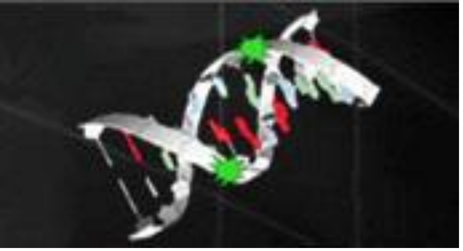

Microdosimetry of Ion Beams

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Challenges in micro-and nanodosimetry for ion beam cancer therapy (MiND-IBCT)
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Outline of presentation

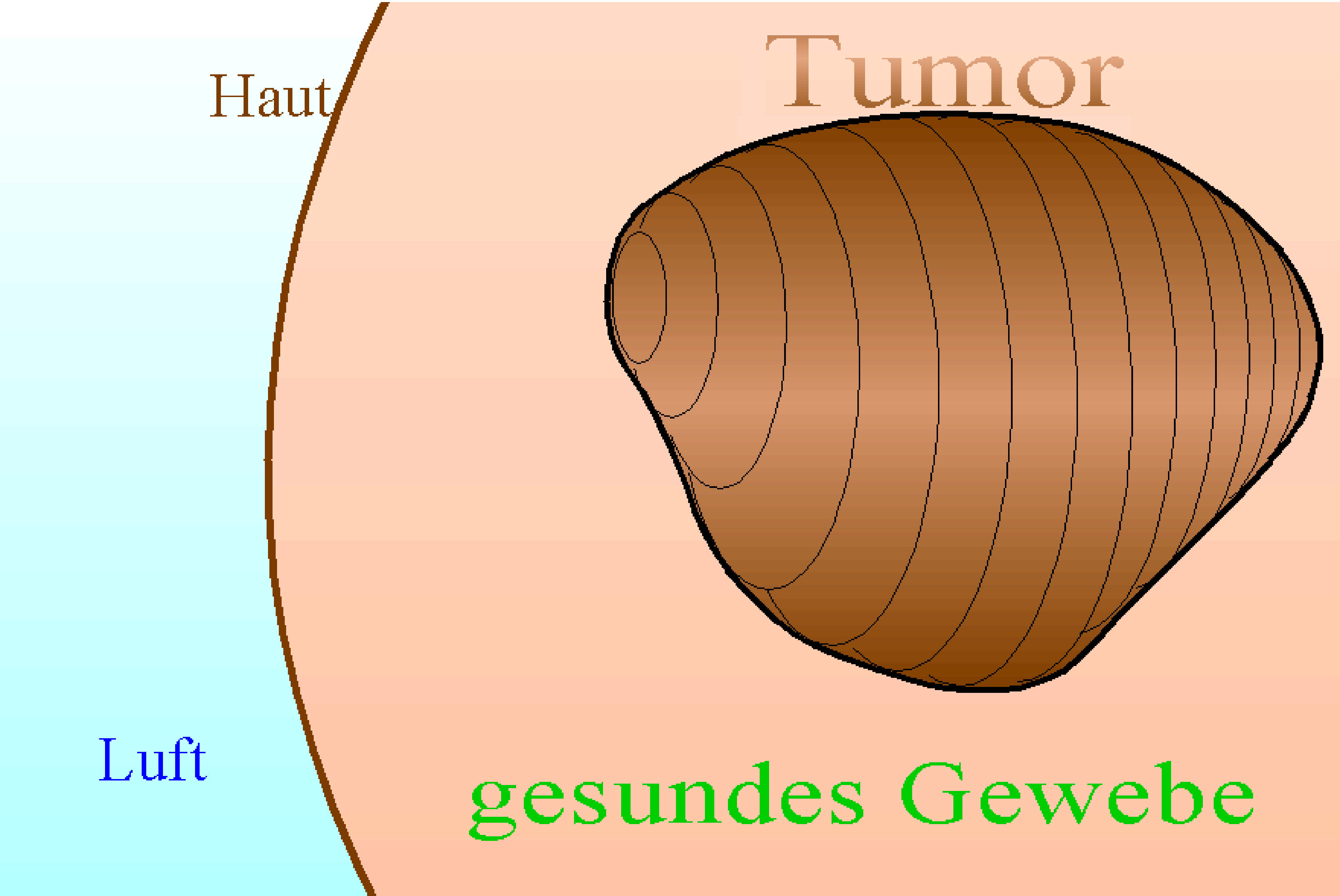
1. **Dosimetry does not measures physical occurrencies at sub-cellular level where mainly single-ionization event occur.**

2. **The energy absorbed in a micrometric sub-cellular site is called *energy imparted* ε. It is an operative quantity.**

3. **In ion therapy, micrometric sites experience only single events, mainly.**

4. **First microdosimetric measurements at CNAO ^{12}C therapeutic beam.**

^{12}C hadrontherapy and the active beam scanning technique



The dose-delivering beam monitor measures the average particle fluence through ~1cm² area

$$D_{exp} = const \cdot J_{gas}$$

The ionization in the transmission chamber

Since, inside the ionization chamber, both **w-value** and **ionization cross-section** variation is small at high ^{12}C energies:

$$D_{exp} \propto \Phi_{^{12}C}$$

For 1 Gy, the carbon ion fluence is $\Phi_{^{12}C} \approx 10^7\ cm^{-2} = 0.1\ \mu m^{-2}$

HOWEVER

Initial radiobiological damage is believed to take place in sub-cellular structures

The sizes of which varies from 1 to 0.002 μm

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THERETORE

1. **Since absorbed dose measures only the average energy imparted to the irradiated macroscopic volume by a given particle fluence.**

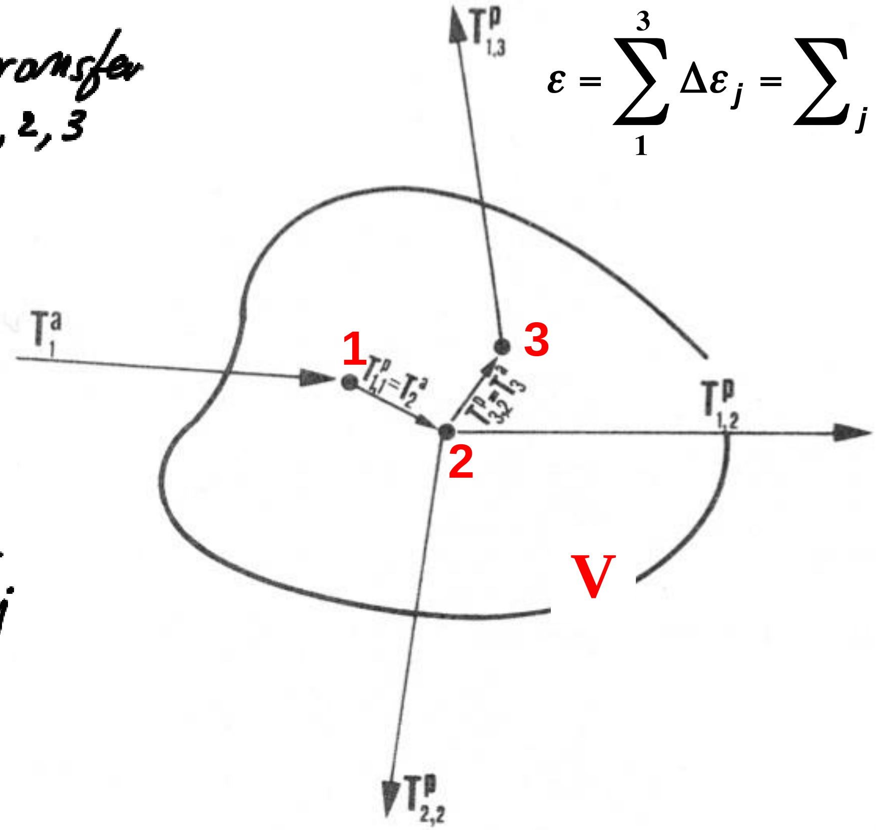
2. **Unlikely, dosimetry is able to monitor biological effects that arise from physical occurrences, which take place at micrometre or nanometre level.**

1. **How monitoring the physical occurrences in micrometric or sub-micrometric sites without abandoning absorbed dose, which is a well established and measurable quantity?**

The answer is in ICRU 36, where the energy ε *imparted to the volume V by a single particle is defined*

Example of inchoate distribution with 3 transfer points P_j with $j = 1, 2, 3$

$$\varepsilon = \sum_{1}^{3} \Delta\varepsilon_j = \sum_j T_j^a - \sum_j \sum_i T_{ij}^p + \sum_j Q_j$$



$j \equiv$ transfer point

$i \equiv$ emerging particle at the transfer point j

Since the particle $j+1$ arriving at P_{j+1} is one of the particles leaving P_j:

$$\varepsilon = T_1^a - \sum_{ij} T_{ij}^p + \sum_j Q_j$$

Where T_{ji}^p is the kinetic energy of all the particles leaving the volume V

The energy imparted by a single event is called microdosimetric event

"It is the energy imparted to the volume V by an ionizing particle entering into the volume V or by a radioactive decay inside it."

The **event size** is the energy-imparted value

$$\varepsilon = T_1^a - \sum_{ij} T_{ij}^p + \sum_j Q_j$$

The event size 0 occurs when

$$T_1^a = \sum_{ij} T_{ij}^p - \sum_j Q_j$$

Since the event size fluctuates, according to all the possible interaction probabilities, *ε is a stochastic variable.* This quantity opens the door to the nuclear physics, which holds technology to measure stochastic variables.

The absorbed dose is then defined on the mean imparted energy to V

The mean imparted energy $\bar{\varepsilon}$ to the volume **V** is a deterministic quantity

$$\bar{\varepsilon} = \frac{\sum_{0}^{N} \varepsilon_j \cdot n_j}{\sum_{0}^{N} n_j}$$

Zero included

N number of single events in V

ε_j energy imparted to V by the jth event

Since the main contribution to the imparted energy is due to electromagnetic interactions, $\bar{\varepsilon}$ can be approximated with the energy released by a charged particle in continuous slowing down approximation (CSDA), when ***V* is larger then secondary electron ranges** .

$$\varepsilon \approx T_1^a - T_1^p$$

$$\bar{\varepsilon} \approx (S/\rho)_V \cdot \rho_V \cdot \bar{d}_V$$

mass stopping power in the volume V

density of the volume V

size of volume V

The lineal energy, *y* *and* the specific energy, *z*

ICRU 36 defines two new stochastic quantities, which resemble ordinary dosimetric quantities

y is "*the quotient of the energy imparted to the volume **V**, by a single particle, and the volume mean chord length".*

$$y = \frac{\varepsilon}{\bar{d}}$$

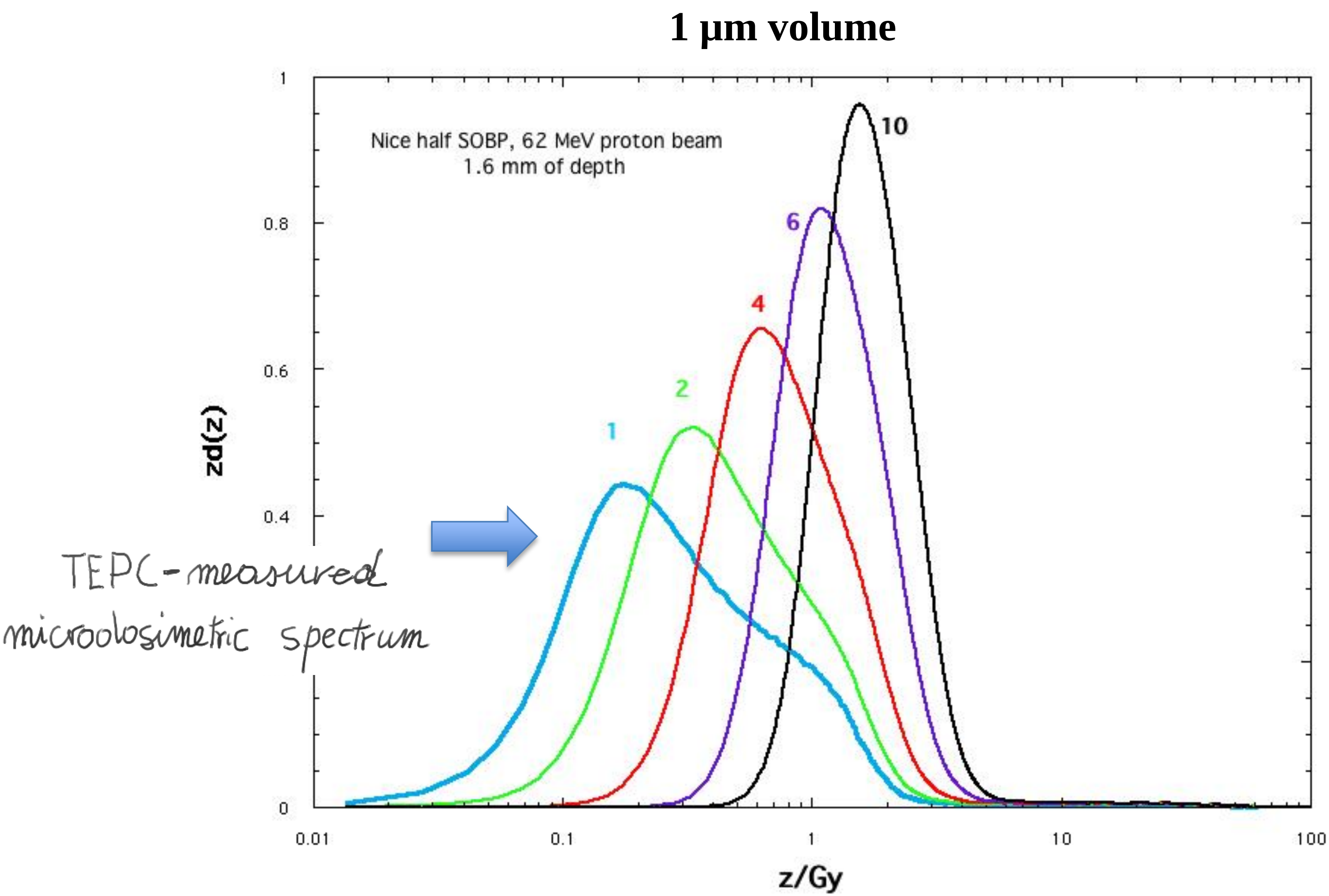
The ***y*** physical dimension is ***keV/µm,*** similarly to ***LET***. The weighted distribution of ***y*** is called ***d(y)***, similarly to the ***LET*** absorbed-dose distribution, ***d(L)*** of complex radiation fields.

z is the *"quotient of the energy imparted to the volume **V**, by **one or more particles**, and the volume mass"*

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

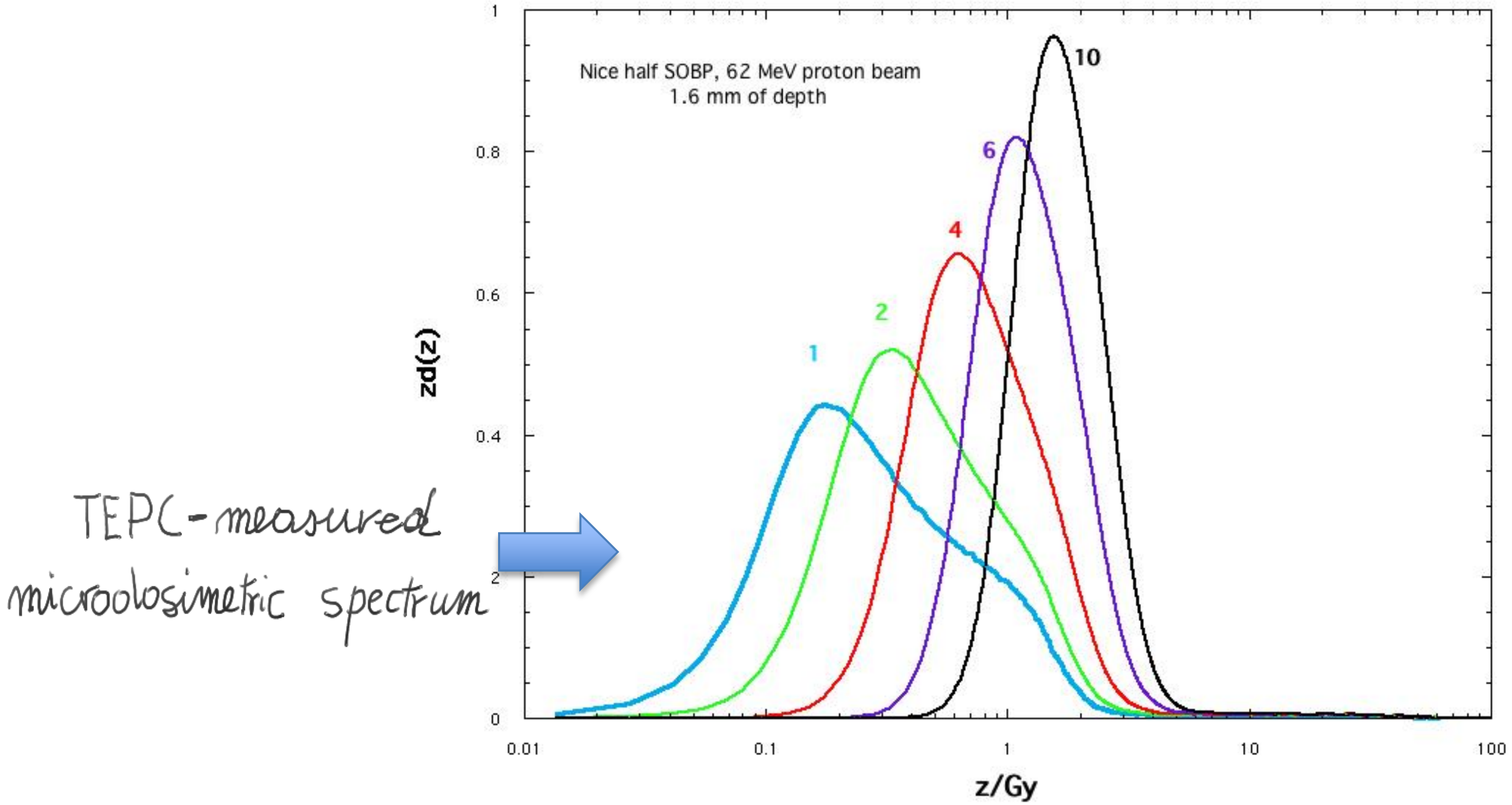
The ***z*** physical dimension is ***Gray***, similarly to absorbed dose ***D***. The weighted distribution of ***z*** is called ***d(z)***, similarly to ***dose*** absorbed-dose distribution (dose components) of complex radiation fields.

How the z distribution changes with event number increase



How many events occur in the volume *V* at the dose *D*?

Is the single-event microdosimetric spectrum meaningful to monitor physical occurrences at micrometre level?



When is the mean specific energy in the site different from *D* ?

The ***critical site*** is the site that one has experienced at least 1 event ≠ 0
Shall we call the specific energy in a critical site ***Z****.

The mean specific energy $\bar{Z}^*$ in critical sites is the mean specific energy $\bar{Z}$ without the 0-event contribution

Re-normalization:
the average is calculated only on the >0 events

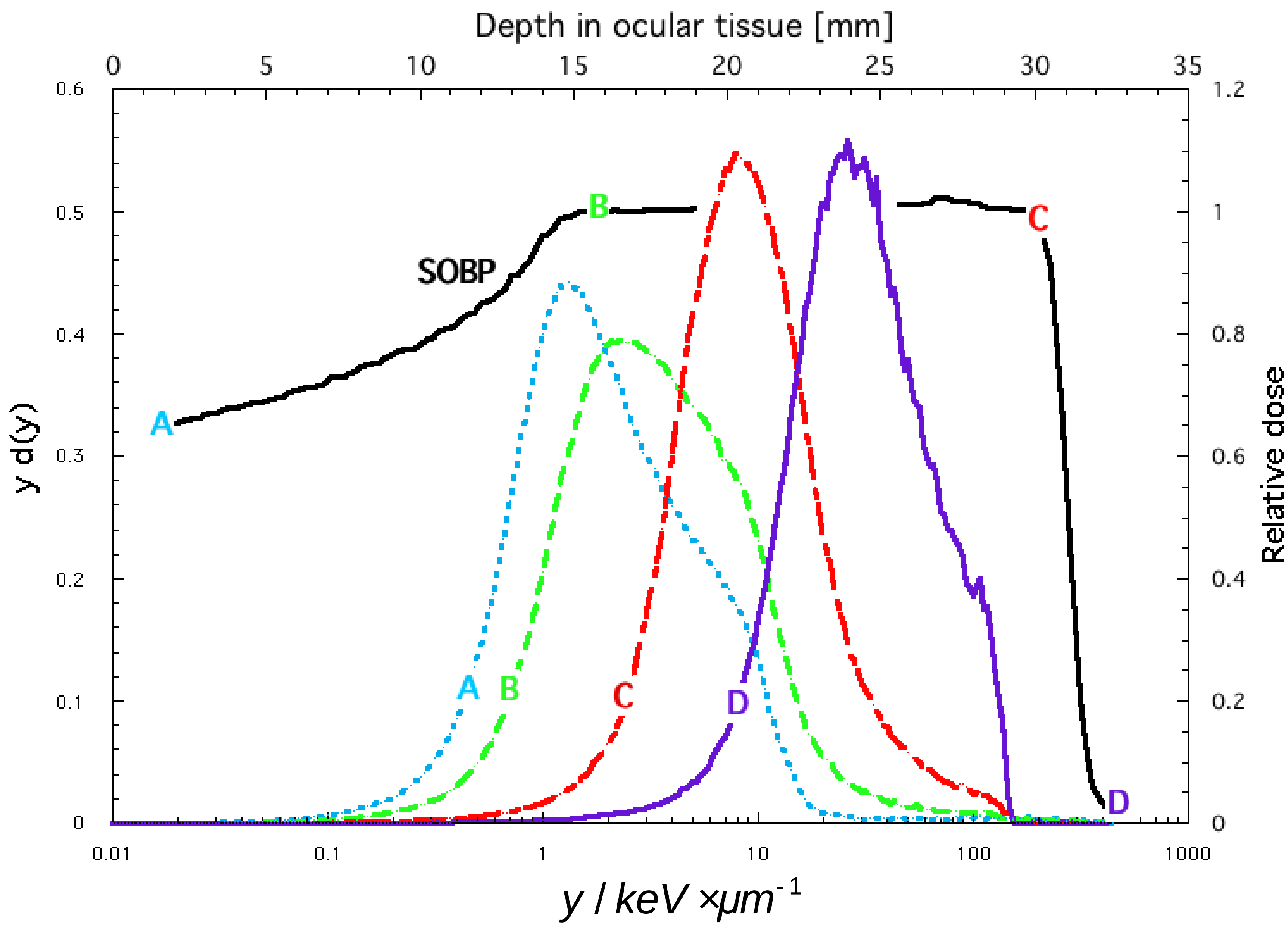
$$\bar{z}^* = \frac{\int_0 z \cdot f(z;D) \cdot dz}{1 - P(0)}$$

Probability to have an event >0 in the volume V

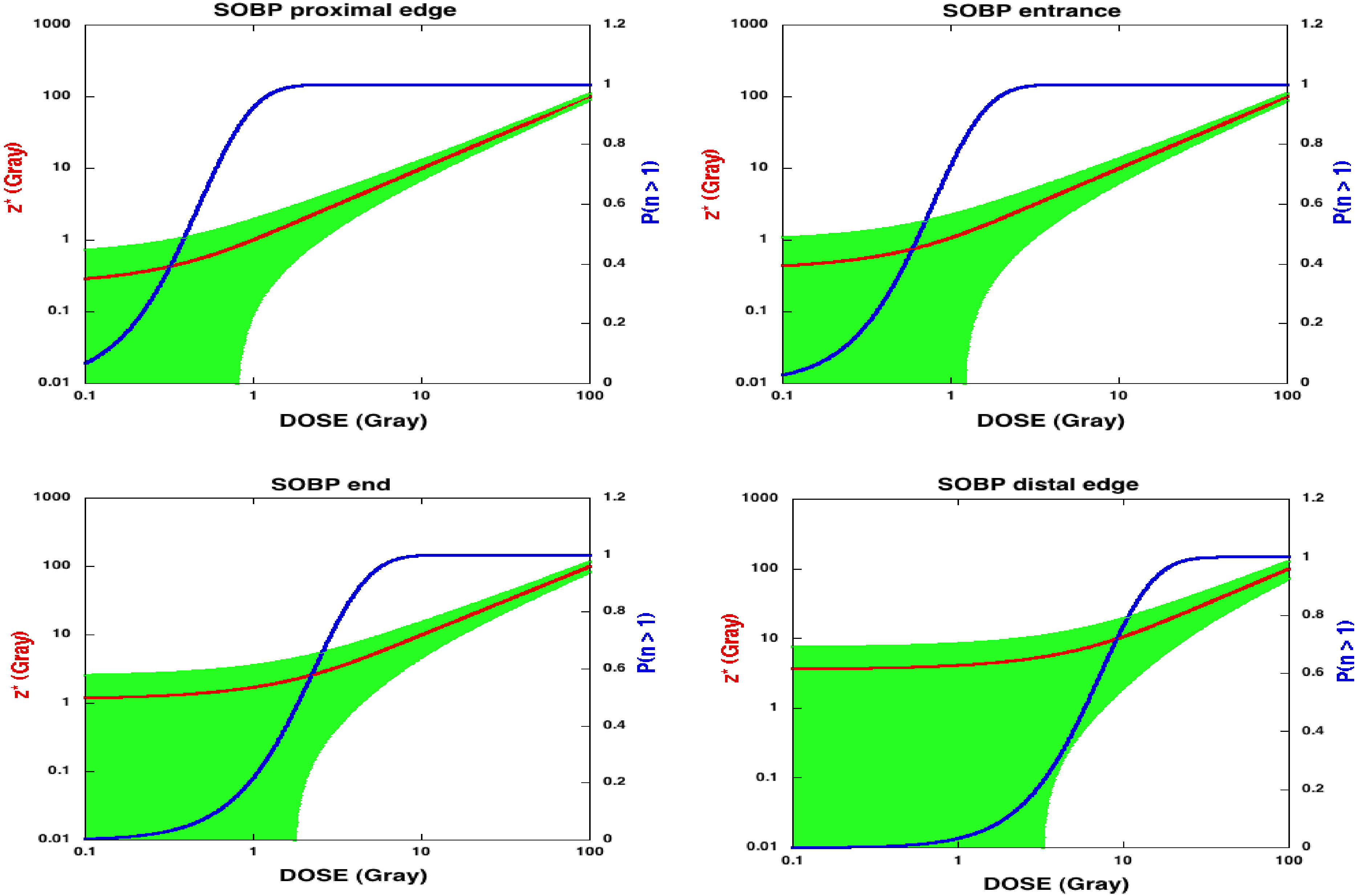
$$\bar{z}^* = \frac{D}{1 - e^{-D/\bar{z}_{1F}}}$$

D ≡ absorbed dose

The therapeutic 62 MeV-proton beam of Lacassagne (Nice) medical centre



Microscopic and macroscopic dose in therapeutic 62 MeV-proton beam



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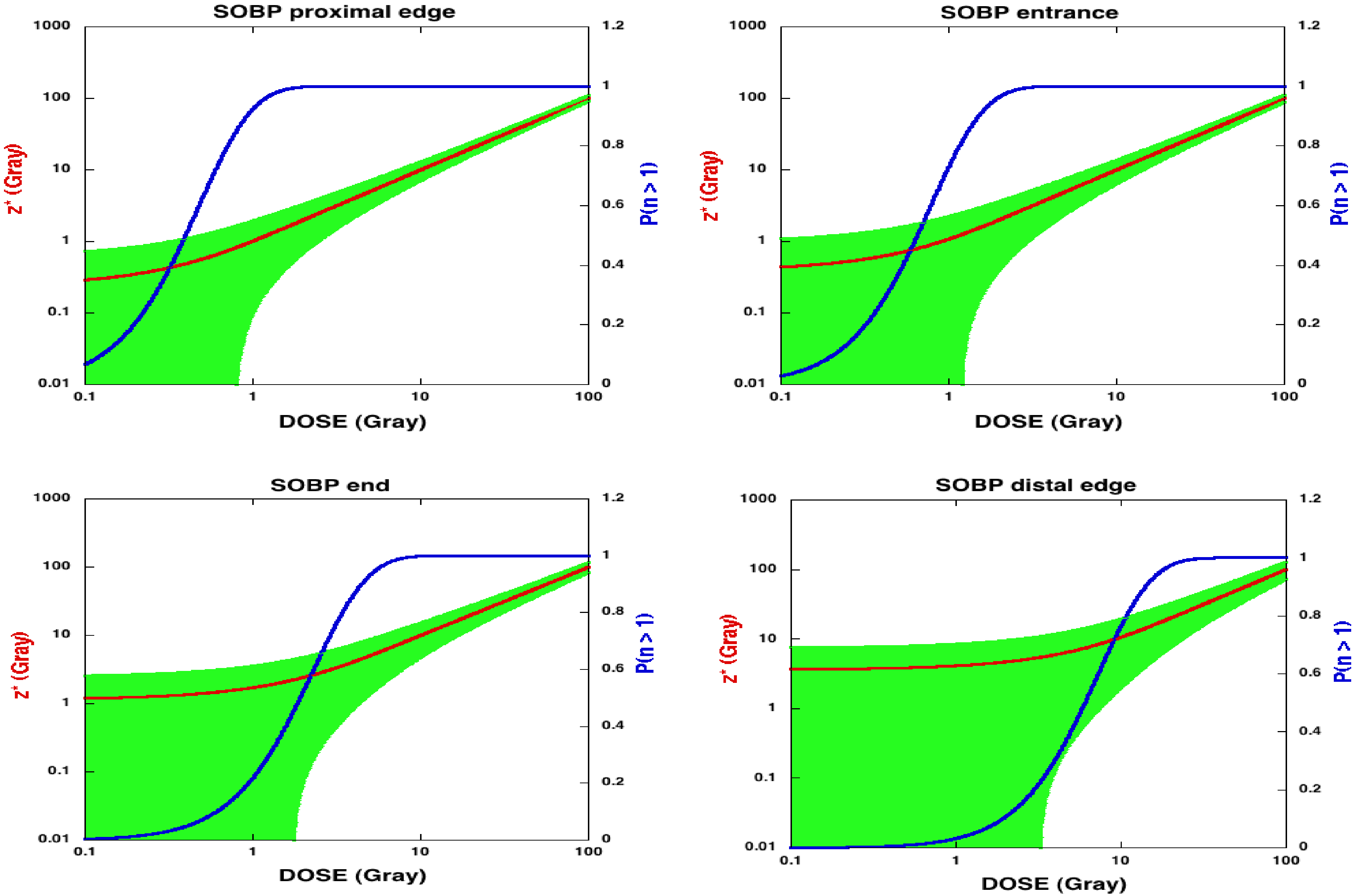

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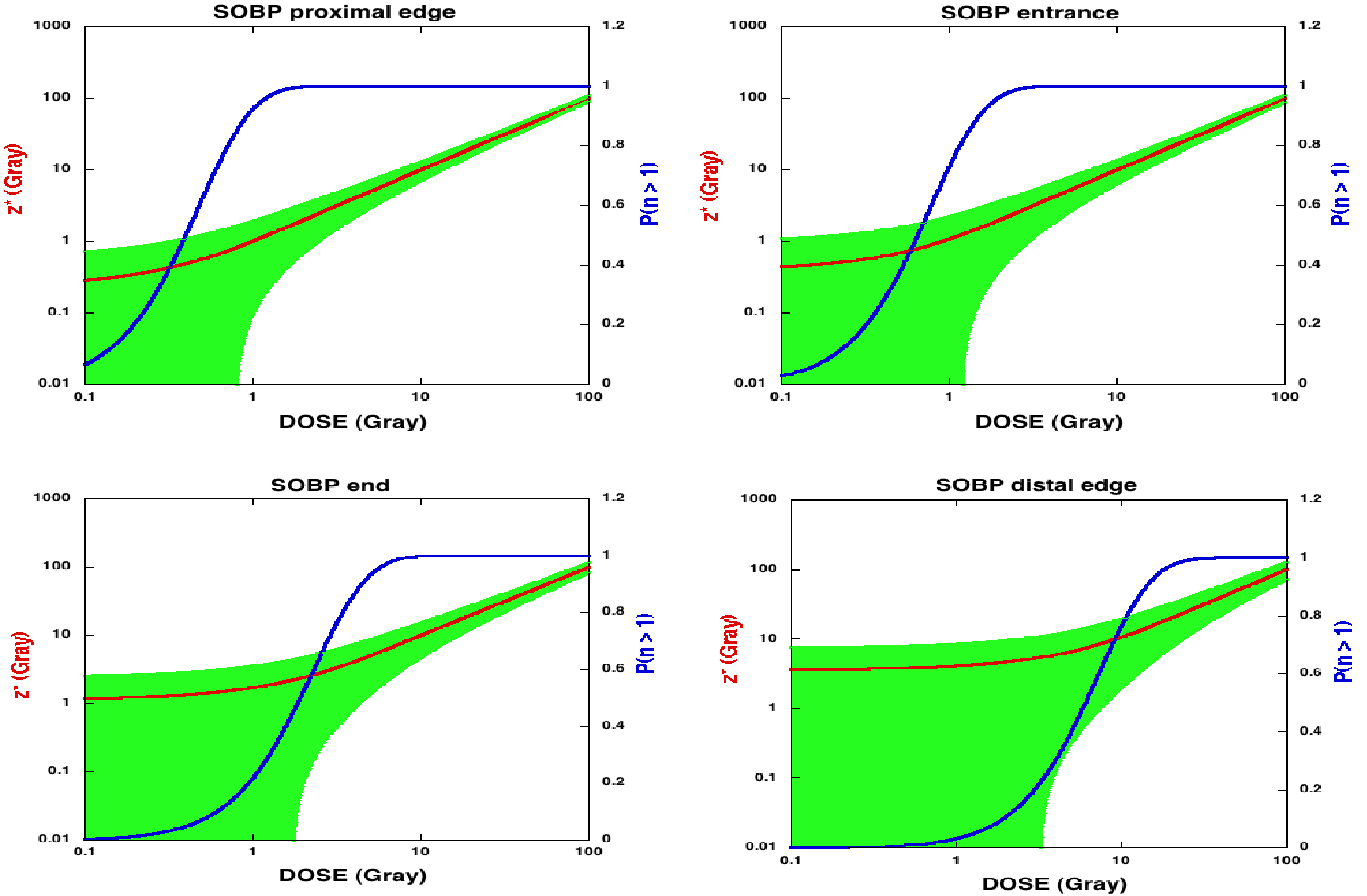

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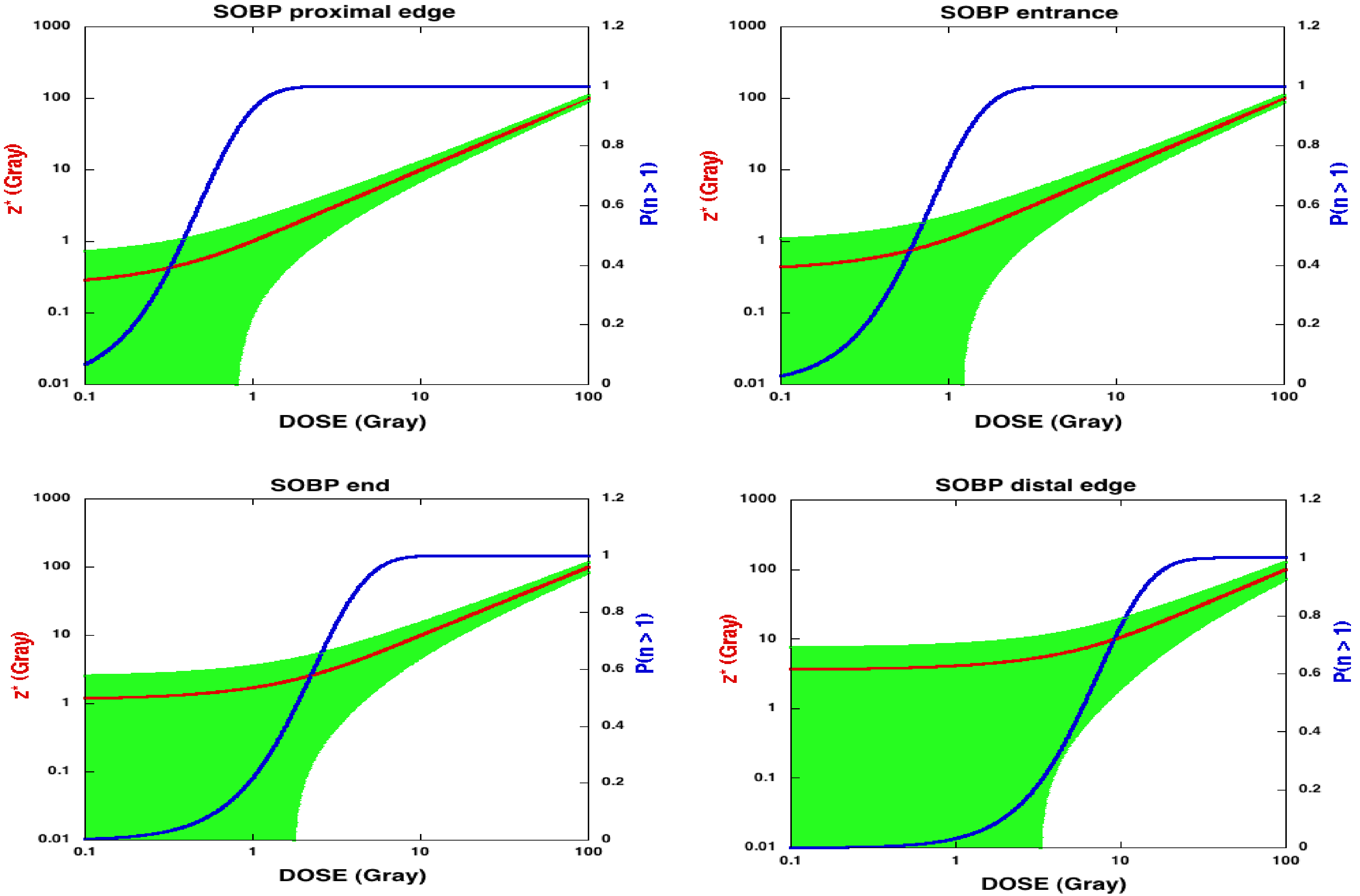
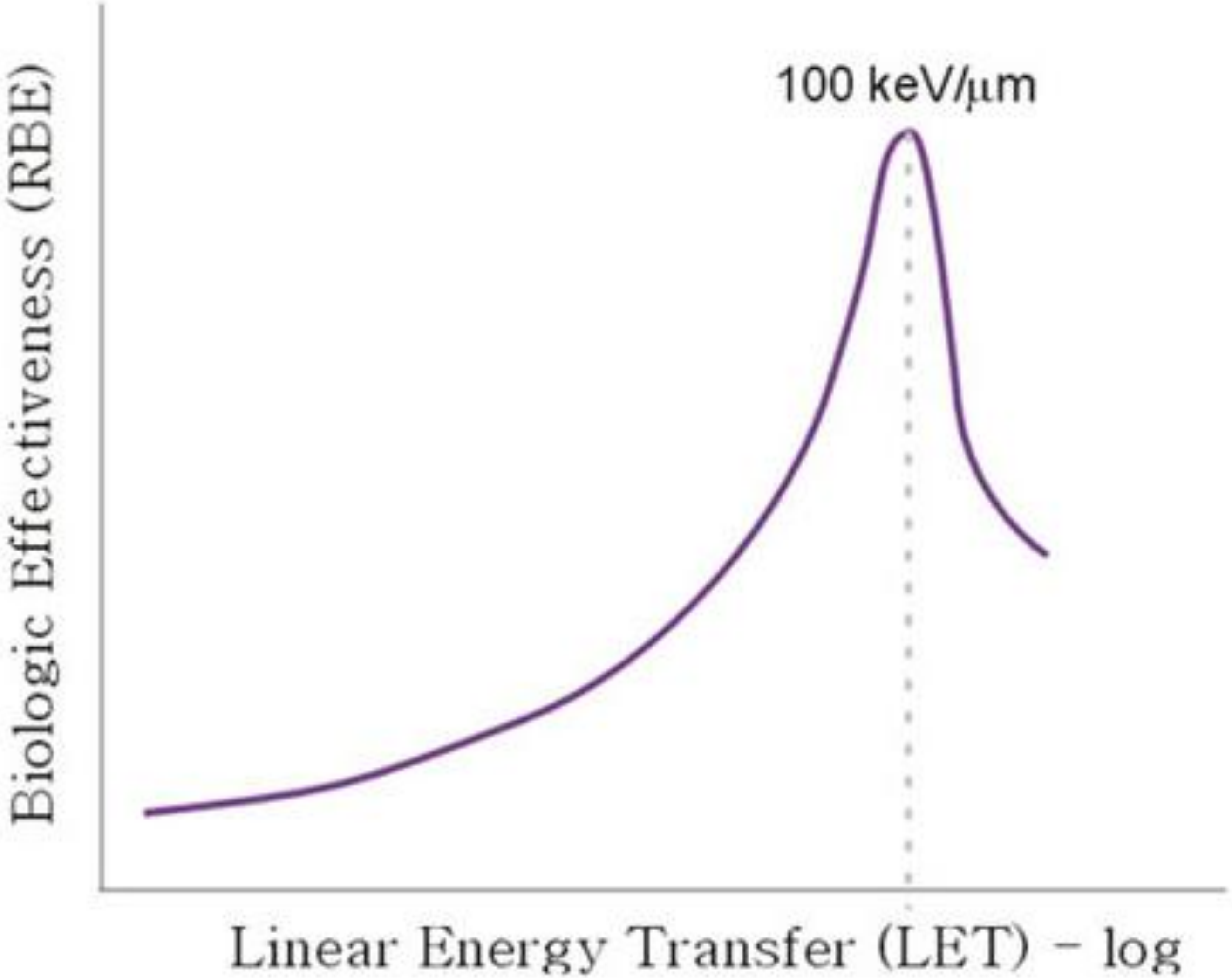
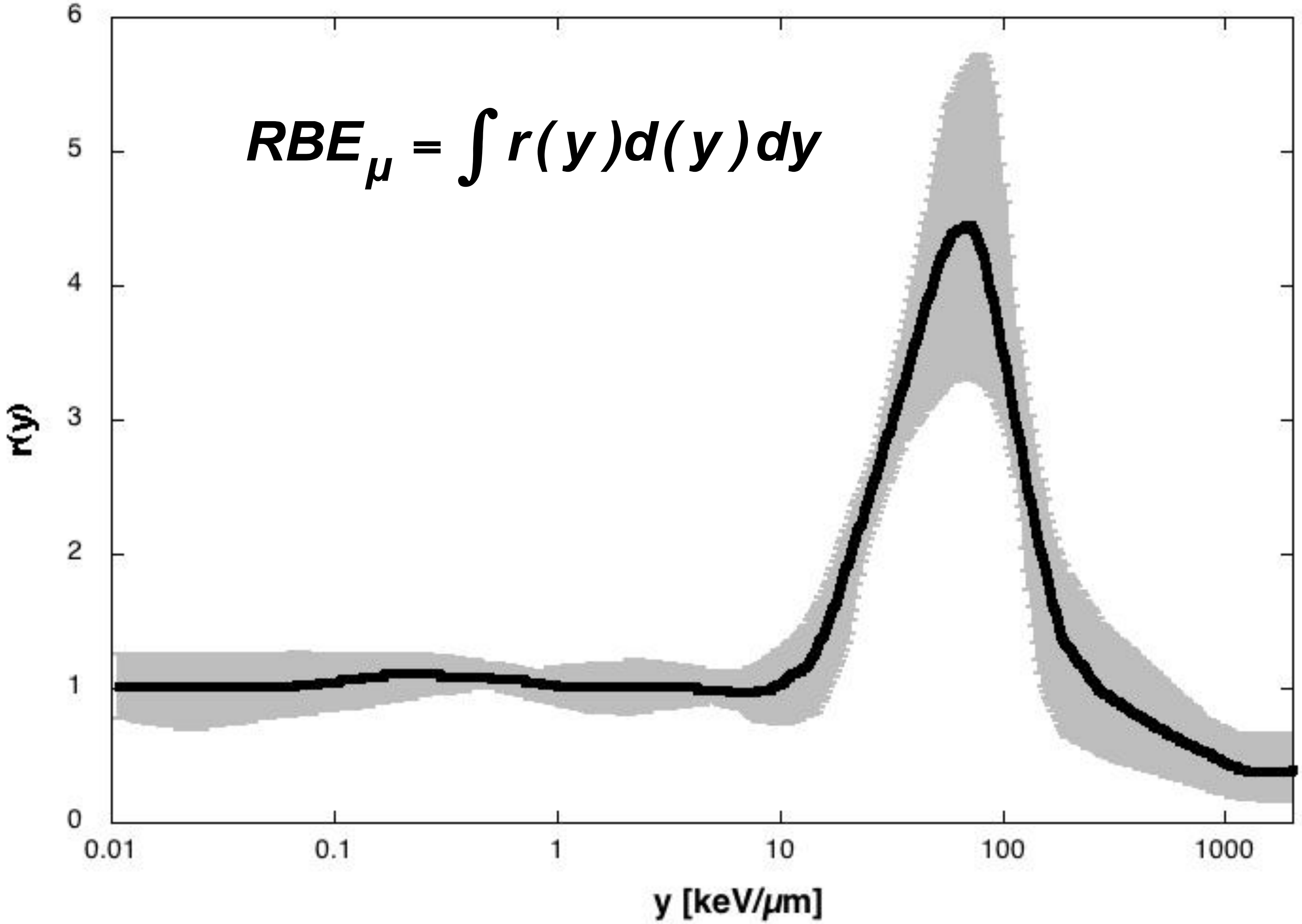


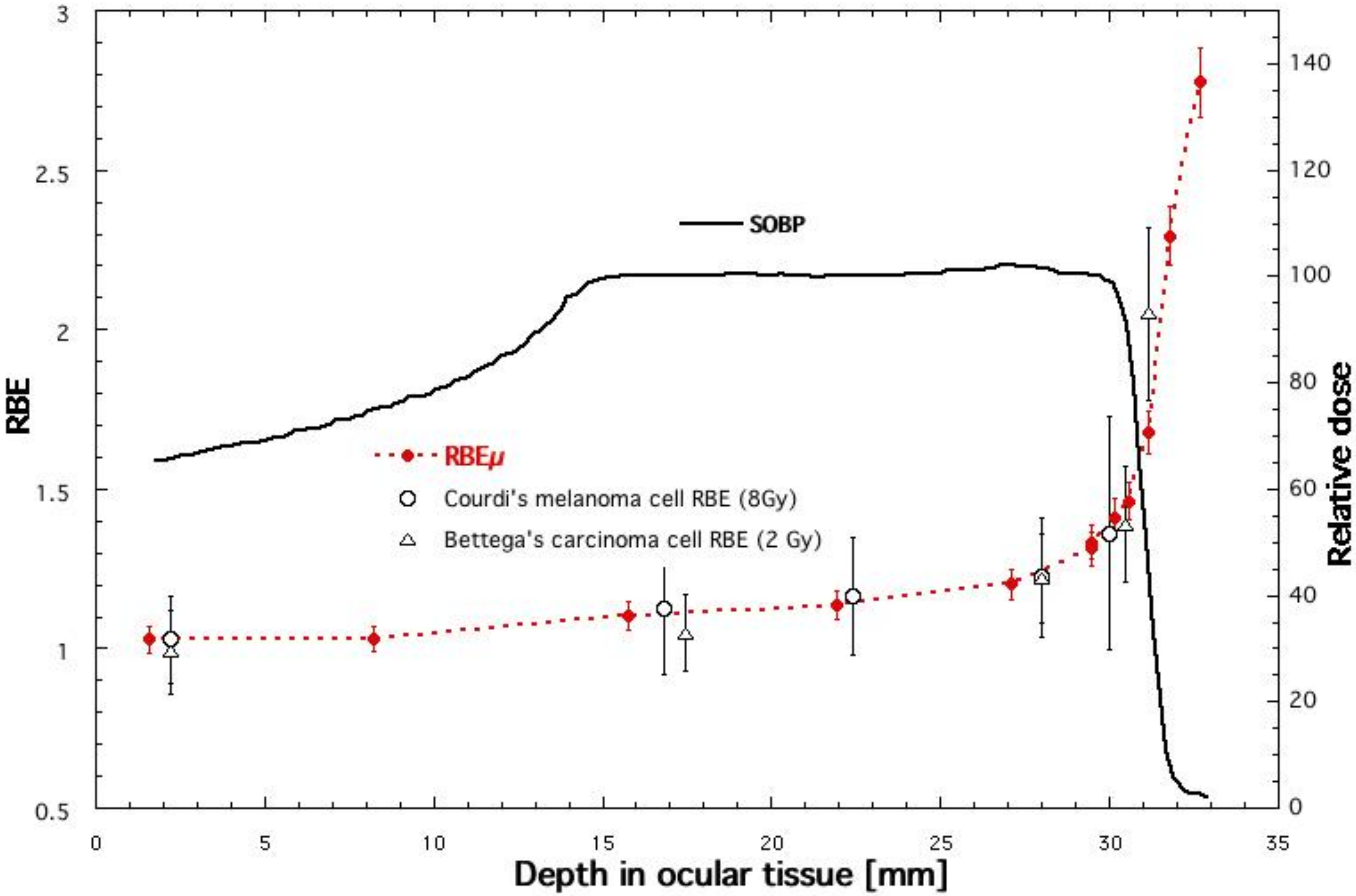
The relative biological effect saturates, the imparted energy ε does not.



Therefore, the weighted distribution *d(y)* has to be further weighted with a saturation function *r(y)*



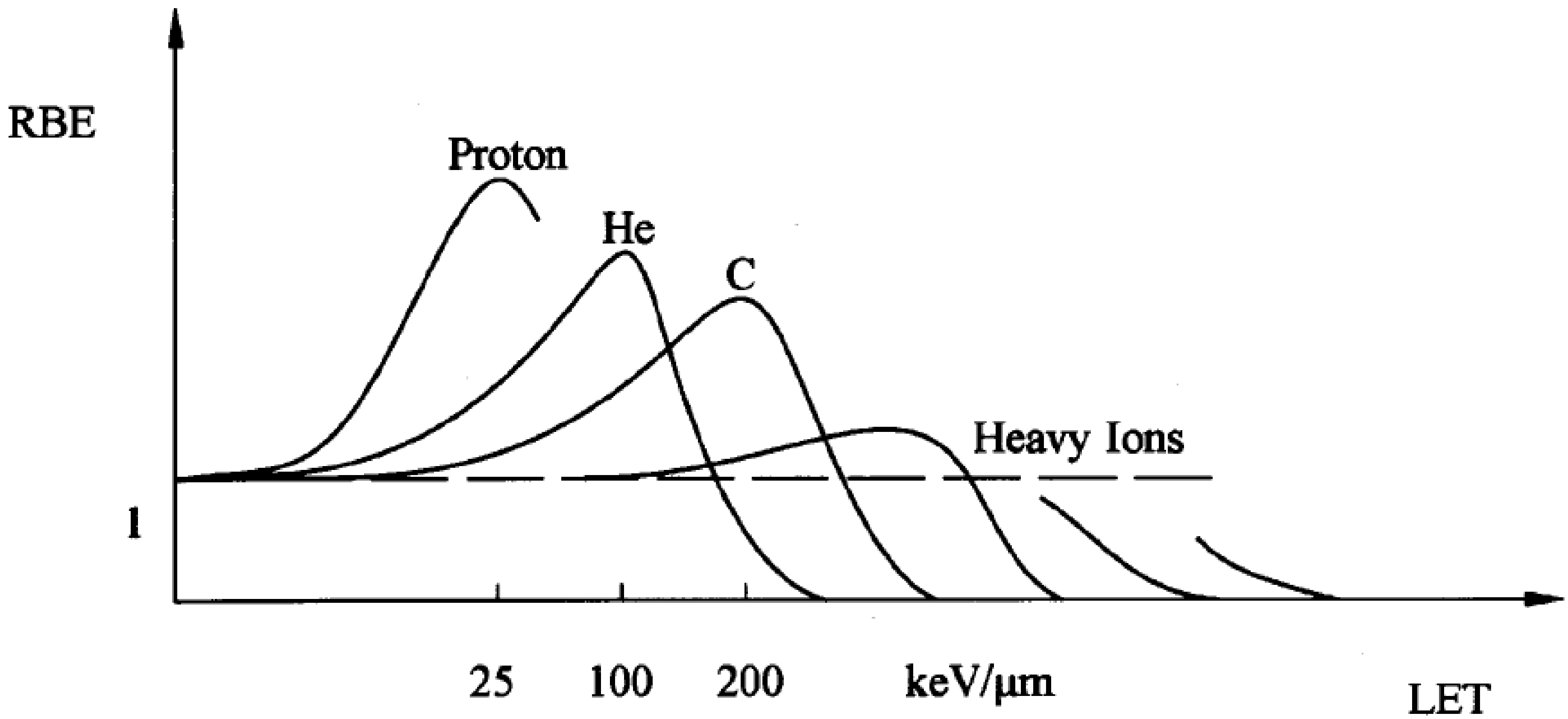
RBE and RBE_μ values of the therapeutic proton beam of Nice



L.De Nardo et al., Physica Medica XX, 71-77, 2004

Schematic comparison of RBE values of different ions

The saturation effect appears at higher LET values as the ion charge increases



From G.Kraft. Prog.Part.Nucl.Phys. 45, 473-544, 2000

CONCLUSIONS

1. **Microdosimetrc measurements in ion beams confirm that the absorbed energy in 1 µm site is poorly correlated with the absorbed dose at 2 Gy. In nanometric sites the physical phenomena are expected to be not correlated at all with the absorbed dose.**

2. **Microdosimetric measurements at 1 µm are able to mimic the biological-effective dose of therapeutic ion beams by using suitable saturation functions.**

1. **The accuracy of the saturation function has to be evaluated by comparison with radiobiological data.**