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
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.


“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”?
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 “quality” became a description of the radiation as it affects the biological response; (Bewley 1973)

From “Radiation Quality and its Influence on Biological Response”

“We now know, of course, that LET is far from adequate to specify radiation quality. (Rossi 1959)

\[ LET = \text{Linear Energy Transfer} \]
To describe radiation effects or mechanisms, need physical specification of:

1. Measure of \textbf{quantity} 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. \textbf{Time} course of delivery: e.g. Dose rate, fractionation
   or fluence rate, etc

4. \textbf{Specification of ‘quality’ of the radiation:}
   \textit{LET as 1}\textsuperscript{st} 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.
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.

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

Adapted from:
Health Physics 1988
55, 231-240
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.

High-LET and low-LET radiations are different at all these levels. Which level(s) dominate the biological effectiveness?

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 Gy = 1 J/kg

ICRU Definition:

4.2.5 Absorbed Dose

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

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

Unit: J kg$^{-1}$

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

Usually applied as an average in a macroscopic 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 source characteristics

Intervening material

Fluence spectrum of charged and neutral particles (particle types and energies)

Track structures

Biological damage and health effects
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:**

<table>
<thead>
<tr>
<th>Dose fraction deposited by electrons</th>
<th>5 keV</th>
<th>1 keV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tritium β</td>
<td>77%</td>
<td>42%</td>
</tr>
<tr>
<td>220 kV X-rays</td>
<td>48%</td>
<td>33%</td>
</tr>
<tr>
<td>Co γ-rays</td>
<td>34%</td>
<td>27%</td>
</tr>
</tbody>
</table>

**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

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:

No single description is adequate or sufficient

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

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

The yield of ionizations in water is about 4-5 per 100 eV
Track entities:

- Developed and used by radiation chemists (Mozumder & Magee 1966: 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):

\[
LE T = \frac{\text{mean energy lost}}{\text{path length}}
\]

(averaged over many particles)
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)

\[ \sim \frac{Z^2}{\beta^2} \]

Hence

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

Note: An alternative is to use \( z^2/\beta^2 \) instead of LET, but generally similar limitations.
The cut-off value ($\Delta$) is usually in electron-volts (eV)

Most commonly used are:

$L_\infty$ 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:

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

Use if effect of interest is $\approx$ proportional to L.

Dose average LET:

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

Use if effect of interest is $\approx$ proportional to $L^2$.

where $t(L)$ is the frequency distribution of L in the field
Linear Energy Transfer (LET), \( L = \frac{\sum \epsilon}{\ell} \) (Averaged over many tracks of this energy)

Restricted LET, \( L_\Delta = \frac{\sum (\epsilon < \Delta)}{\ell_{\text{total}}} \)

If \( \epsilon > \Delta \) Cut off and treat as separate track
Linear Energy Transfer (LET), \( L = \frac{\sum \epsilon}{\ell} \)

Restricted LET, \( L_\Delta = \frac{\sum (\epsilon < \Delta)}{\ell_{\text{total}}} \)

(Averaged over many tracks of this energy)

If \( \epsilon > \Delta \) Cut off and treat as separate track

Particle track
\((\text{electron})\)  

\(>\Delta\)

\(>\Delta\)

Wide spectrum of LETs and a variety of ‘averages’

ICRU Report 16 (1970)
Ionizing radiations can kill cells:
e.g. Cell survival after alpha-particle irradiation compared to X-rays (in V79 cells)

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

\[
\frac{\text{Dose B}}{\text{Dose A}} \approx 5
\]

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

\(\text{RBE} = \text{Relative Biological Effectiveness}\)
\(= \text{Ratio of doses for identical level of biological effect}\)

Adapted from:
Radiat Res 93, 343 (1982)
Ionizing radiations mutate genes in cells:

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

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:

[Diagram showing a graph with dose vs. mutant frequency, comparing alpha-particles to 250 kV X-rays.]

Adapted from:
Radiat Res 93, 343 (1982)
Relative Biological Effectiveness for Cell Inactivation by Ionizing Radiations

RBE increase is evidence for role of clustered or correlated damage.

RBE decrease ~due to $1/L$ decreasing number of particle tracks per dose.

BUT LET alone is an inadequate descriptor of radiation quality.

Data points are examples for low velocity ions.

But on what size scale?

Adapted from Int J Radiat Biol 65, 7-17 (1994)
Some applications of LET

- Absorbed Dose ↔ Fluence relationship
  
  For fluence $F$ of particles of LET $L$, the absorbed dose $D$ is
  
  $$D = kFL$$
  
  where $F = n/A = \text{number of particles/unit area}$
  
  $$= 0.16FL \text{ for } A (\mu m), D (\text{Gy}), L (\text{keV/}\mu m)$$

- 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

- 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)

Reliance on LET as the sole radiation-quality parameter is a notable limitation --- All other aspects of track structure are ignored

Quality factor, Q, as function of LET as defined by:

\[ Q\text{, as function of LET} \]

100 keV/\(\mu\)m

ICRP 60, 1991 and ICRP 103, 2007

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

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

<table>
<thead>
<tr>
<th>Radiation type and energy range</th>
<th>Prescribed $w_R$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photons, all energies</td>
<td>1</td>
</tr>
<tr>
<td>Electrons and muons, all energies</td>
<td>1</td>
</tr>
<tr>
<td>Neutrons, energy &lt; 10 keV</td>
<td>5</td>
</tr>
<tr>
<td>Neutrons, energy 10 keV to 100 keV</td>
<td>10</td>
</tr>
<tr>
<td>Neutrons, energy &gt;100 keV to 2 MeV</td>
<td>20</td>
</tr>
<tr>
<td>Neutrons, energy &gt;2 MeV to 20 MeV</td>
<td>10</td>
</tr>
<tr>
<td>Neutrons, energy &gt;20 MeV</td>
<td>5</td>
</tr>
<tr>
<td>Protons, other than recoil protons, &gt;2 MeV</td>
<td>5</td>
</tr>
<tr>
<td>$\alpha$ particles, fission fragments, heavy nuclei</td>
<td>20</td>
</tr>
</tbody>
</table>

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).
Amorphous track: Radial dose distribution

(a) Linear Energy Transfer (Section 3)

Let = $\frac{\text{mean energy lost}}{\text{path length}}$

(b) Proportional Counter Quantities (Section 4)

Lineal energy = $\frac{\text{energy deposited}}{\text{mean chord}}$

Specific energy = $\frac{\text{energy deposited}}{\text{mass}}$

(c) Radial Profile

(c) Radial Profile

(d) Track Entities (Section 5.3)

Spurs: $0 - 100\;\text{eV}$

Blob: $100 - 500\;\text{eV}$

Short track: $500 - 5000\;\text{eV}$

AMORPHOUS TRACK (averaged over many particles)
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 ~ 1/r²)

- Energy density in track depends on both Z and V
  Unrestricted LET ≈ Stopping Power \( \sim \frac{Z^2}{\beta^2} \)
  (as dominant term of Bethe-Block stopping power formula)
Radial dose distribution

Ave. Dose at radius t from ion path:

\[ D(t) = \frac{\text{Energy}}{\text{Mass}} \text{ at radius } t \]

\[ \varepsilon(t, \delta t) = \frac{\text{\varepsilon(t, \delta t)}}{2\pi t \delta t \delta \ell \rho} \]

\( \varepsilon(t, \delta t) \) is energy deposited in element \( \delta t \delta \ell \)

(\( \delta \ell = \text{length of element} \))

\[ D(t) \sim \frac{1}{t^2} \text{ over most of the profile} \]

Note then that

\[ \varepsilon(t) \sim \frac{1}{t} \]

i.e. energy falls off much more slowly than does dose

Adapted from: Cucinotta et al, Radiat Environ Biophys 38, 81-92 (1999)
For heavy charged particles (i.e. protons and heavier):

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

$$D_r \sim \frac{1}{r^2}$$

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

Energy, $\varepsilon_r$, deposited in annulus at distance r, falls off much more more slowly, as

$$\varepsilon_r \sim \frac{1}{r}$$

Note: Mass of annulus increases proportionally with r

Hence, $D_r \sim \frac{\varepsilon_r}{m_r} \sim \frac{1}{r} \cdot \frac{1}{r} \sim \frac{\varepsilon_r}{r^2}$

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 **energy** spread by ions of same LET

\[
\int_{t=0}^{t=\infty} \varepsilon(t) \, dt \quad \frac{\int_{t=t}^{t=\infty} \varepsilon(t) \, dt}{\int_{t=0}^{t=\infty} \varepsilon(t) \, dt}
\]

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

\[\text{i.e. Linear energy deposited within the cell nucleus is only } \approx 40\% \times 151 \approx 60 \text{ keV/\mu m}\]

**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/\(\mu m\).

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 $Z^2/\beta^2$ instead of LET to specify Quality Factor, and paramaterizes NASA Quality Factor as a function of ‘Katz’ parameters ($\Sigma_0$, $\kappa$ and $m$).

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.
‘Proportional counter’

microdosimetry

(a) LINEAR ENERGY TRANSFER (Section 3)

LET = mean energy lost
path length

(b) ‘PROPORTIONAL COUNTER’ QUANTITIES

Lineal energy = energy deposited
mean chord

Specific energy = energy deposited
mass
The Rossi Counter: Low pressure tissue equivalent proportional counter (TEPC). A major development of the 1950s & 60s

Electric Pulse ~ # ionizations ~ $\varepsilon$ (energy imparted)

Lineal Energy:
$$y = \frac{\varepsilon}{\lambda} \text{ (keV/\mu m)}$$

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

Measures actual stochastic events in a microscopic simulated tissue volume

From measured lineal energy spectrum of single tracks from neutrons $(d,Be)$
Experimental Simulation of microscopic volume of tissue:

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

Energy loss for charged particle through counter gas

\[ \text{Energy loss} = \text{tissue volume} \]

For scaling factor K:

\[ \frac{\rho_{\text{gas}}}{\rho_{\text{tissue}}} = \left( \frac{S_t}{S_g} \right) \left( \frac{p_g}{p_t} \right) = \frac{1}{K} \]

\( \rho \) = 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’).
Lineal energy, $y = \frac{\varepsilon}{\frac{2}{3}d}$ keV/µm

Specific energy, $z_1 = \frac{\varepsilon}{m}$ Gy
Spectrum of lineal energy and specific energy for $^{60}$Co γ-rays in sphere of diameter 1 µm

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:**

$$\phi = \frac{1}{z_F}$$
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, 
$$z_F = 1 \text{ mGy}$$ (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**
(i.e. narrow tracks)

crossing spherical targets:

$$y_F \approx L$$  \hspace{1cm} $$z_1 \approx 0.204 \frac{L}{d^2}$$  \hspace{1cm} $$\phi \approx \frac{d^2}{0.204 L}$$

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

y, L in keV/µm
z in Gy
D in µm
Some Applications of $y, z$

- Hit-frequency evaluations: $\phi = \frac{1}{z_F}$

**Basic radiobiology and risk modelling:**

- Theory of Dual Radiation Action
  
  Developed hand-in-hand with Rossi Counter during 1970s
  
  for radiobiology and cancer risk: $\text{Effect} = \alpha D + \beta D^2 = k(D + z_D^2)$
  
  Proposed as fundamental and mechanistic, but assumptions invalidated by experimental tests.
  
  Remains usable as phenomenological model for limited purposes.

- Microdosimetric Kinetic Model (MKM) of cell death.
  
  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).

- 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);

Track structure:

(a) Linear Energy Transfer (averaged over many particles)

(b) Proportional Counter Quantities (Section 4)

(c) Radial Profile (Section 5.1)

(d) Track Entities (Section 5.3)

(e) Track Structure Simulation
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)

Hypothesis of critical properties:

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

Goodhead & Nikjoo (1989, IJRB 55, 513-529)
Frequency distribution of energy deposition, $\varepsilon$, 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)

Radiat Res 153, 459-468

* HZE = particles of high charge and energy
• 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)

1 keV electron

0.5 keV electron

DNA

Note ionization clustering on scale of DNA
Example of **Complex Clustered Damage in DNA** 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

Complex DSB

Yield of DSB is proportional to dose

"number of tracks"

Each DSB arises from a single track

DSB = Double-Strand Break in DNA

(Rottkamm & Lobrich, PNAS, 2003)
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

Complex Clustered Damage (3 or more components):
- Complex DSB
- 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)

DTG 16.10.13
The proportion of Complex DSB increases with LET. The degree of complexity increases with LET.

Charged particle tracks in nuclear emulsions

Fluorescent foci marking DSB in cell nuclei

Gamma-ray irradiation:

Fe ion irradiation:

Complex Clustered damage in DNA

(Cucinotta & Durante, Lancet Oncol 2006)

Magnification

DTG 4.2.14
Repair of DSBs induced by HZE particles in normal human skin fibroblasts

Dose: 1Gy

- γ-rays
- Fe (1 GeV/n)
- Fe (300 MeV/n)
- Silicon (1 GeV/n)
- Oxygen (1 GeV/n)

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)


[Courtesy of David Chen]
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:

- (2013) Mutat Res 756, 213

DTG 17.10.13
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 \( Z^2/\beta^2 \)

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