radiotherapy:

- General indicator of increasing effectiveness & decreasing OER (Oxygen Enhancement Ratio)
- RBE model for "biological dose" for application in treatment planning for heavy ion RT at HIMAC (Kanai et al RR, Radiat Res **147**, 78-85 (1997))

Based on linear-quadratic survival dose-response, with parameters empirically dependent on LET.

In operational radiation protection:

Q(L) relationship is used to calculate the operational dose equivalent used in monitoring

$$H = k \int Q(L) \left| L \frac{\partial \Phi(L)}{dL} \right| dL$$

Q weights absorbed dose (Gy) to obtain dose equivalent (Sv)

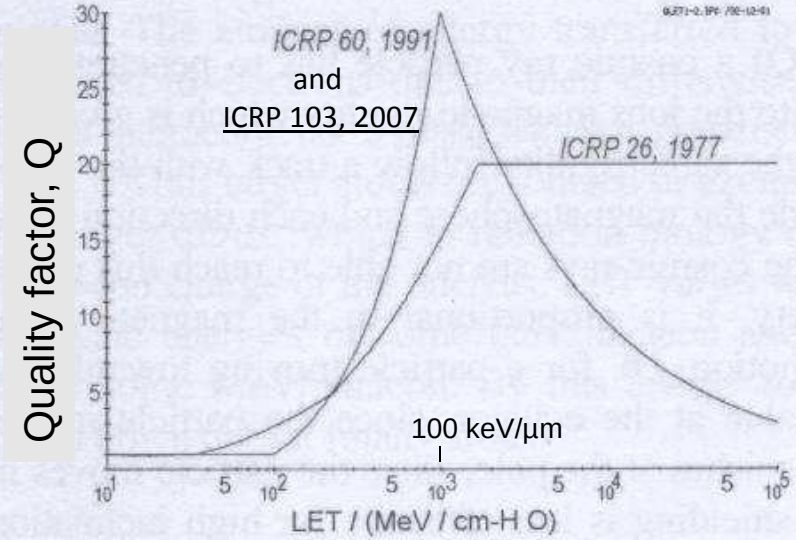


Figure 1.8 Quality factor, Q, as function of LET as defined by: (ICRP 60, 1991 and ICRP 26, 1977)

Based on ICRP committee judgements from experimental/theoretical considerations, because ~no epidemiological data are available for most high-LET radiations.

yields the equivalent dose deposited at the given point with $Q(L)$ representing the quality factor dependence on LET as in Figure 1.8 and k being an appropriate unit conversion factor.

Reliance on LET as the sole radiation-quality parameter is a notable limitation

--- All other aspects of track structure are ignored

Note: For most radiation protection ICRP-defined radiation weighting factors, w_R, are used to convert absorbed dose to equivalent dose (ICRP 103 (2007)).

ICRP-prescribed values of radiation weighting factor

NOTE: ~ all based on experimental/theoretical info, because ~no epi

Radiation type and energy range	Prescribed w_R	
	ICRP(1991)	ICRP(2007)
Photons, all energies	1 ★	1 ★
Electrons and muons, all energies	1 ★	1 ★
Neutrons, energy < 10 keV	5	Continuous fnc of energy, min 2.5, max 21
10 keV to 100 keV	10	
>100 keV to 2 MeV	20	
>2 MeV to 20 MeV	10	
>20 MeV	5	
Protons, other than recoil protons, >2 MeV	5	2 (also pions)
α particles, fission fragments, heavy nuclei	20	20

★ Implies equal risk per unit effective dose to body
" " equivalent dose to a tissue
" " absorbed dose to a tissue

} For ALL photon and electron irradiations -- a major simplification

ICRP treats: absorbed dose from low-energy beta emitters (few keV)
exactly as if from orthovoltage X-rays (~100 keV)
or from high-energy gamma-rays (~ 1 MeV).

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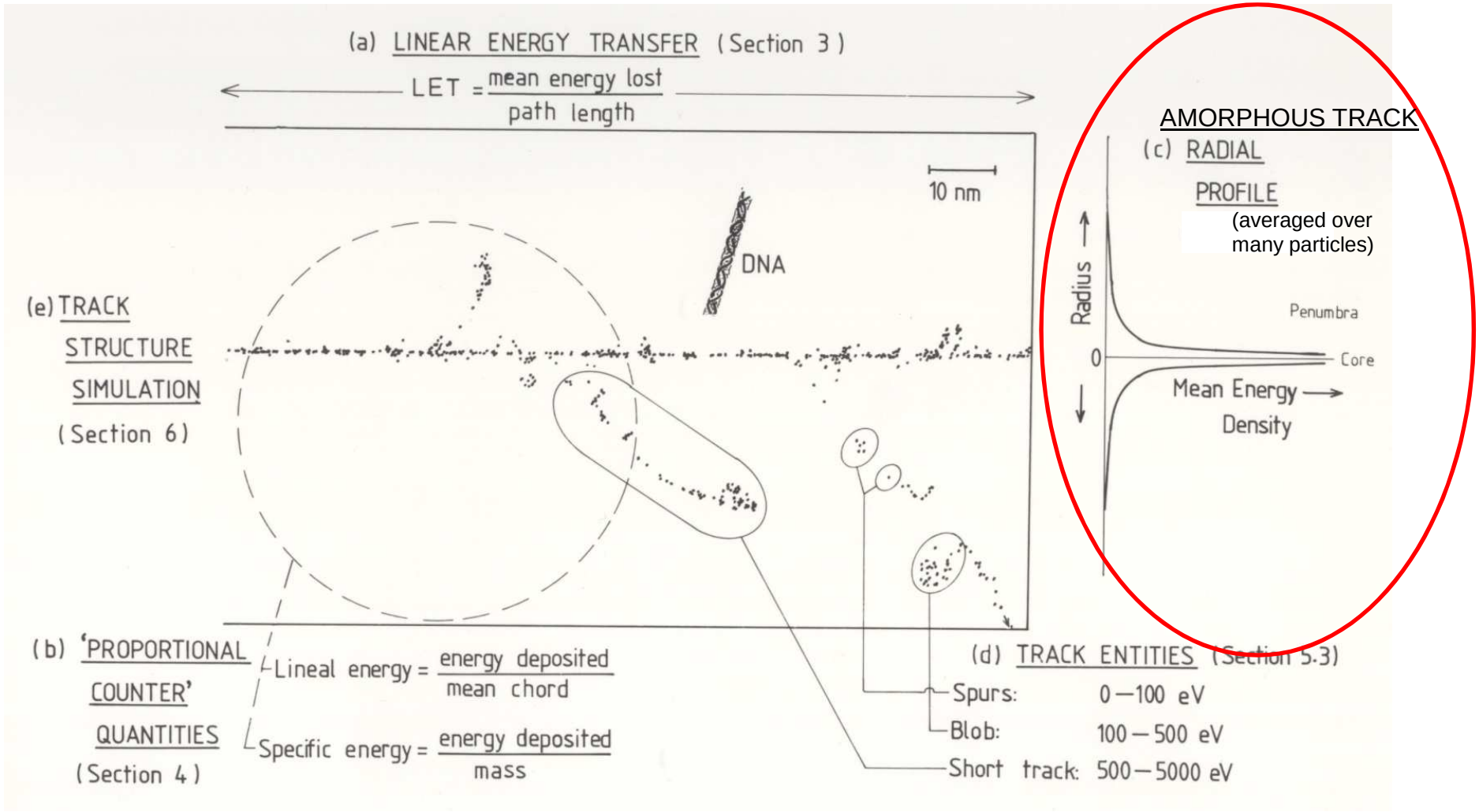
Amorphous track: Radial dose distribution



Amorphous track:

Consider radial dose distribution

- **Indicates average lateral spread of particle track**

  (Averaged over many particles of same Z, E)

- **BUT totally ignores stochastics of track**

- **Maximum width of track depends on particle velocity (V), i.e. on Energy/nucleon (not on Z)**

- **Ions of equal V, have ~ same relative track width and radial dose distribution ($D_r \sim 1/r^2$)**

- **Energy density in track depends on both Z and V**

  Unrestricted LET ≈ Stopping Power $\sim Z^2/\beta^2$

  (as dominant term of Bethe-Block stopping power formula)

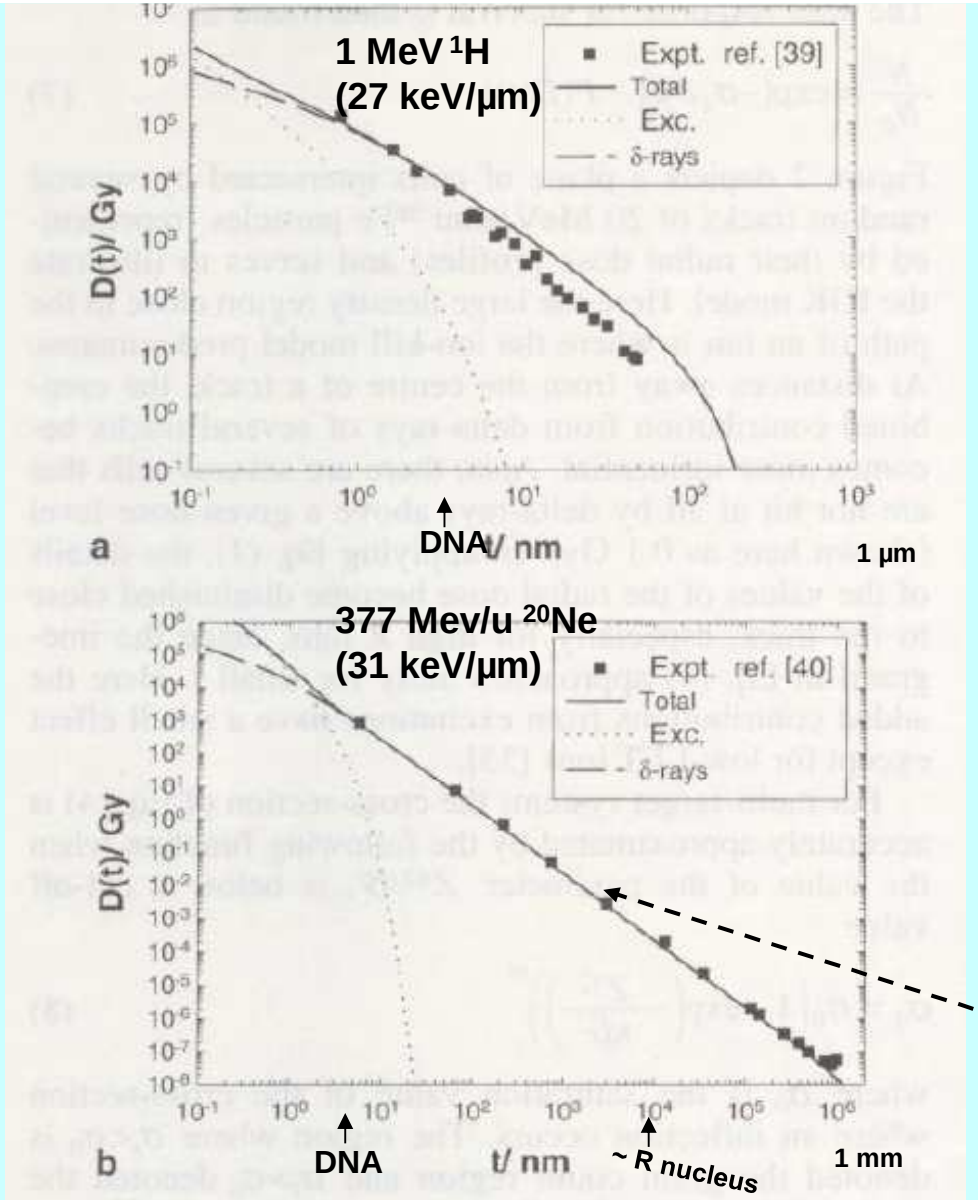


Fig. 1a–b Comparison of calculations of radial dose distributions to experiments [39, 40]. Calculations show contributions from excitations and secondary electrons. **a** ^{1}H at 1 MeV (linear energy transfer, LET=27 keV/μm), **b** ^{20}Ne at 377 MeV/u (LET=31 keV/μm)

Adapted from: Cucinotta et al , Radiat Environ Biophys 38, 81-92 (1999)

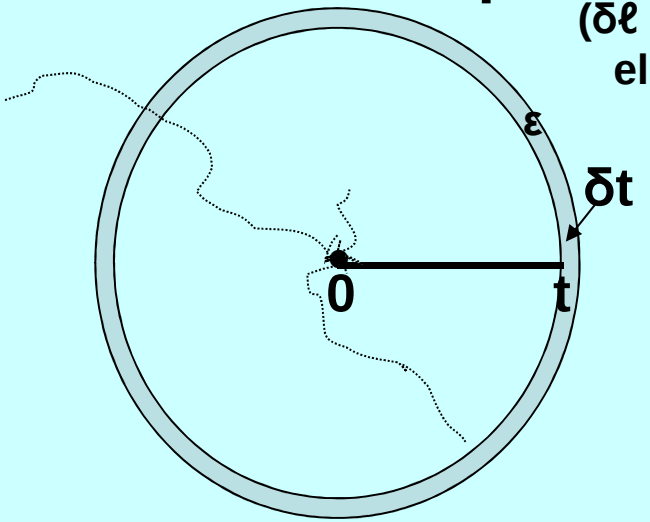
Radial dose distribution

Ave. Dose at radius t from ion path:

$$D(t) = \frac{\text{Energy}}{\text{Mass}} \quad \text{at radius t}$$

$$= \frac{\varepsilon(t,\delta t)}{2\pi t.\delta t.\delta \ell.\rho}$$

ε(t,δt) is energy deposited in element δt.δℓ (δℓ = length of element)



$D(t) \sim 1/t^2$ over most of the profile

Note then that

$\varepsilon(t) \sim 1/t$

i.e. <u>energy</u> falls off much more slowly than does <u>dose</u>

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For heavy charged particles (i.e. protons and heavier):

With increasing distance r from track centre
the local dose, D_r falls off as

$$D_r \sim 1/r^2$$

Note: 1. Often misinterpreted as the track being too narrow:

Energy, ε_r, deposited in annulus at distance r, falls off much more more slowly, as

$$\varepsilon_r \sim 1/r$$

Note: Mass of annulus increases proportionally with r

Hence, $D_r \sim \varepsilon_r / m_r \sim 1/r \,.\, 1/r \sim \varepsilon_r / r2$

2. Beware early descriptions based on “core and penumbra”.

Misleading because:

~ 50 % of deposited energy was arbitrarily assigned to the “core” --- **not valid**;

Definitions of “core” questionable.

Compare <u>energy</u> spread by ions of same LET

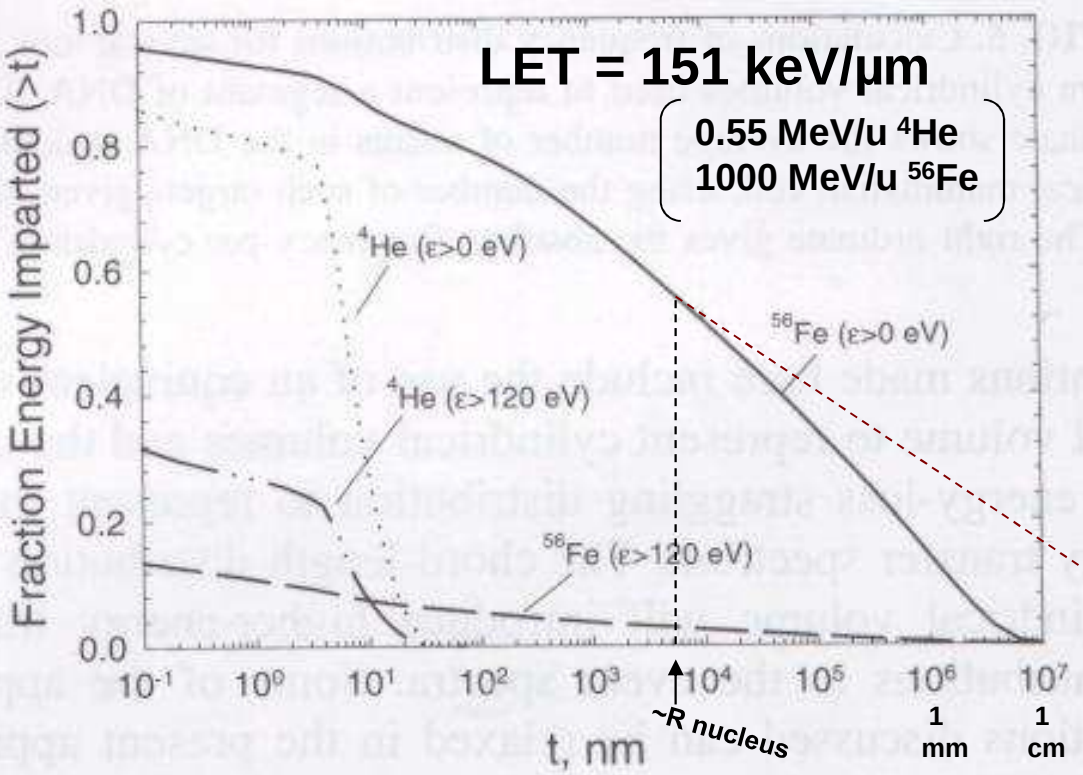


FIG. 9. Calculations of the fraction of energy imparted in a nucleosome from radial distances greater than *t*. This fraction is shown for the total energy imparted (0 eV) and for the fraction of energy imparted above 120 eV from ions of identical LET: **151 keV/μm.**

Fraction of energy imparted (>t):

$$\int_{t=t}^{t=\infty} \varepsilon(t).dt \Big/ \int_{t=0}^{t=\infty} \varepsilon(t).dt$$

For the high velocity Fe ions:
nearly 60% of the track energy escapes a traversed cell nucleus

i.e. Linear energy deposited <u>within</u> the cell nucleus is only ~ 40% x 151 ≈ 60 keV/μm

Adapted from: Cucinotta et al, Radiat Res <u>153</u>, 459-468 (2000)

Applications of amorphous track/radial profile

Basic studies:

- Katz amorphous track structure model for effects of radiation on cells

  Phenomenological model for radiobiological responses of cells to heavy charged particles.
  Integrates radial dose profile for heavy ions with radiation response from gamma- or X-rays.
  e.g. Katz et al, Radiat Res **47**, 102-125 (1971)

Radiation protection:

- NASA risk model uses Z^{*2}/β^2 instead of LET to specify Quality Factor, and paramaterizes NASA Quality Factor as a function of 'Katz' parameters (Σ_0, κ and m).

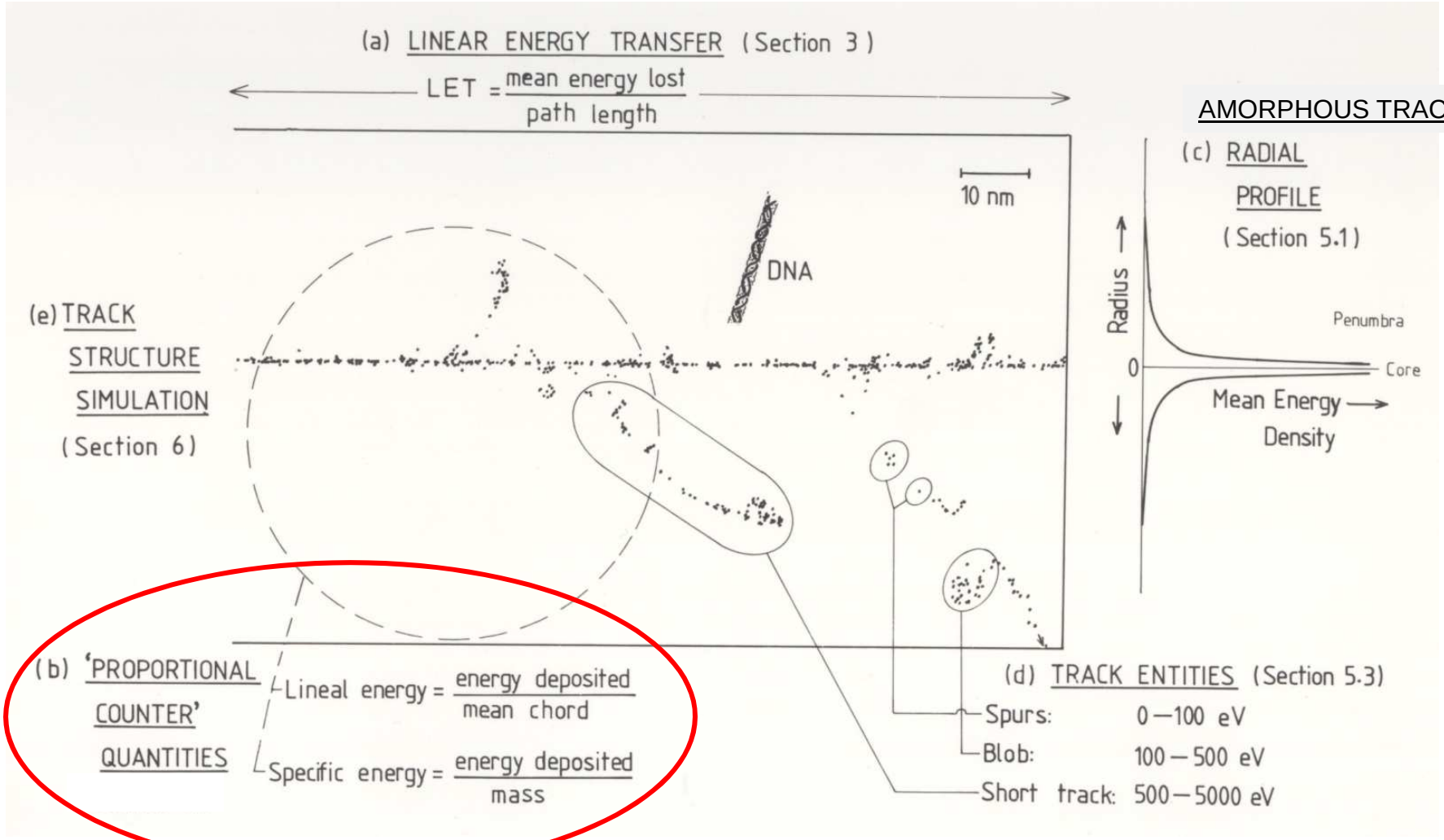
  (Cucinotta et al (2013) PLoS ONE 8(10): e74988.doi:10.1371)

Radiotherapy:

- Used in Local Effects Model (LEM) for radiotherapy with C ions (GSI)

  Phenomenological model for cell killing by heavy ions.
  Conceptual similarities to Katz model.
  e.g. Elsässer and Scholz, Radiat Res **167**, 319–329 (2007)

‘Proportional counter’ microdosimetry



The Rossi Counter:

Low pressure tissue equivalent proportional counter (TEPC).
A major development of the 1950s & 60s

Lineal Energy:

$$y = \frac{\varepsilon}{\ell} \text{ (keV/μm)}$$

Specific Energy:

$$z_1 = \frac{\varepsilon}{m} \text{ (Gy)}$$

Electric
Pulse ~ # ionizations
~ ε (energy imparted)

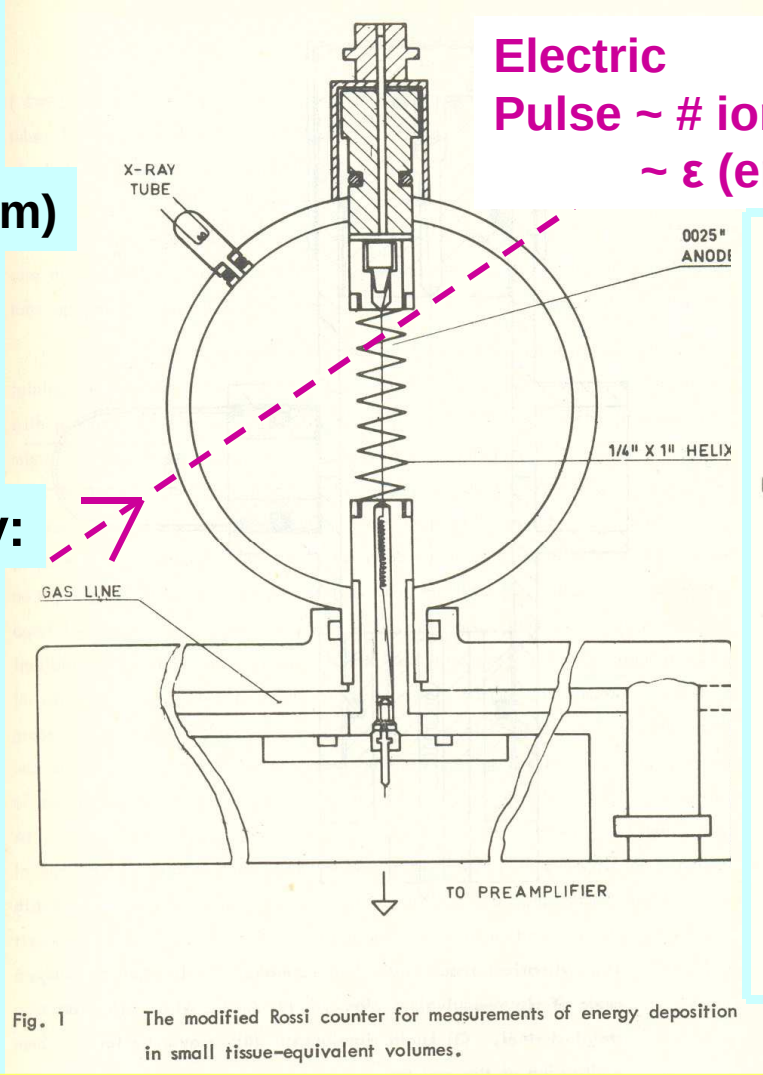
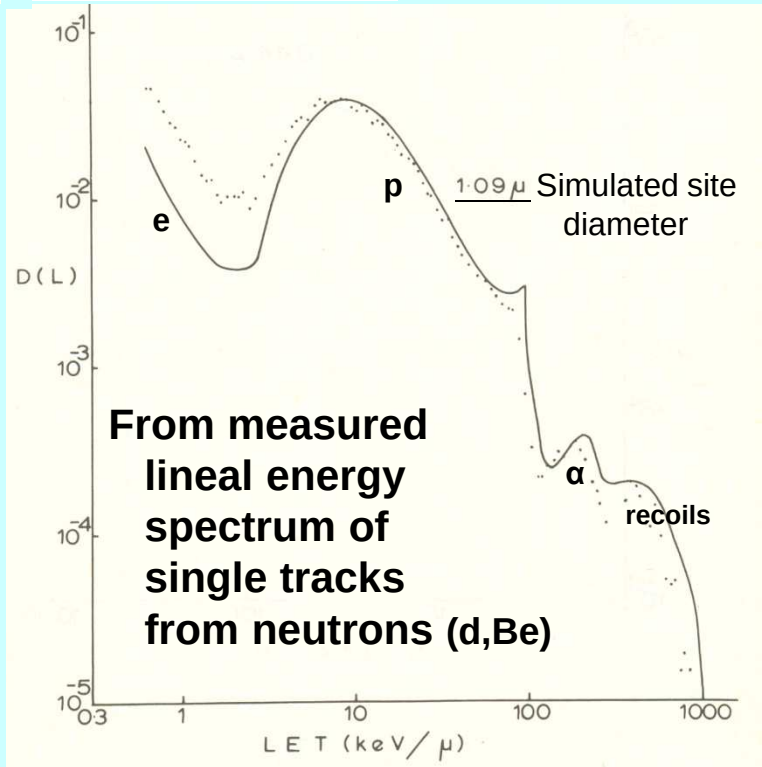


Fig. 1 The modified Rossi counter for measurements of energy deposition in small tissue-equivalent volumes.



Measures <u>actual</u> stochastic events in a microscopic simulated tissue volume

16.10.13

Experimental Simulation of microscopic volume of tissue:

Fill proportional counter with 'tissue-equivalent' gas at low pressure, such that that:

Energy loss for charged particle through counter gas
= " " " " " " tissue volume

For scaling factor K: $\frac{\rho_{gas}}{\rho_{tissue}} = \left(\frac{S_t}{S_g}\right)\left(\frac{p_g}{p_t}\right) = \frac{1}{K}$

ρ = density
S = stopping power
p = path length
S_t/S_g approx = 1

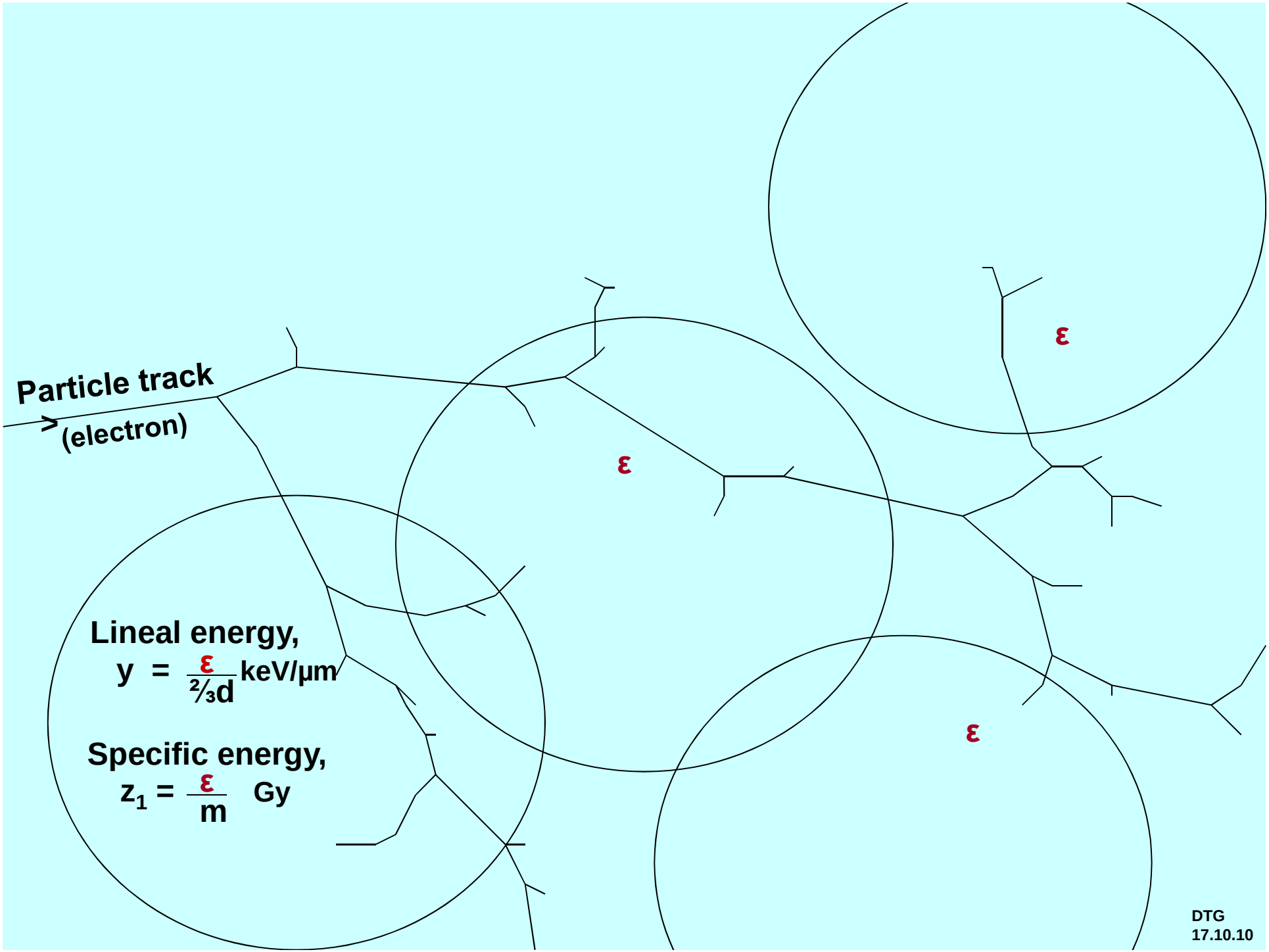
Typical scaling factor of 20,000 simulates 1 μm sphere in tissue with low-pressure gas in a 2 cm spherical prop counter

Most common is ~ 1 μm simulation
Also 0.5 μm to 10 μm (sub-nucleus to nucleus or cell sizes)

Practical limit of simulation: Down to tissue sites of ~ 0.3 μm diameter

(still very large compared to DNA, nucleosomes, etc)

Later: Also solid state microdosimeters.
Much smaller volumes ('nanodosimetry').


Particle track
(electron)
ε
ε
ε
Lineal energy,
y = ε / ⅔d keV/μm
Specific energy,
z1 = ε / m Gy
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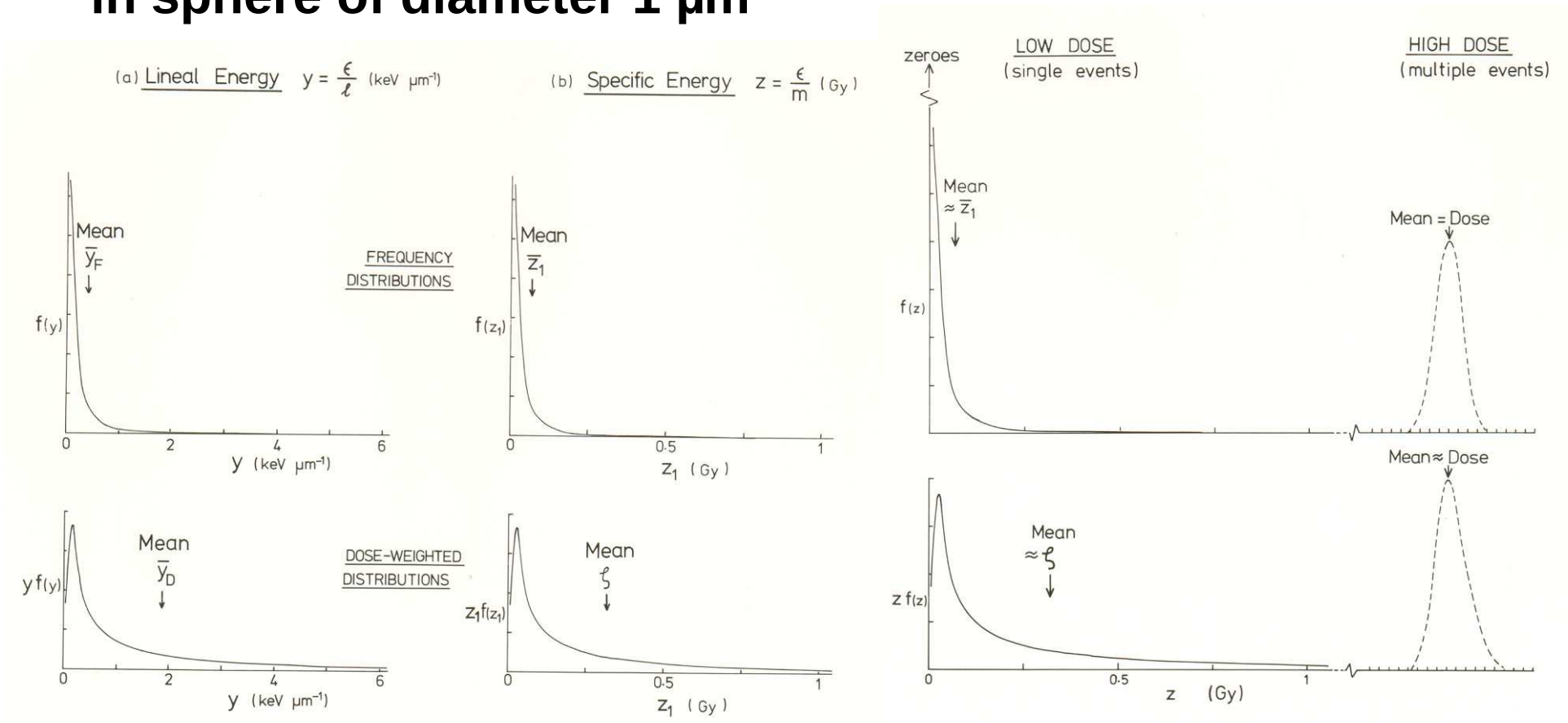
17.10.10

Spectrum of lineal energy and specific energy for ^{60}Co γ-rays in sphere of diameter 1 μm



Radiat Res 91, 45-76 (1982)

Obtained from experimental measurements with Rossi proportional counter.

Note: More usually plotted with log-scale abscissae (and ordinates therefore multiplied by y (or z) to preserve area normalization).

Useful relationship

Event frequency:

$$\phi = \frac{1}{\bar{z}_F}$$

gives average number of events ('hits') in the target volume per unit absorbed dose

Example: For a sphere of diameter 8 µm in tissue irradiated with Co gamma-rays, $\bar{z}_F$ = 1 mGy (from measurements with Rossi counter).
Hence: For natural background radiation of 1 mGy per year, each cell nucleus of diameter ~ 8 µm is hit by radiation on average once per year

---

Approximations for irradiation with low-velocity charged particles of LET = L , (i.e. narrow tracks) crossing spherical targets:

$$y_F \approx L \qquad y_D \approx \frac{9}{8} L$$

$$z_1 \approx 0.204 \frac{L}{d^2}$$

$$\Phi \approx \frac{d^2}{0.204\ L}$$

y, L in keV/µm
z in Gy
D in µm

Some Applications of y, z

- Hit-frequency evaluations: $\phi = \frac{1}{\bar{z}_F}$

Basic radiobiology and risk modelling:

- Theory of Dual Radiation Action for radiobiology and cancer risk: Effect = $\alpha D + \beta D^2 = k(D + z_D^2)$

  Developed hand-in hand w Rossi Counter during 1970s

  Curr Top Radiat Res Q 8,85-158 (1972); Radiat Res 75, 471-488 (1978)

  Proposed as fundamental and mechanistic, but assumptions invalidated by experimental tests.

  See: Radiat Prot Dosim 122, 3-15 (2006)

  Remains usable as phenomenological model for limited purposes.

- Microdosimetric Kinetic Model (MKM) of cell death. [Hawkins, Int J Radiat Biol 69, 739 (1996); Radiat Res 160, 61 (2003); Radiat Res 172, 761 (2009)]

  Incorporates aspects of TDRA and other models as practical mathematical formalism.

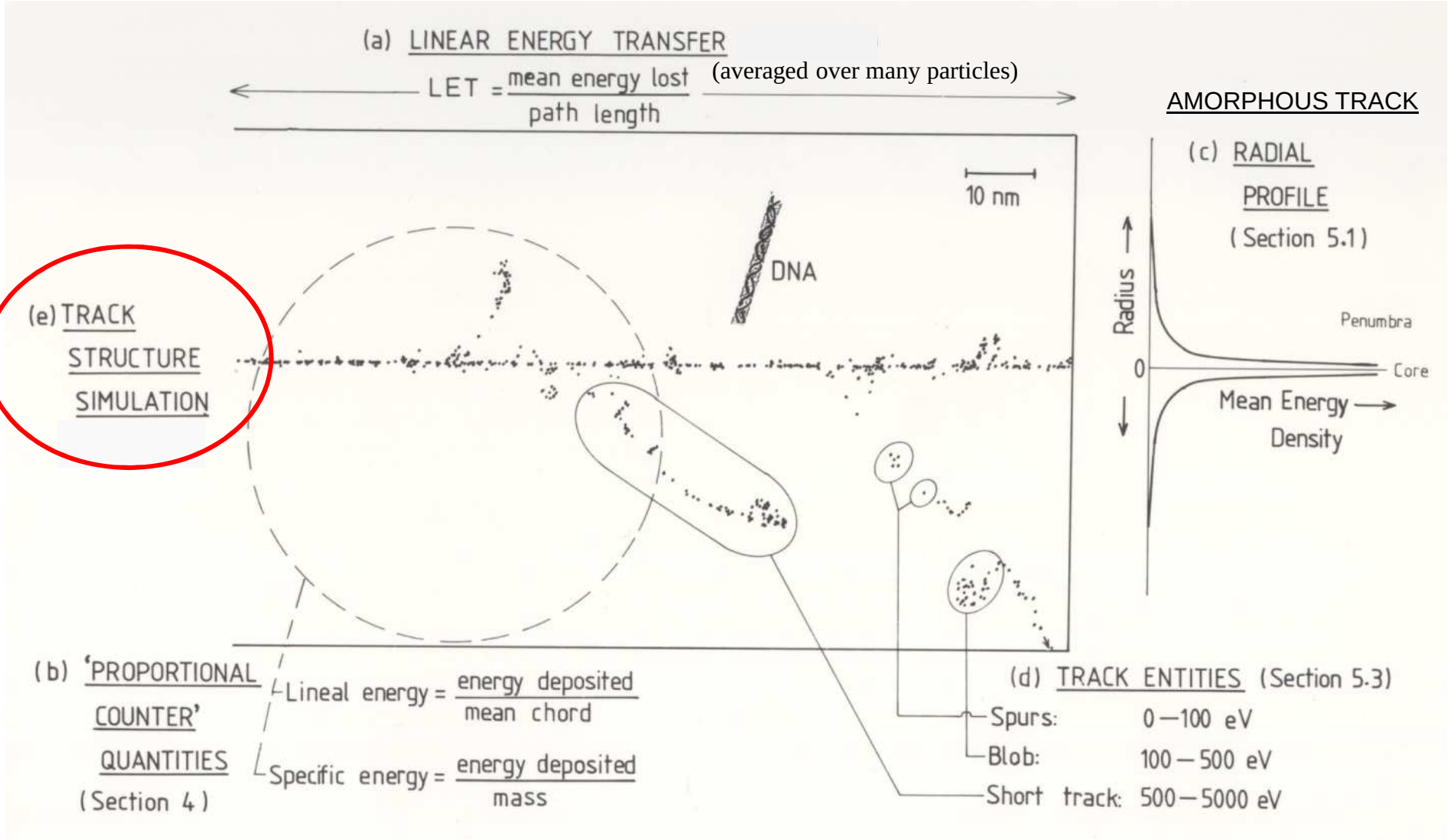
Radiation Protection:

- (Task Group proposed specifying Q as fnc of mean lineal energy (y) instead of fnc LET, but never adopted by ICRP). (ICRU Report 14, 1986)
- Wide practical application in dosimeters: e.g. Measure y spectrum in mixed radiation field (prop counter and other devices), unfold as LET spectrum and hence evaluate Q(L) and equivalent dose rate.

Radiotherapy:

- Mathematical approach based on MKM for "biological dose" for planning of C-ion radiotherapy at HIMAC (Japan). Kase et al, Radiat Res **166**, 629-638 (2006); Sato et al, Int J Radiat Biol **88**, 143-150 (2012); Sato et al, Radiat Res **178**, 341-356 (2012)

Track structure:



Track structure

- **Event-by-event simulations**
- **Provide ~ complete microscopic description of radiation**
- **BUT what to do with all the information ???**

Reduce to the well-known microdosimetric/radiation-quality quantities ?

Calculate 'novel' microdosimetric/radiation-quality quantities ??

Quantities on the nanometre scale (cf DNA, etc) ?

Use for modelling:

- **to provide new insights and generate new hypotheses on radiation mechanisms and effects**
- **to provide quantitative descriptions of known phenomena/data**

Modelling from track simulations

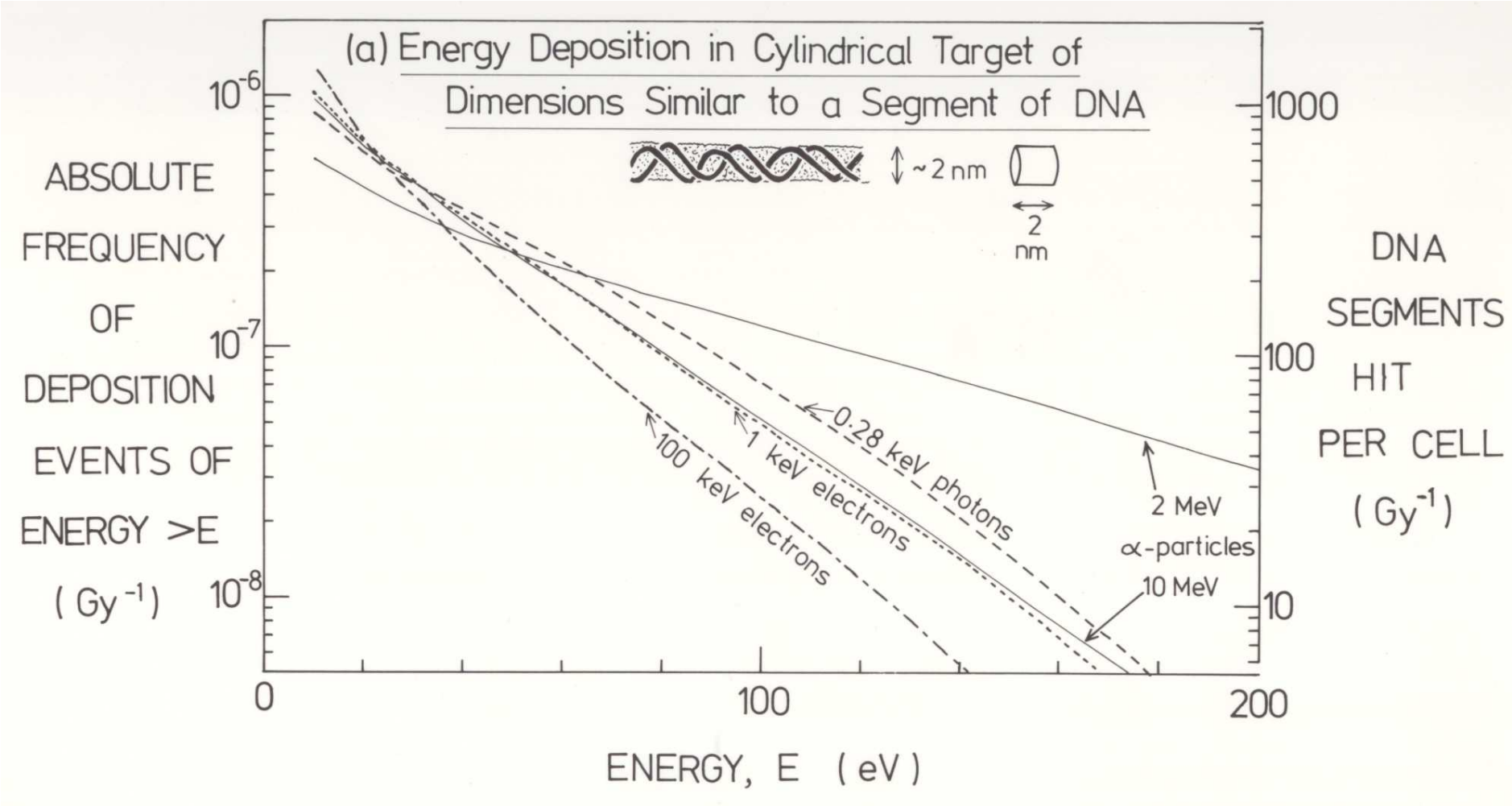
1. **A personal example:**

DNA Clustered damage

Spectra of ‘hit sizes’ in DNA-sized targets from different radiation qualities

(Calculated by sampling Monte-Carlo track-structure simulations)

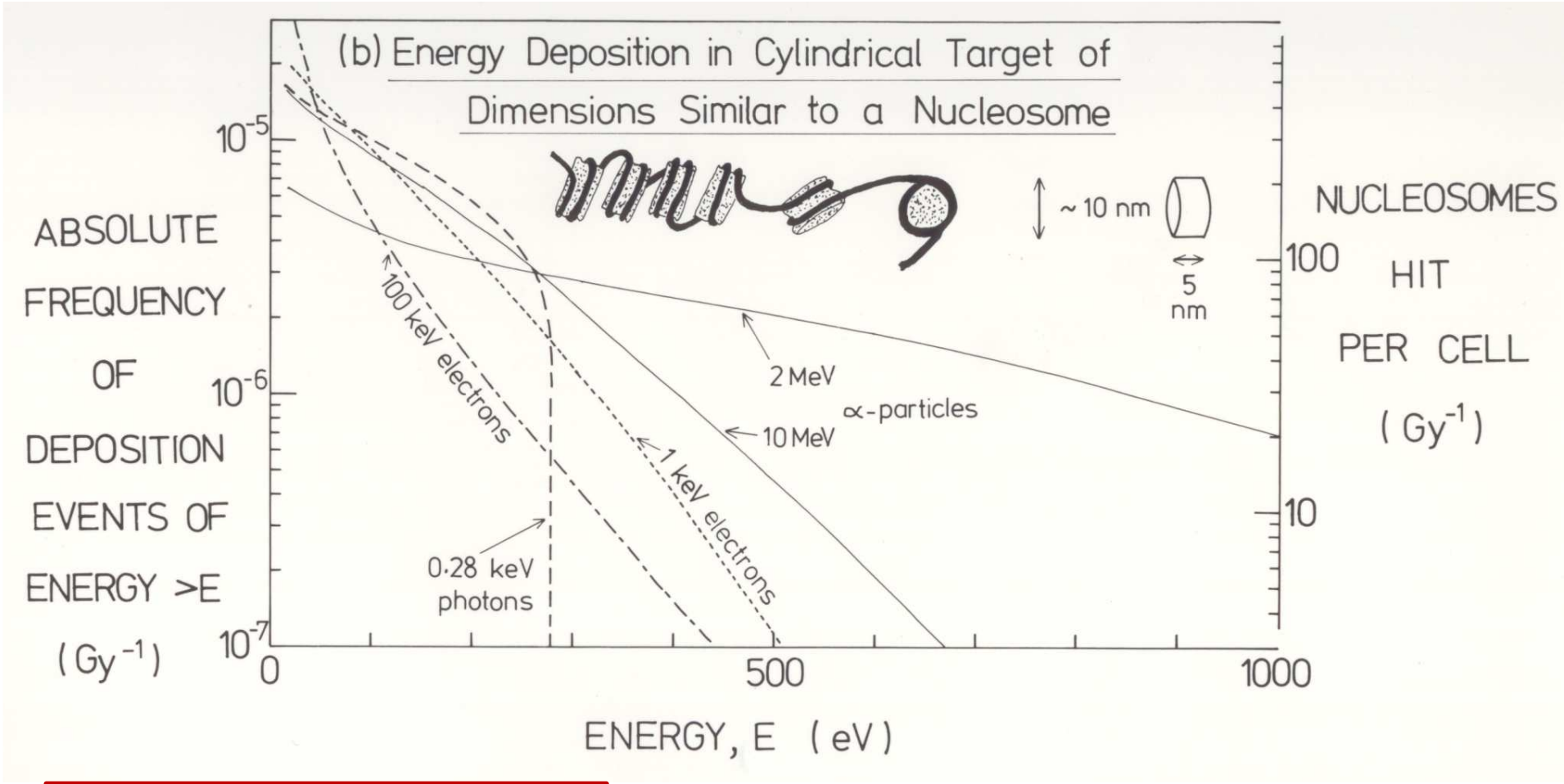
Goodhead & Nikjoo (1989, IJRB 55, 513-529)



Spectra of ‘hit sizes’ in nucleosome-sized targets from different radiation qualities

(Calculated by sampling Monte-Carlo track-structure simulations)

Goodhead & Nikjoo (1989, IJRB 55, 513-529)



Hypothesis of critical properties:

For Low-LET: ~ 100 eV in ~ 3-4 nm
High-LET: ~ 300 eV in ~ 10 nm

Frequency distribution of energy deposition, ε, in target volumes of interest for HZE* exposures:

from deterministic model, which combines:
results from Monte-Carlo scoring of electrons
with average-track model of ions (amorphous track)

Cucinotta et al (2000)
Radiat Res 153, 459-468

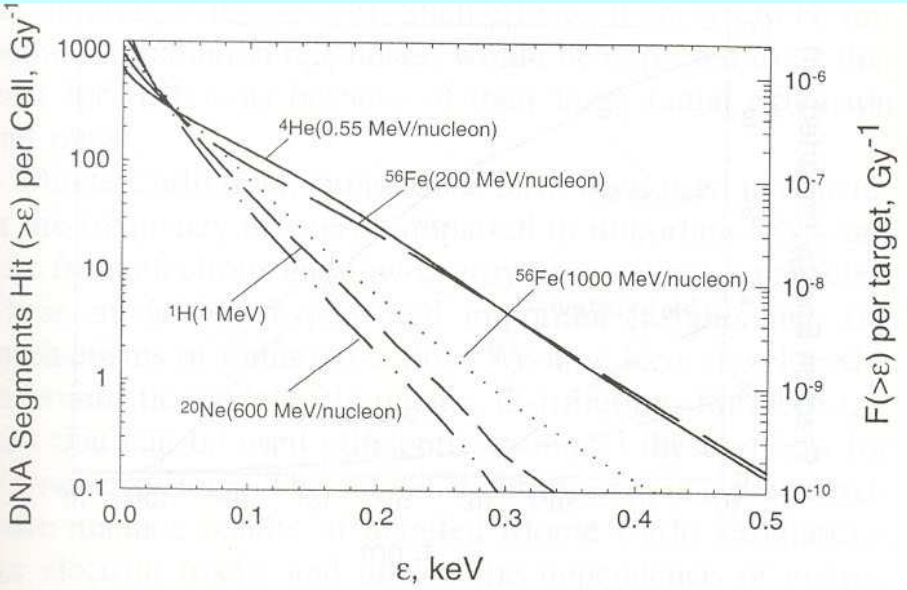


FIG. 5. Calculations of frequency distributions for several ions in 2 × 2-nm cylindrical volumes used to represent a segment of DNA. The left ordinate shows the average number of events in the DNA structure in a typical mammalian cell, using the number of such targets given in Table 1. The right ordinate gives the absolute frequency per cylindrical target.

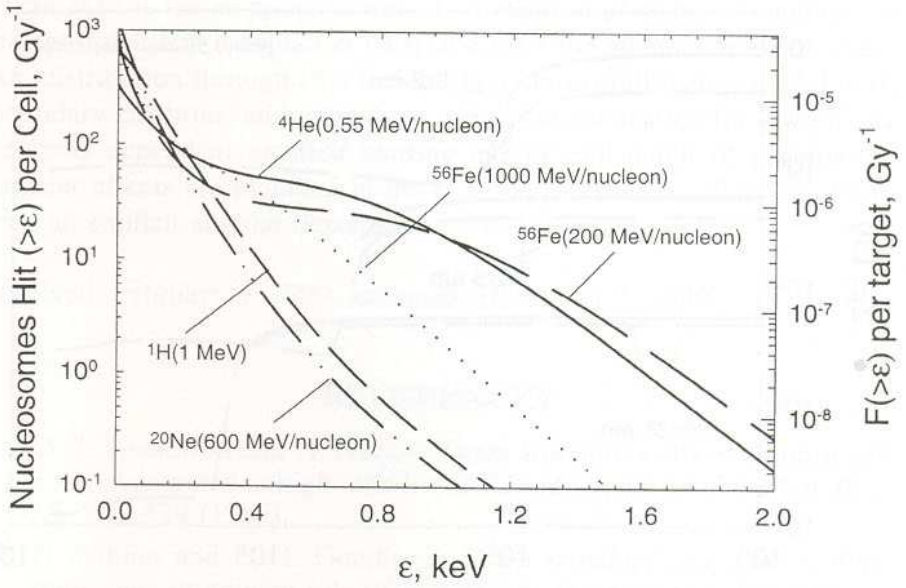


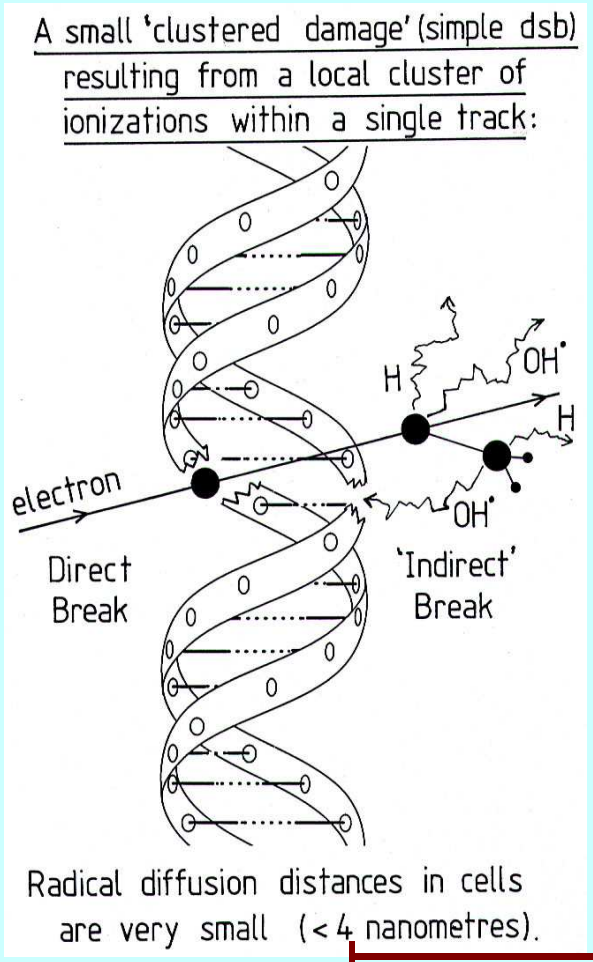
FIG. 6. Calculations of frequency distributions for several ions in a 10 × 5-nm cylindrical volume (nucleosome). The left ordinate shows the average number of events in the nucleosome structure in a typical mammalian cell, using the number of such targets given in Table 1. The right ordinate gives the absolute frequency per nucleosome cylindrical target.

* HZE = particles of high charge and energy

DTG
4.2.14

- **Well known that chromosome aberrations, and smaller mutations, can result from Double-Strand Breaks (DSB) in DNA**

- **Ionizing radiation is efficient at producing DSB**
  ---- because of clustering of ionizations within individual tracks



This simple Double-Strand Break has been produced by:
- **one direct ionization, and**
- **one OH radical diffusing from an ionization in water very nearby**

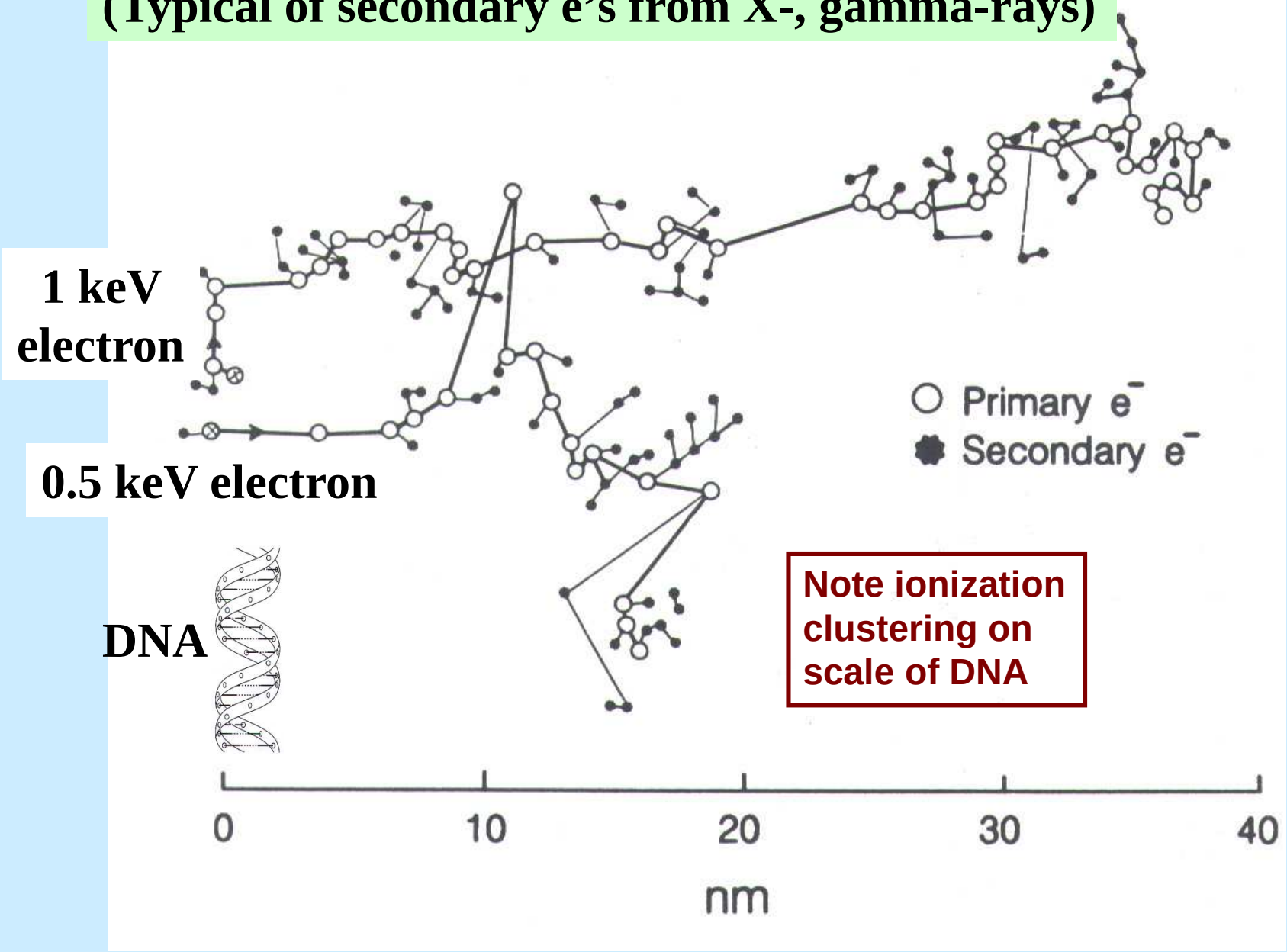
ie Both were from a small cluster of ionizations in a single electron track

Other DSB can be due:
- **to two direct ionizations (ie Direct only)**
- **or to two OH radicals (ie Indirect only)**

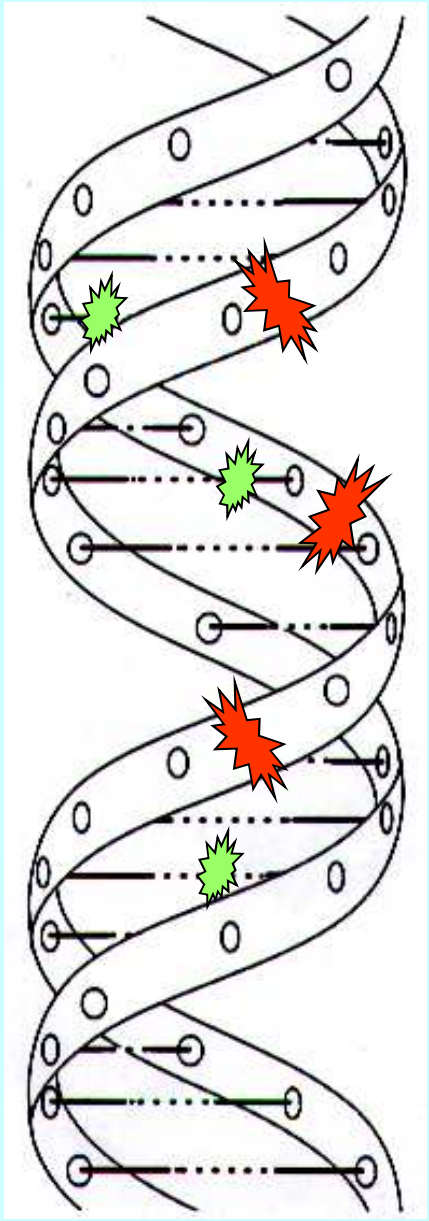
DSB result from clustering of ionizations on nm scale

Two low-energy-electron tracks

(Typical of secondary e's from X-, gamma-rays)

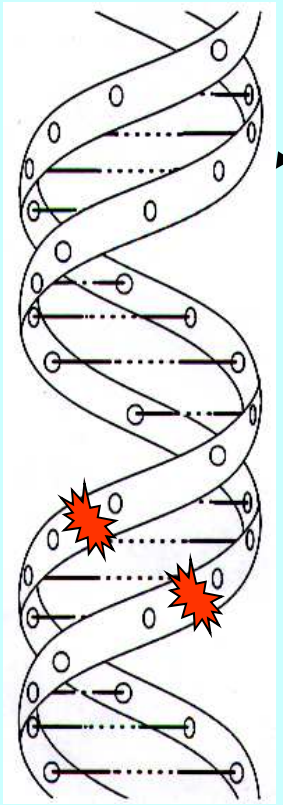


Example of <u>Complex</u>
<u>Clustered Damage in DNA</u>
resulting from a single electron track from low-LET radiation

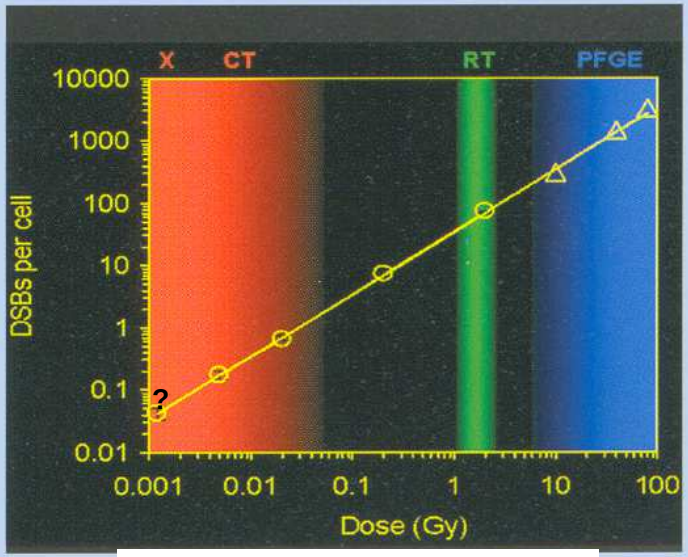


2 nm

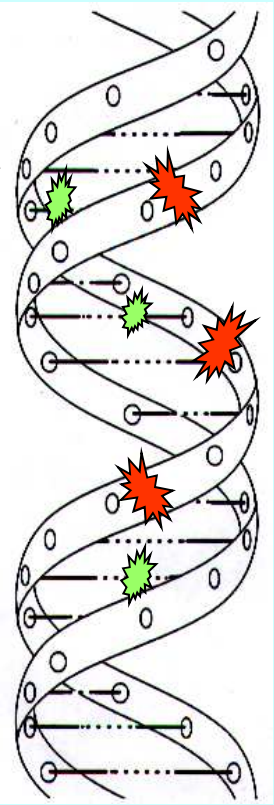
Examples of Clustered Damage in DNA resulting from a single electron track from low-LET radiation



Simple DSB



(Rottkamm & Lobrich, PNAS, 2003)



Complex DSB

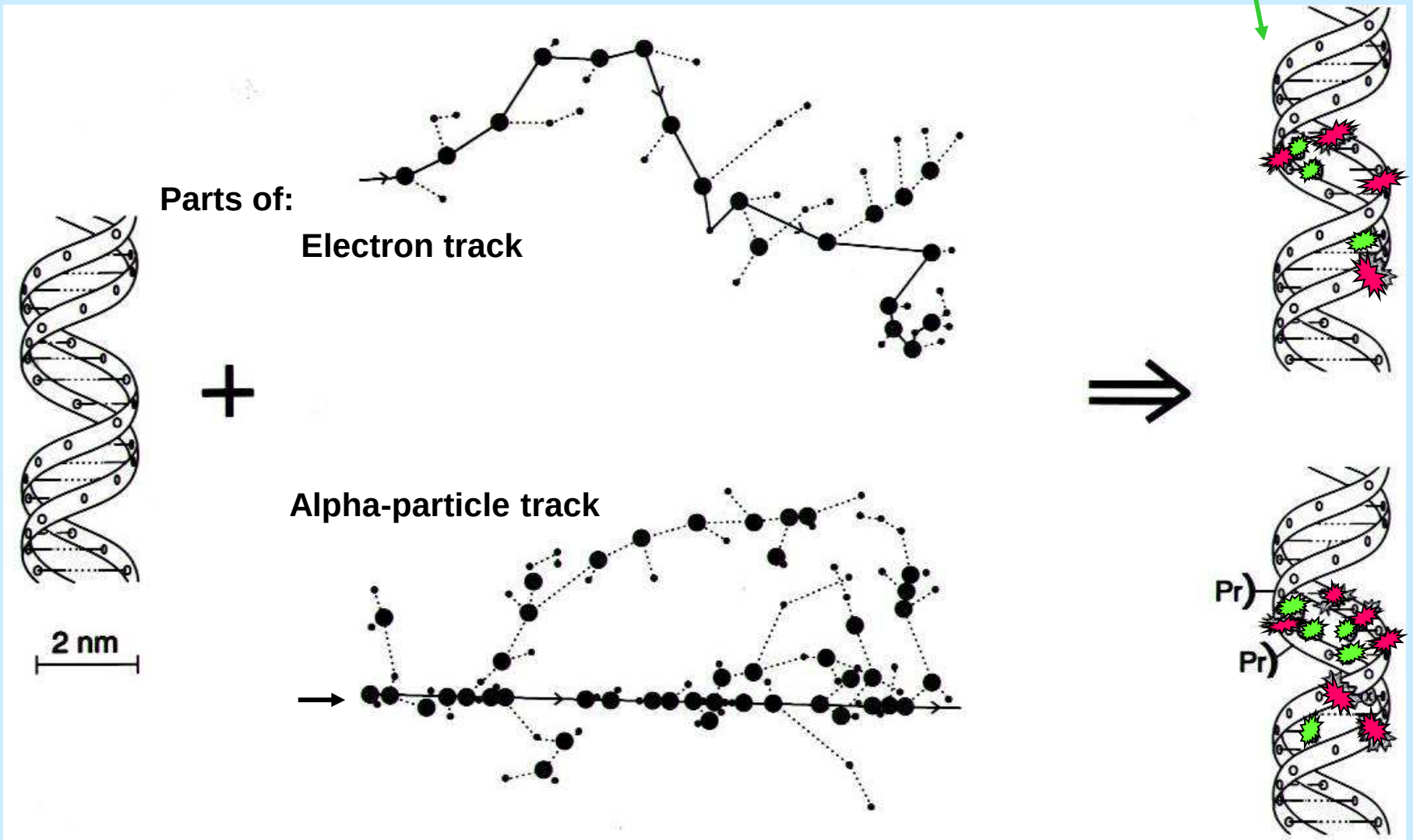
Yield of DSB is proportional to dose

" " number of tracks

Each DSB arises from a <u>single</u> track

DSB = Double-Strand Break in DNA

Single tracks of ‘low’- LET or high- LET radiation can produce Complex Clustered Damage in DNA

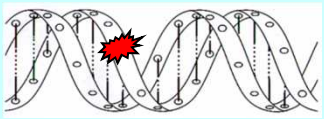


[Goodhead, IJRB 65, 7 (1994)]

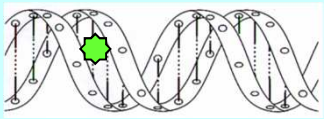
Clustered Damage in DNA

Simple damage (1 component):

Single strand break (SSB)

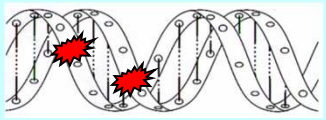


Damaged base (BD)

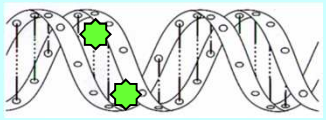


Simple Clustered Damage (2 components):

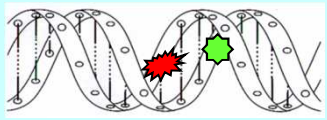
Double strand break (DSB)



Double base damage



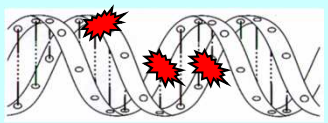
SSB + BD

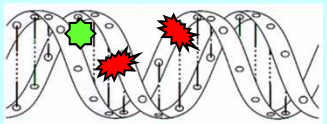


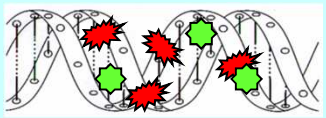
Also pairs on same strand

Complex Clustered Damage (3 or more components):

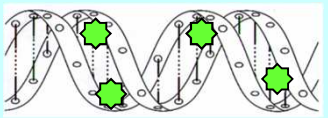
eg Complex DSB

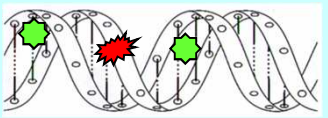






eg Other combinations





Low-LET X, γ: ~ 20% of dsb are complex via 1 or more additional strand break(s)*
~ 50% " " " " " additional break(s) and/or base damage(s)*

High-LET α: ~ 70% " " " " " 1 or more additional strand break(s)*
~ 90% " " " " " additional break(s) and/or base damage(s)*

All radiations produce a substantial proportion of complex DSB

* Nikjoo et al, Radiat Res 148, 485 ('97); 156, 577 ('02);
IJRB 71, 467 ('97) 156, 577 ('02); Rad Prot Dosim 99, 77 ('02)

* Goodhead, Health Physics 97, 394-406 (2009)

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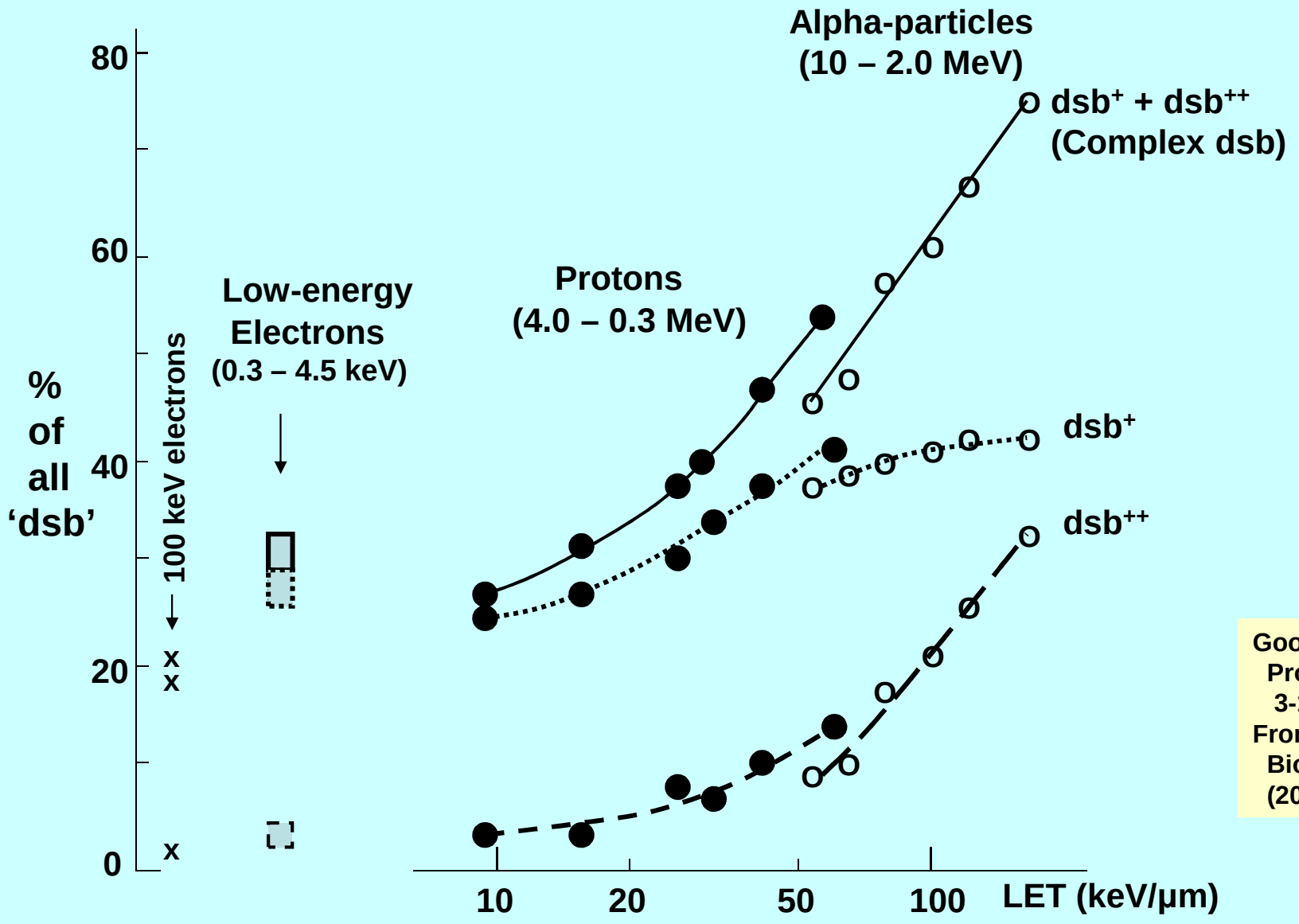
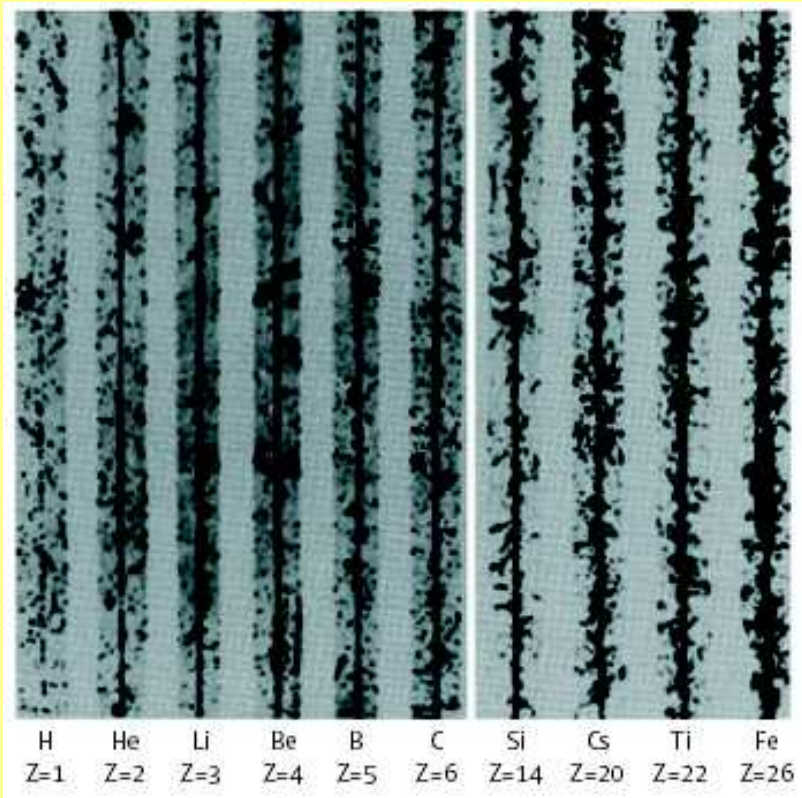
16.10.13

The proportion of Complex DSB increases with LET.
The degree of complexity increases with LET.



Goodhead, Radiat Prot Dosim, 122, 3-15 (2006);
From Int J Radiat Biol 156, 577-583 (2001)

Charged particle tracks in nuclear emulsions



100 µm

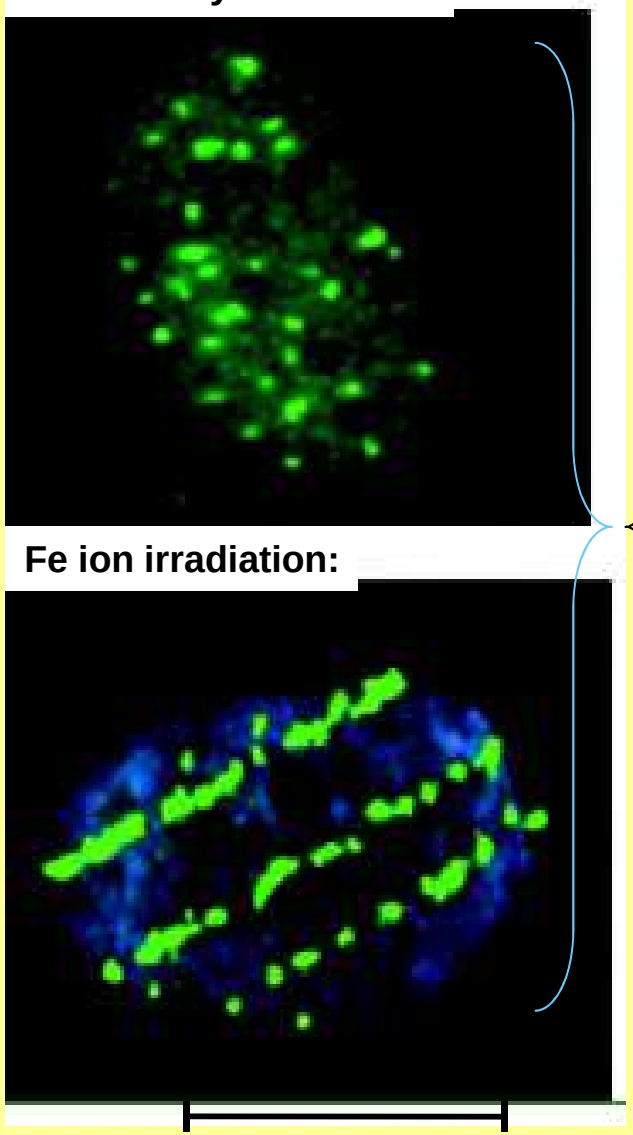
Cell nucleus

(Cucinotta & Durante, Lancet Oncol 2006)

Fluorescent foci marking DSB in cell nuclei

Gamma-ray irradiation:

Fe ion irradiation:

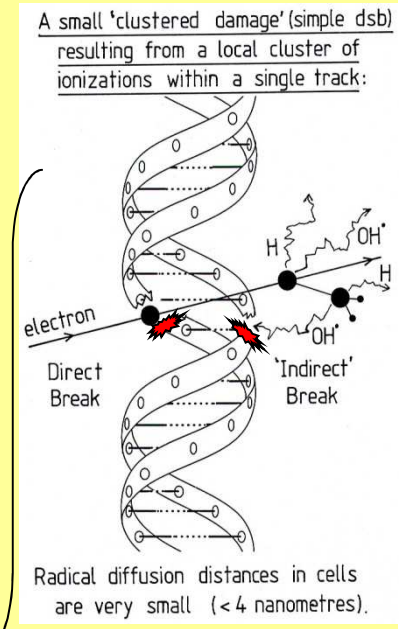


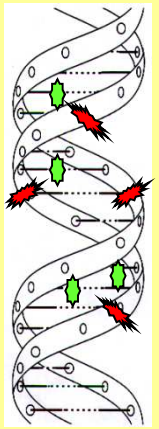
10 µm

X 20

X 1600

Magnification



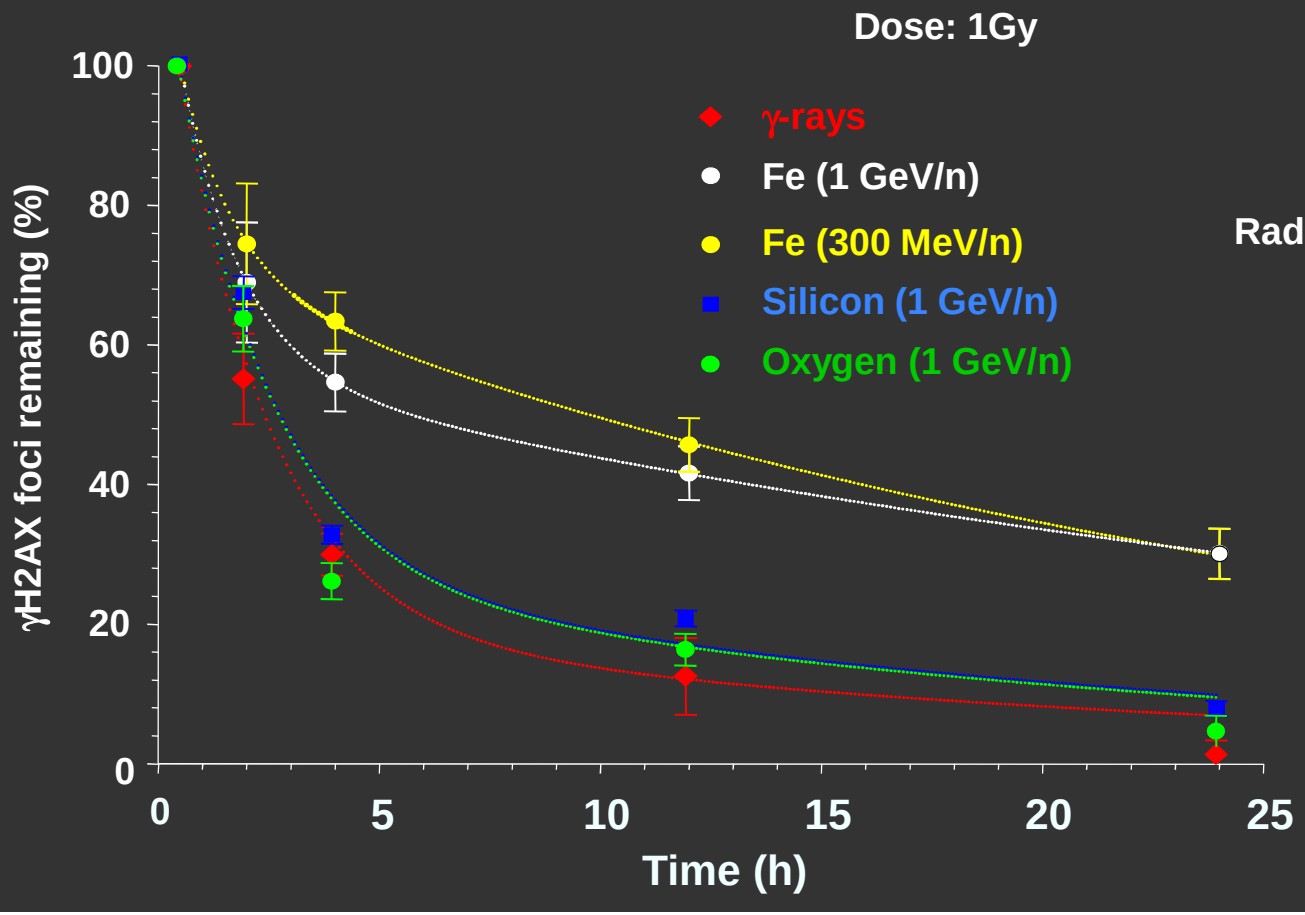


Complex Clustered damage in DNA

2 nm

DTG 4.2.14

Repair of DSBs induced by HZE particles in normal human skin fibroblasts



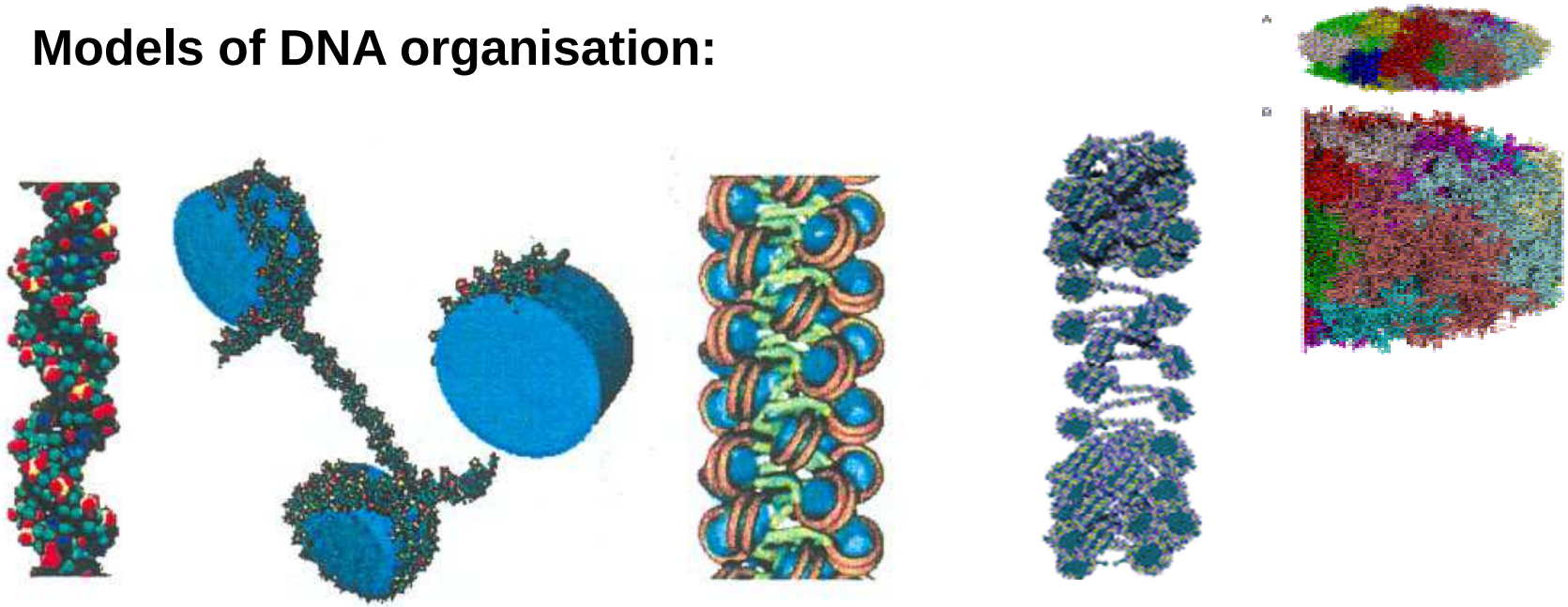
[Courtesy of David Chen]

(Asaithamby et al, Radiat Res 169, 437 (2008))

Such results are consistent with track structure predictions that there should be more-complex DSB from the more densely ionizing radiations (and hence more difficulty for repair)

2. Modelling at GSF/Helmholtz (Munich)

Models of DNA organisation:



Combine with M-C track-structure simulations to estimate damage from impact of tracks from radiations of many types

- **DNA fragments,**
- **Chromosome aberrations,**
- **etc, etc**

e.g. Friedland et al:

(2003) Radiat Res 159, 401
(2005) Radiat Phys Chem 72, 279
(2006) Radiat Prot Dosim 122,116
(2010) Radiat Res 173. 263
(2010) Radiat Res 173, 677
(2013) Mutat Res 756, 213

Closing comments:

Differences in radiation quality can lead to:

- **differences in biological effectiveness for the same quantity of radiation (e.g. the same absorbed dose)** --- can quantify ~as RBEs

- **qualitative differences in biological effects** --- cannot use scaling to specify

Effects of internal emitters depend on

- **Dose localization/inhomogeneity**

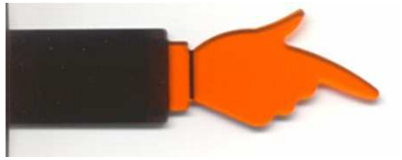
AND

- **Radiation quality**

Practical attempts to account for radiation quality include:

Radiation protection (very approx.):	w_R (radiation weighting factor) or Q (quality factor) as function of LET
More detailed risk assessments:	Best available information on specific RBEs
NASA astronauts' risk model:	QF as function of Z^{*2}/β^2
Therapy, non-cancer effects, etc:	e.g. Estimate 'Gy-Equivalent' doses for the system

All have substantial short-comings ---- Much research to be done !!!



THE END