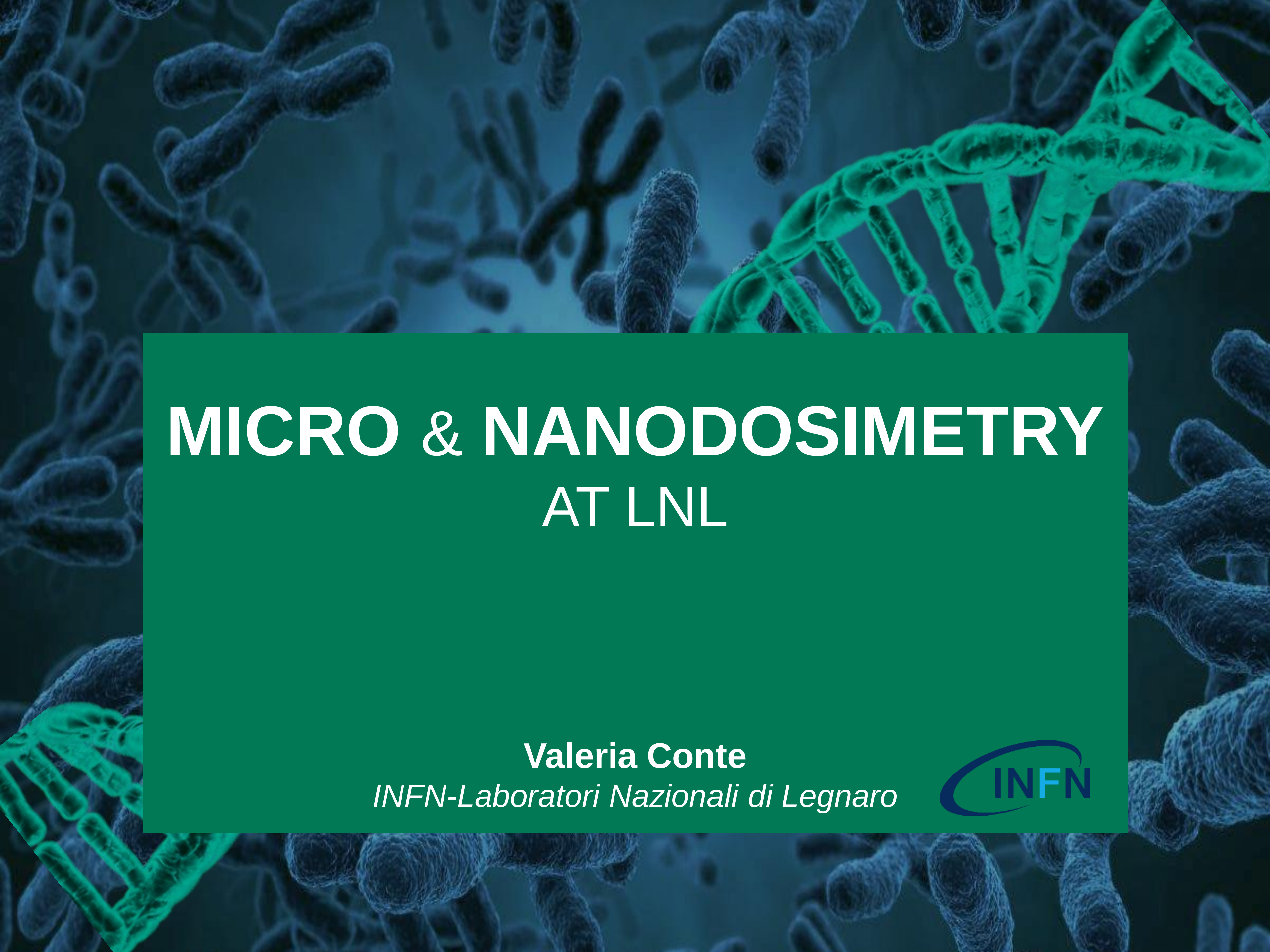
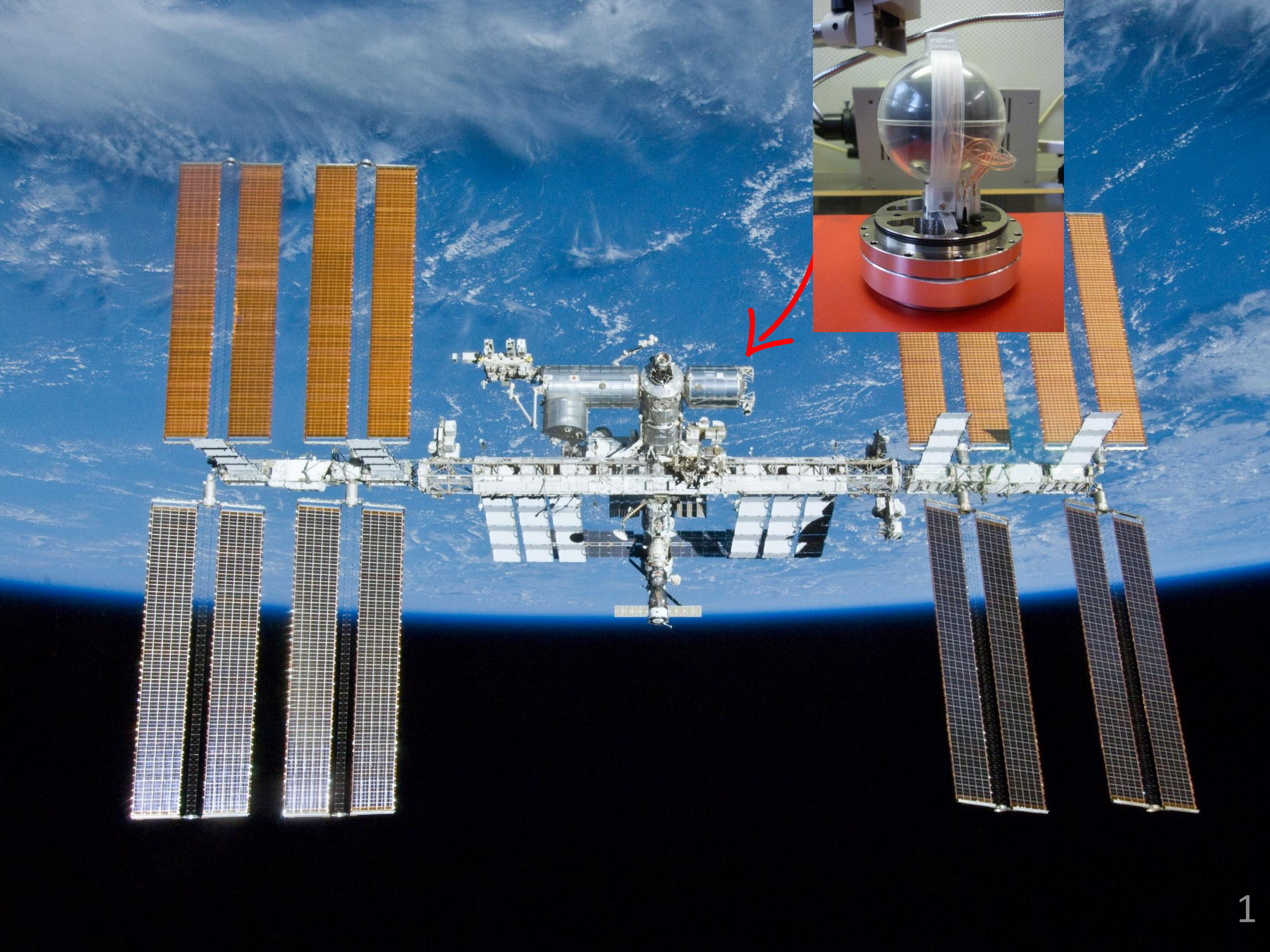
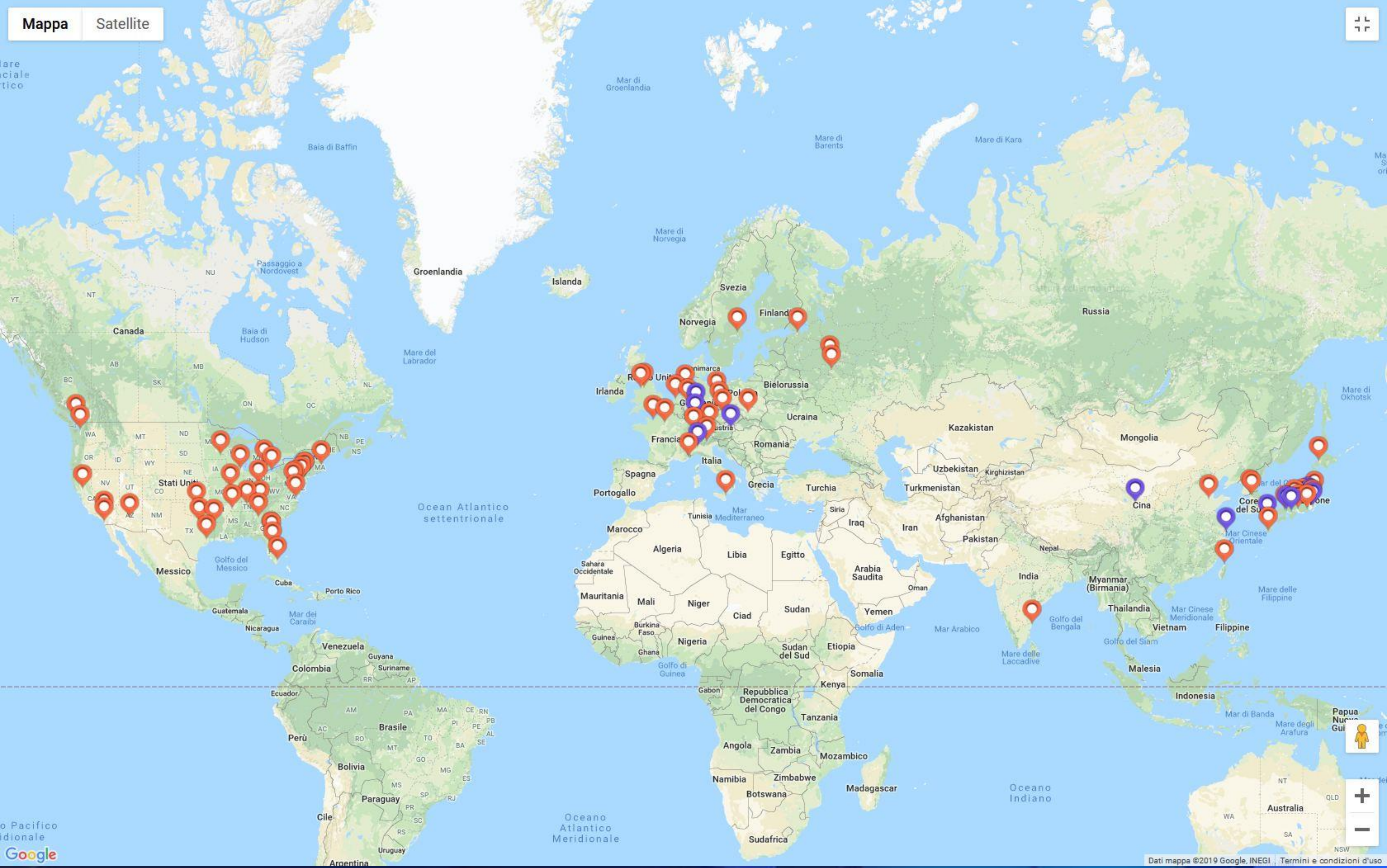


MICRO & NANODOSIMETRY
AT LNL

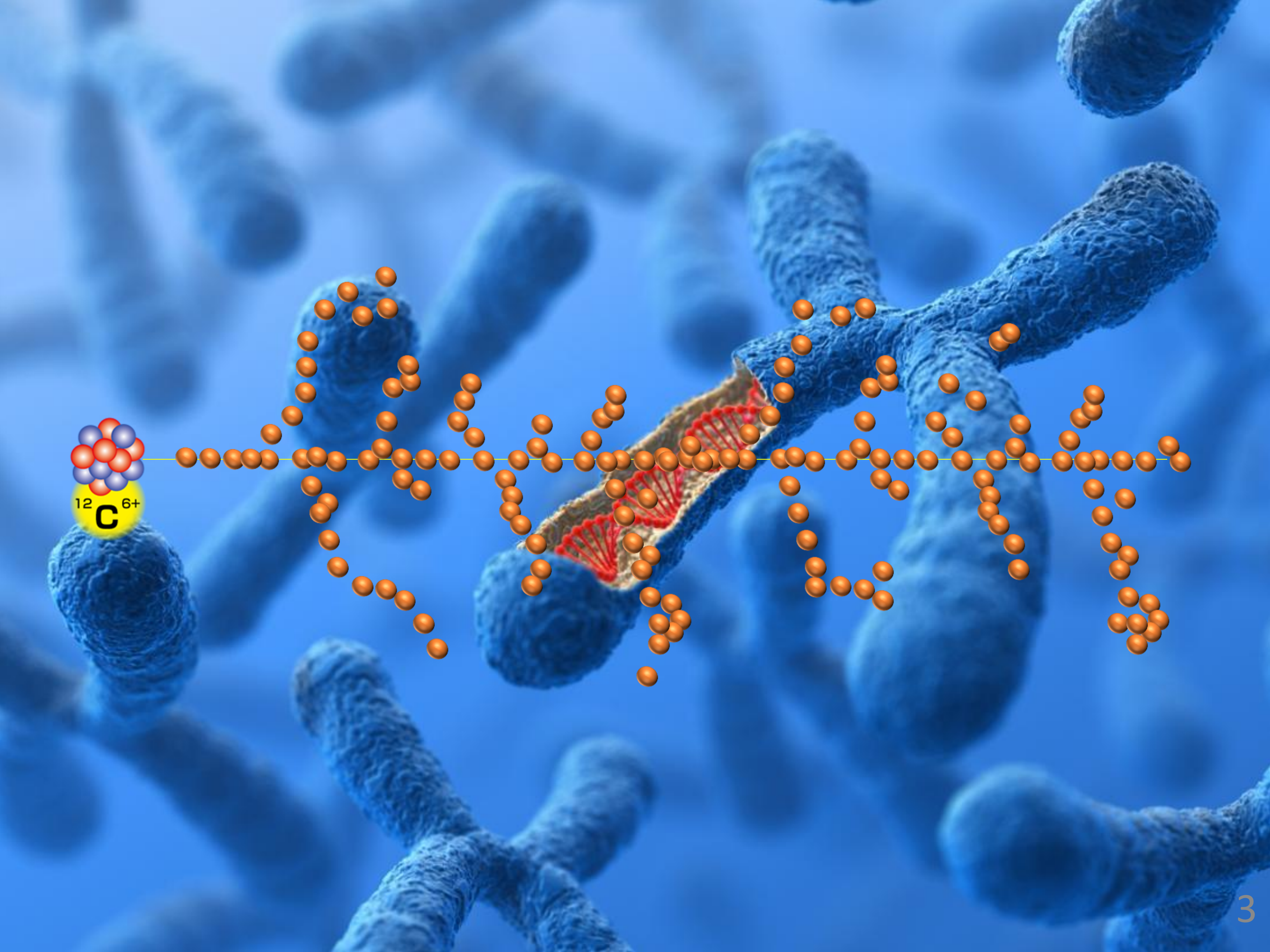
Valeria Conte
INFN-Laboratori Nazionali di Legnaro



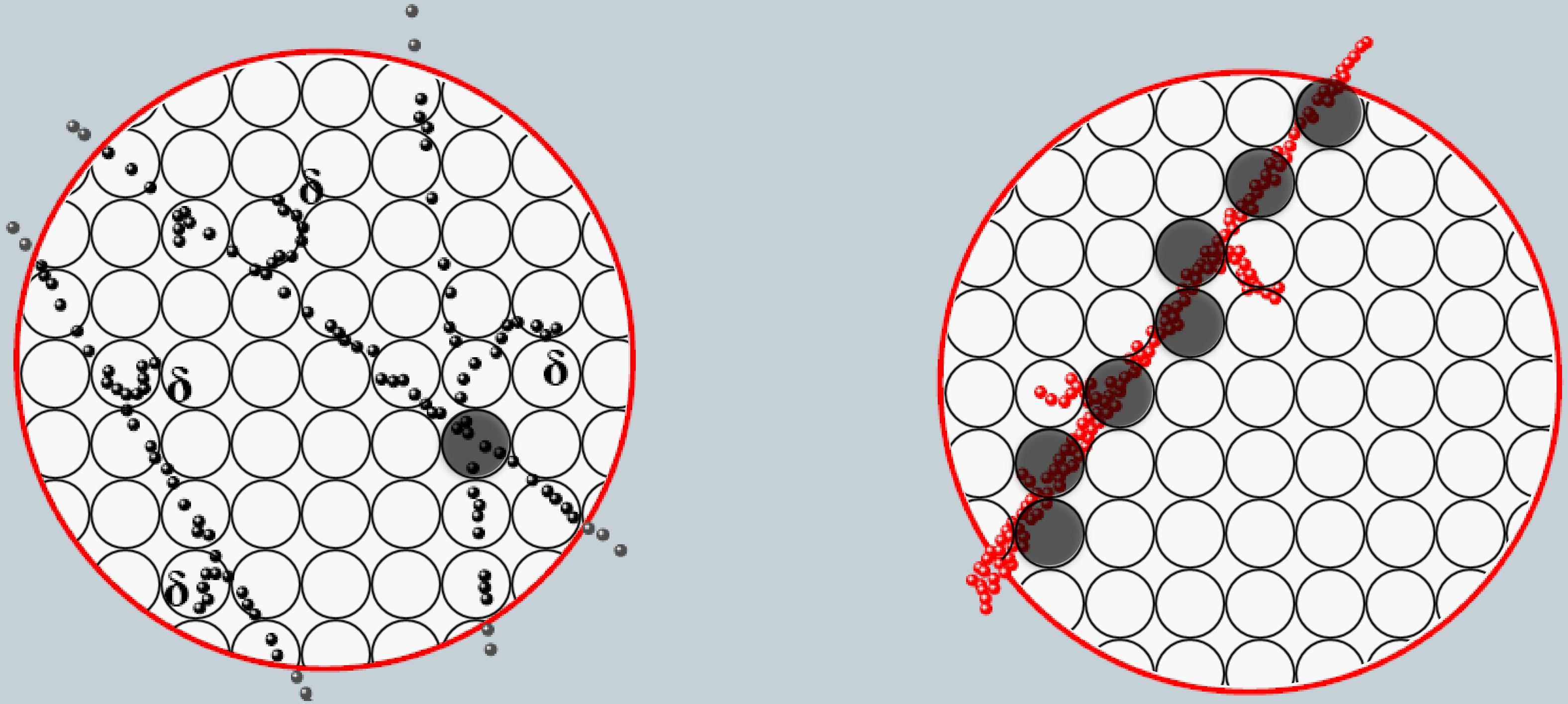
82 centres worldwide – 25000 patients treated last year



82 centres worldwide – 25000 patients treated last year


12
C
6+

DENSE TRACKS ARE MORE EFFECTIVE THAN SPARSE TRACKS



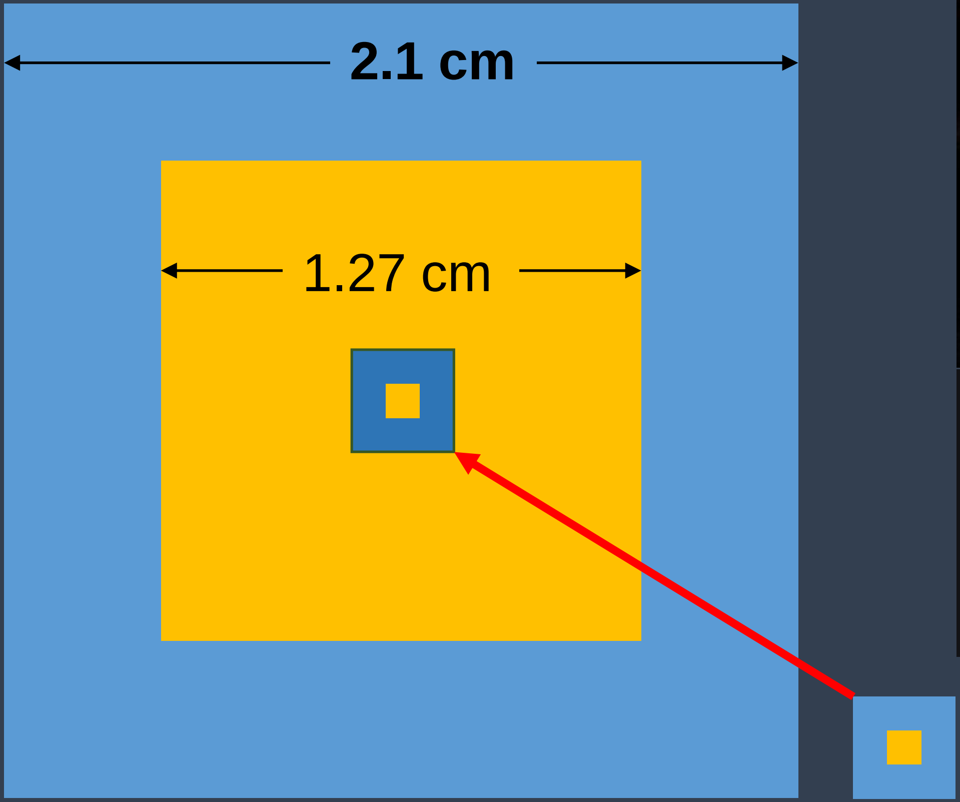
Warning: the Dose does not define the spatial pattern of energy deposition

“microdosimetry counters and their associated data logging and analysis require considerable care and are best left to experts”

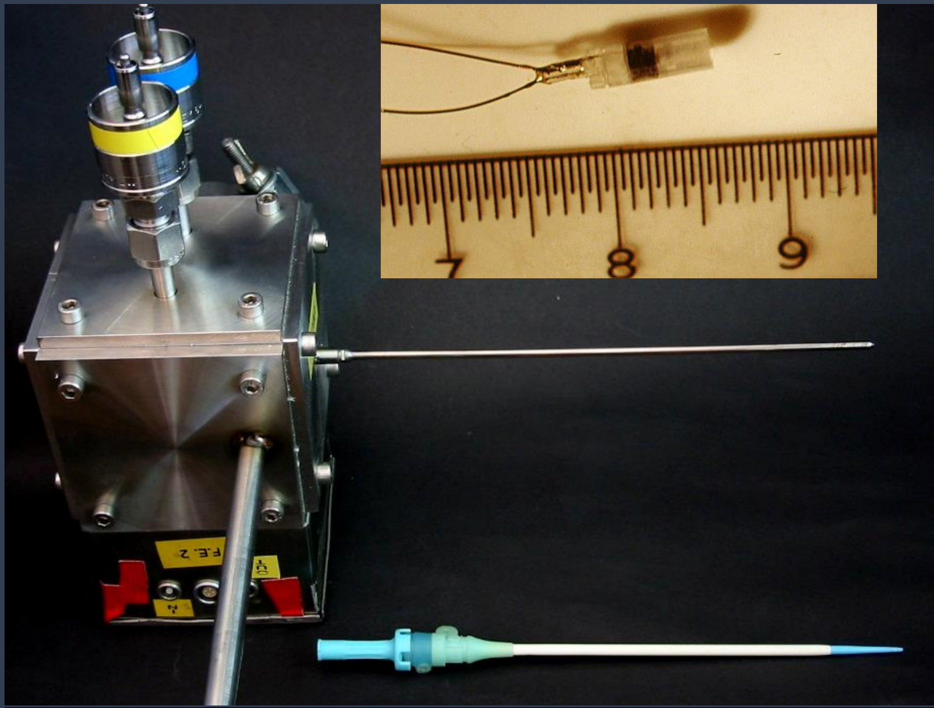
Particle Therapy Co-Operative Group

MINI-TEPC FOR HIGH INTENSITY BEAMS

The FWT LET-1/2 TEPC



The LNL MINI-TEPC



external diam. 2.7 mm

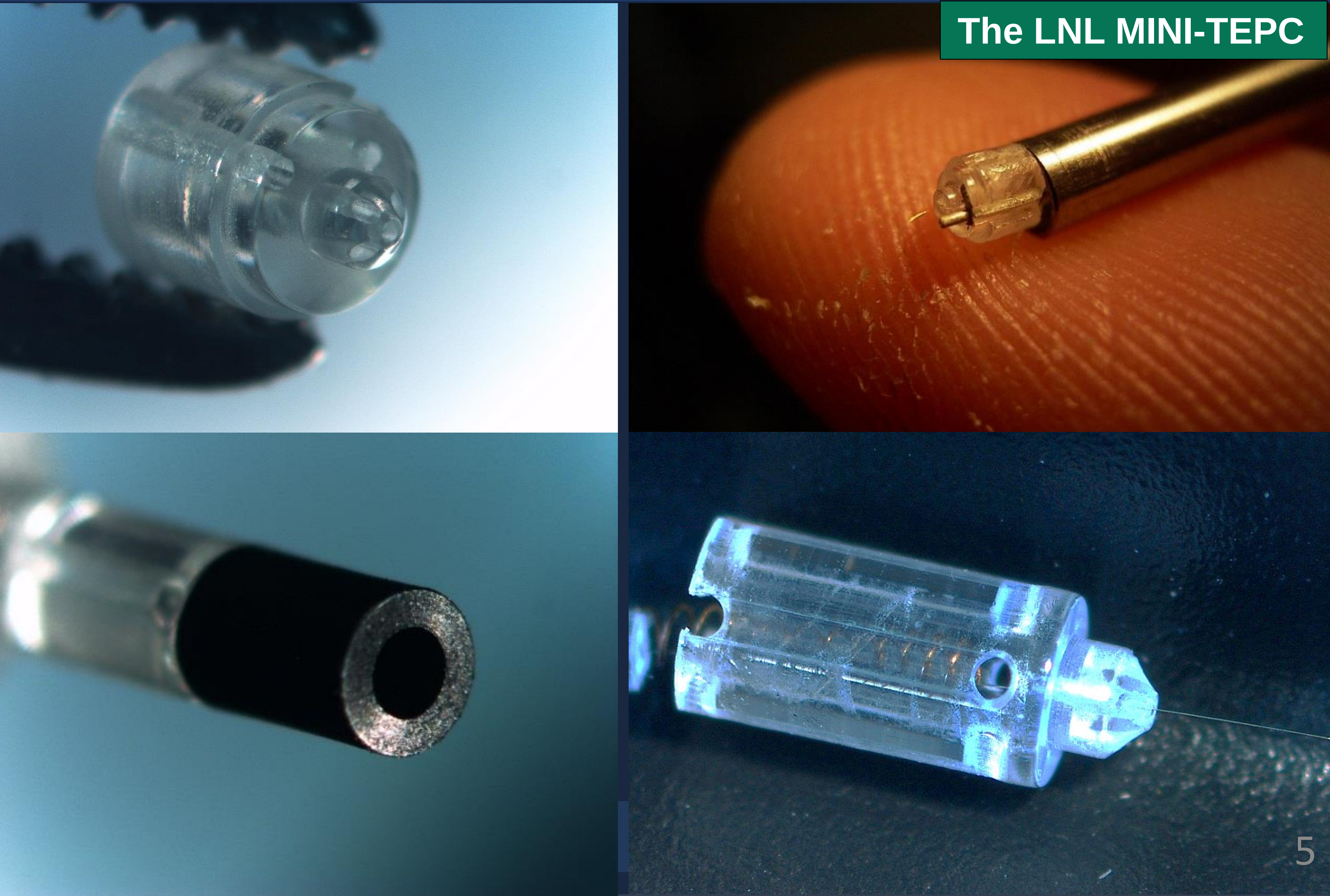
the same of 8 French cannula

inside diam. 0.9 mm

2.7 mm

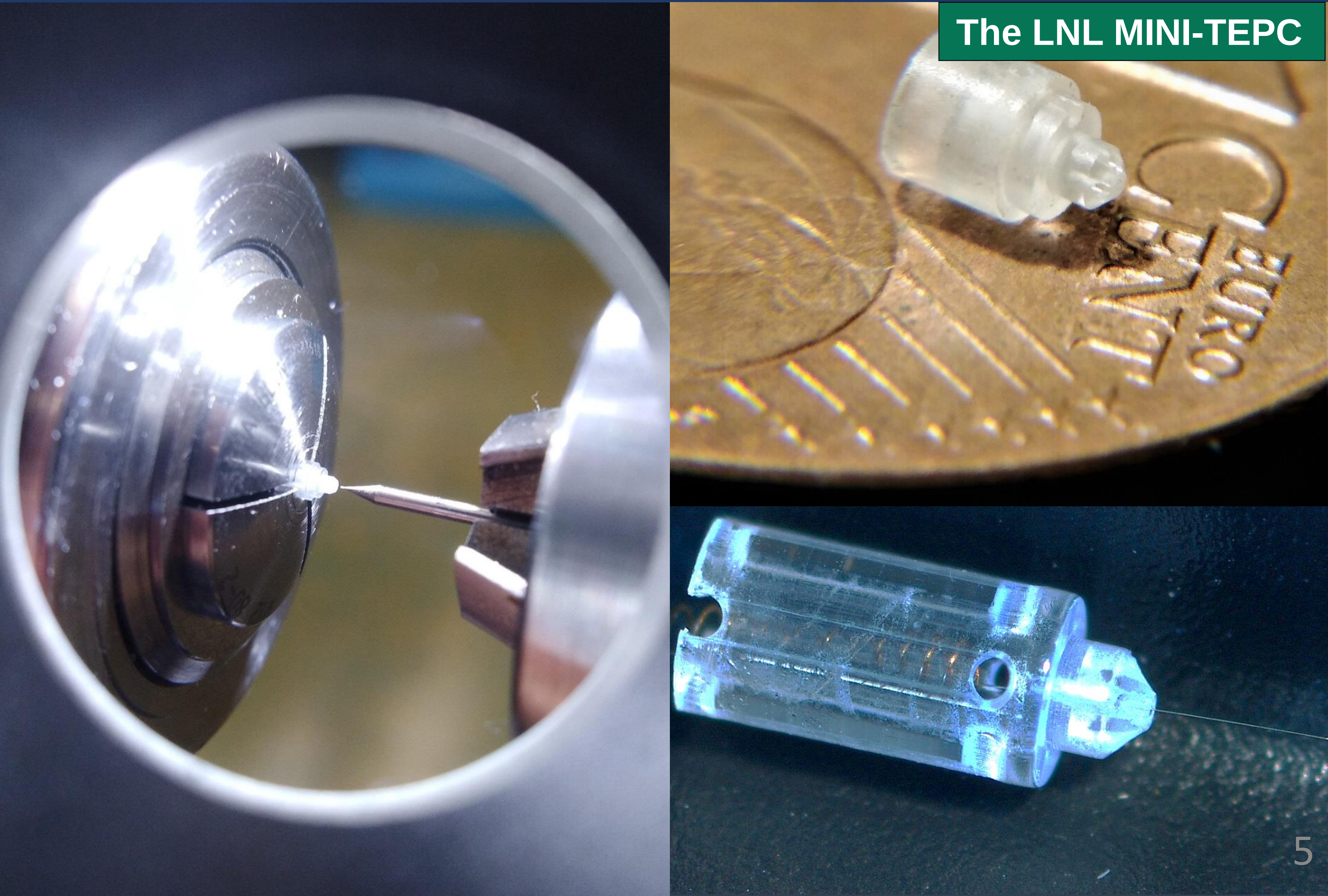
0.9 mm

MINI-TEPC FOR HIGH INTENSITY BEAMS



The LNL MINI-TEPC

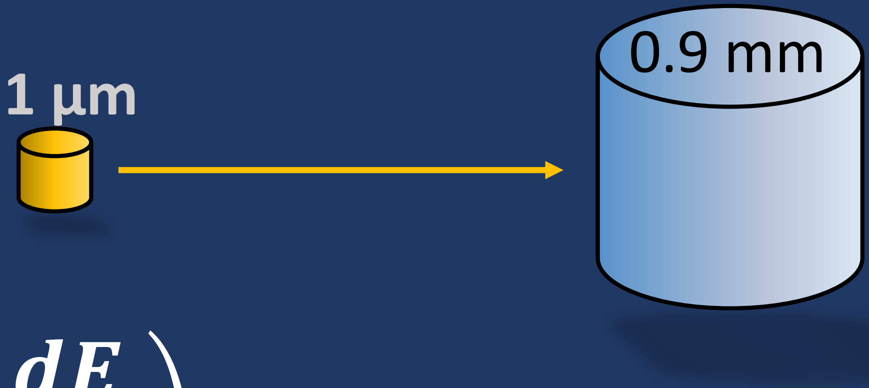
MINI-TEPC FOR HIGH INTENSITY BEAMS



The LNL MINI-TEPC

MICRODOSIMETRY

Macroscopic counters mimic the μm SIZE by using tissue-equivalent gas as the detection medium.



$$d_t \times \rho_t \times \left(\frac{dE}{\rho dx}\right)_t = d_{gas} \times \rho_{gas} \times \left(\frac{dE}{\rho dx}\right)_{gas}$$

MICRODOSIMETRY

Macroscopic counters mimic the μm SIZE by using tissue-equivalent gas as the detection medium.

definition of quantities

lineal energy $y = \frac{\varepsilon}{\bar{l}}$ $[y] = \mathbf{keV/\mu m}$

$\mathbf{f}(y)$ frequency probability density of y

$\mathbf{d}(y)$ dose probability density of y

The p(65)+Be therapeutic neutron beam of Nice

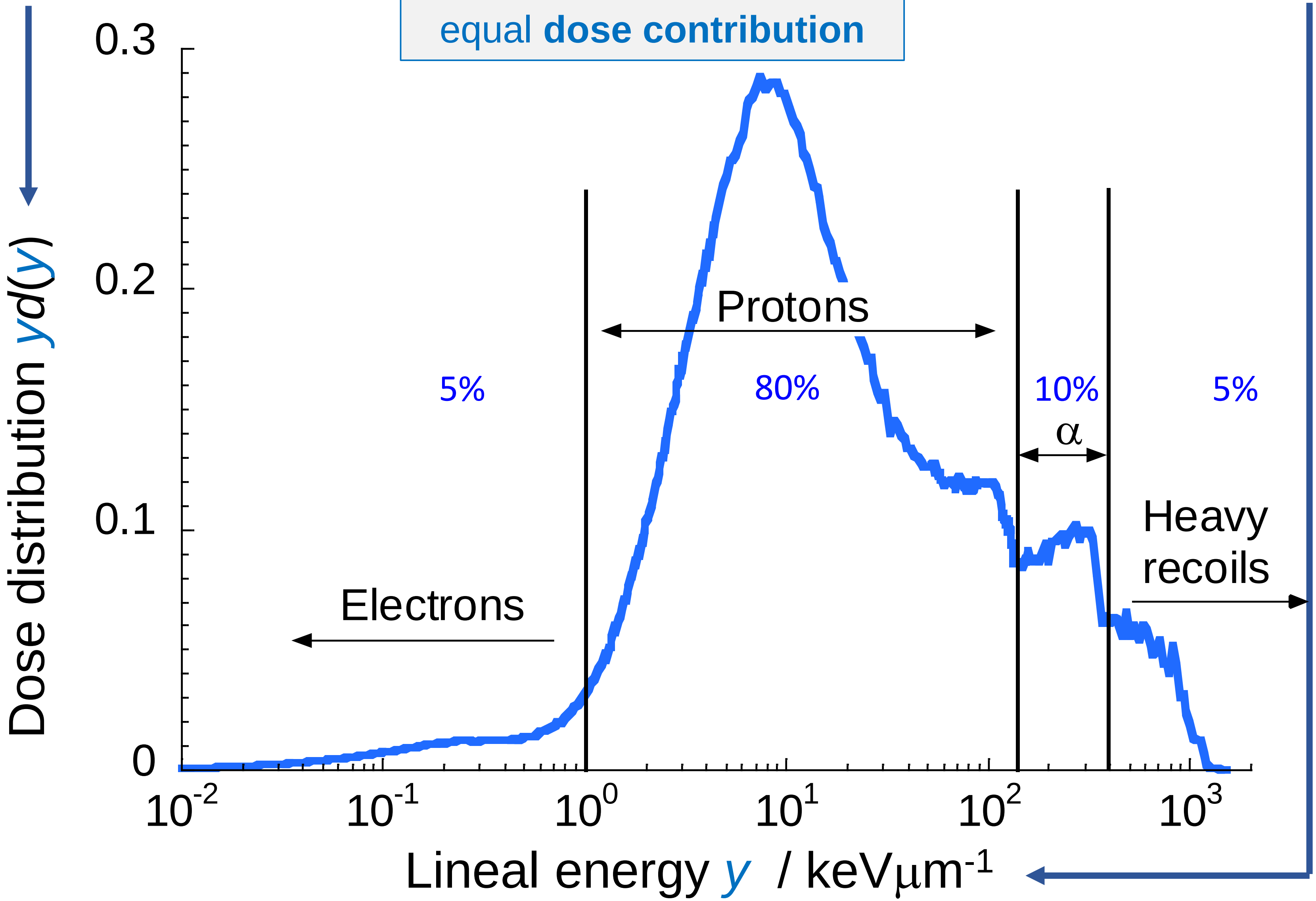
ordinate: ***y**d(**y**)*

Equal area under curve

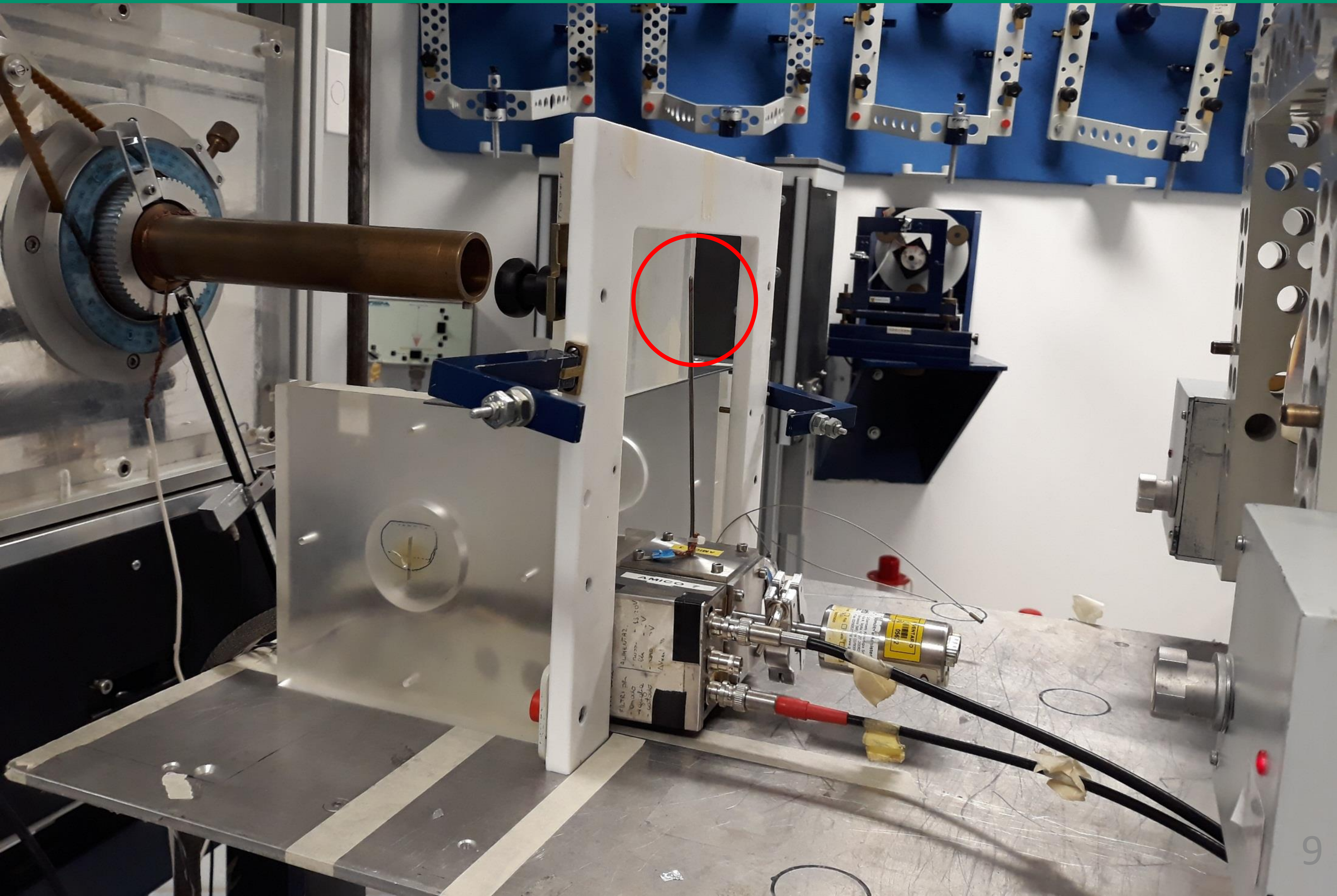
═

equal **dose contribution**

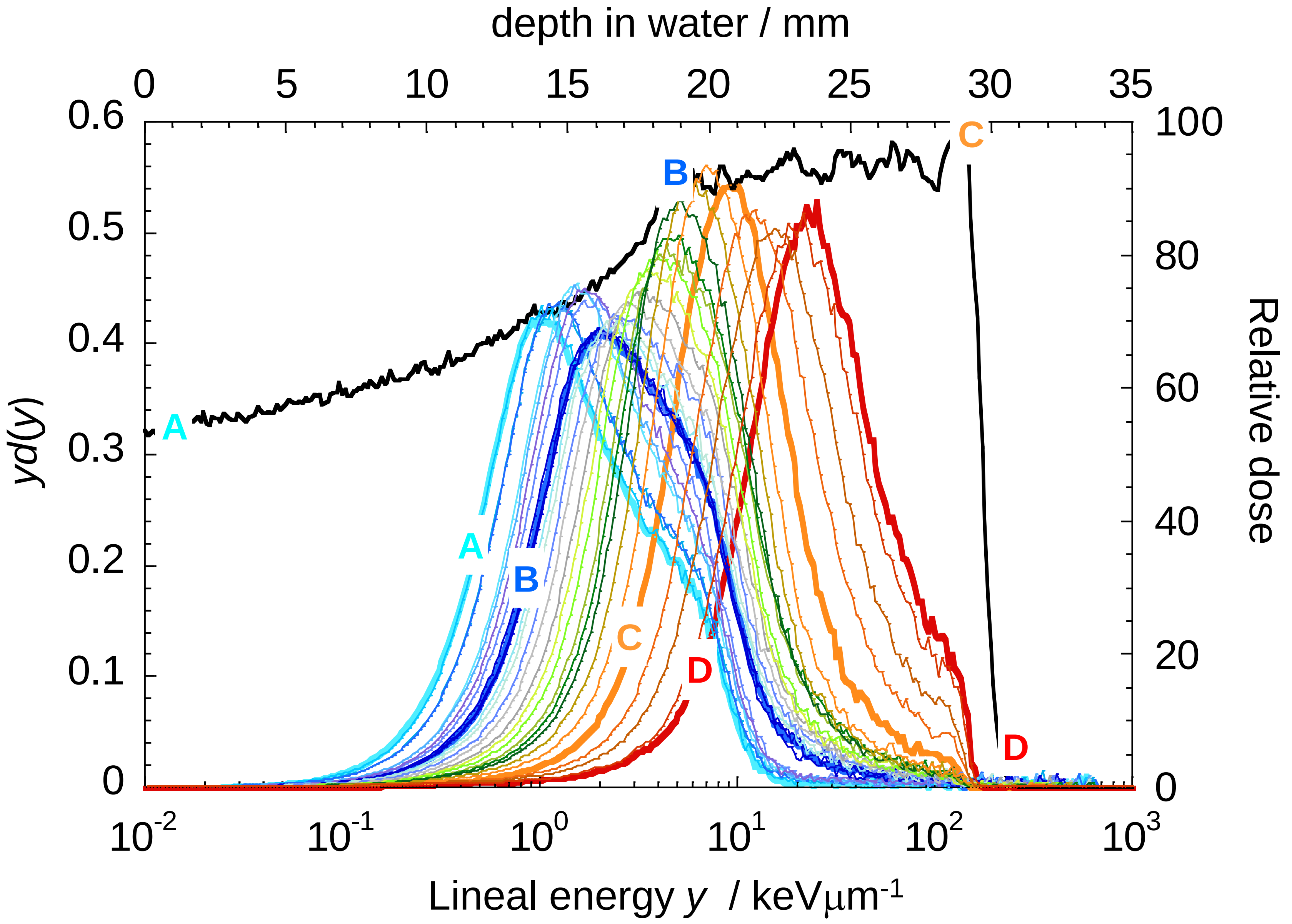
Log scale of ***y***



MICRODOSIMETRY at the 62 MeV Therapeutic Proton Beam of CATANA

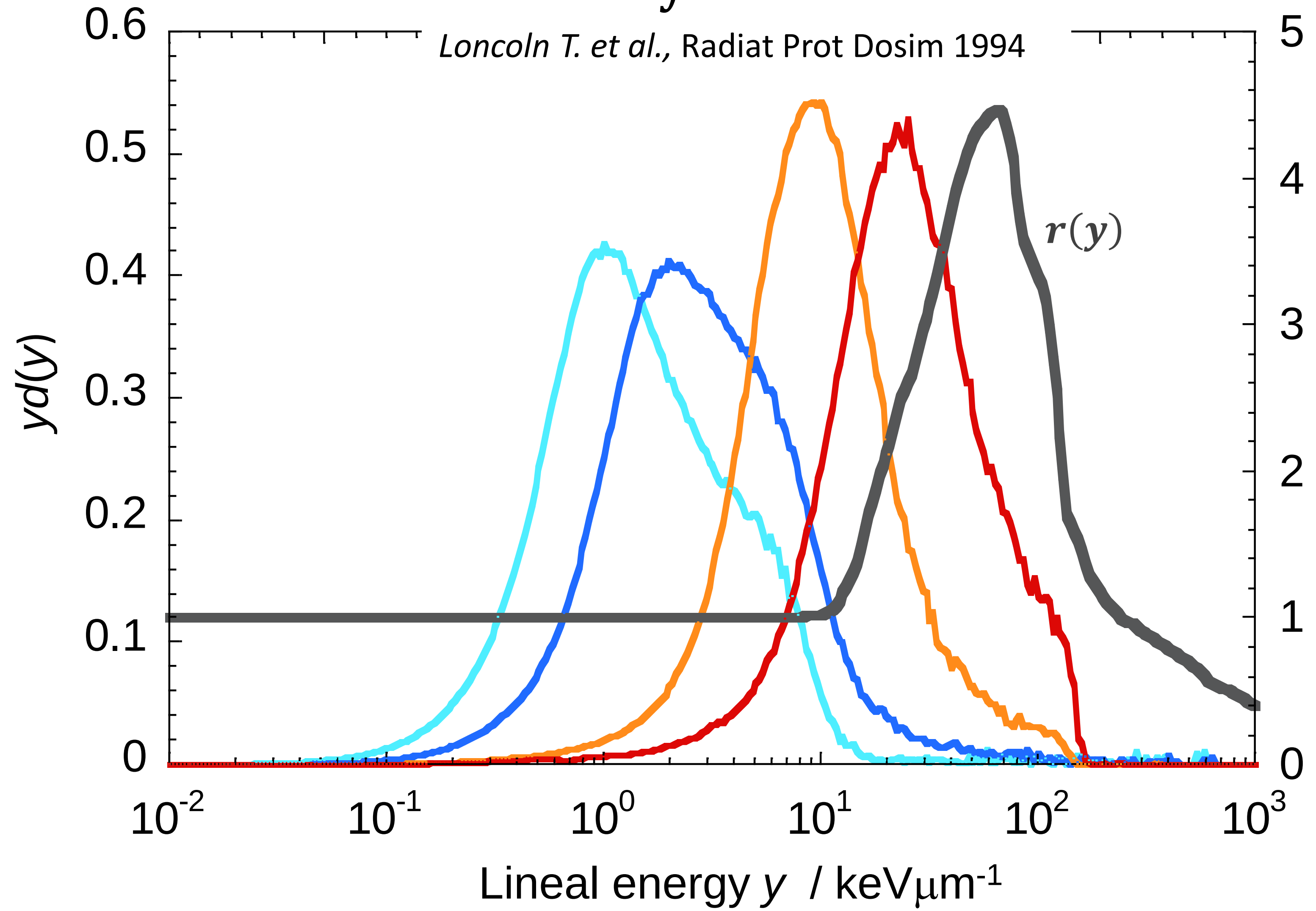


MICRODOSIMETRY at the 62 MeV Therapeutic Proton Beam of CATANA



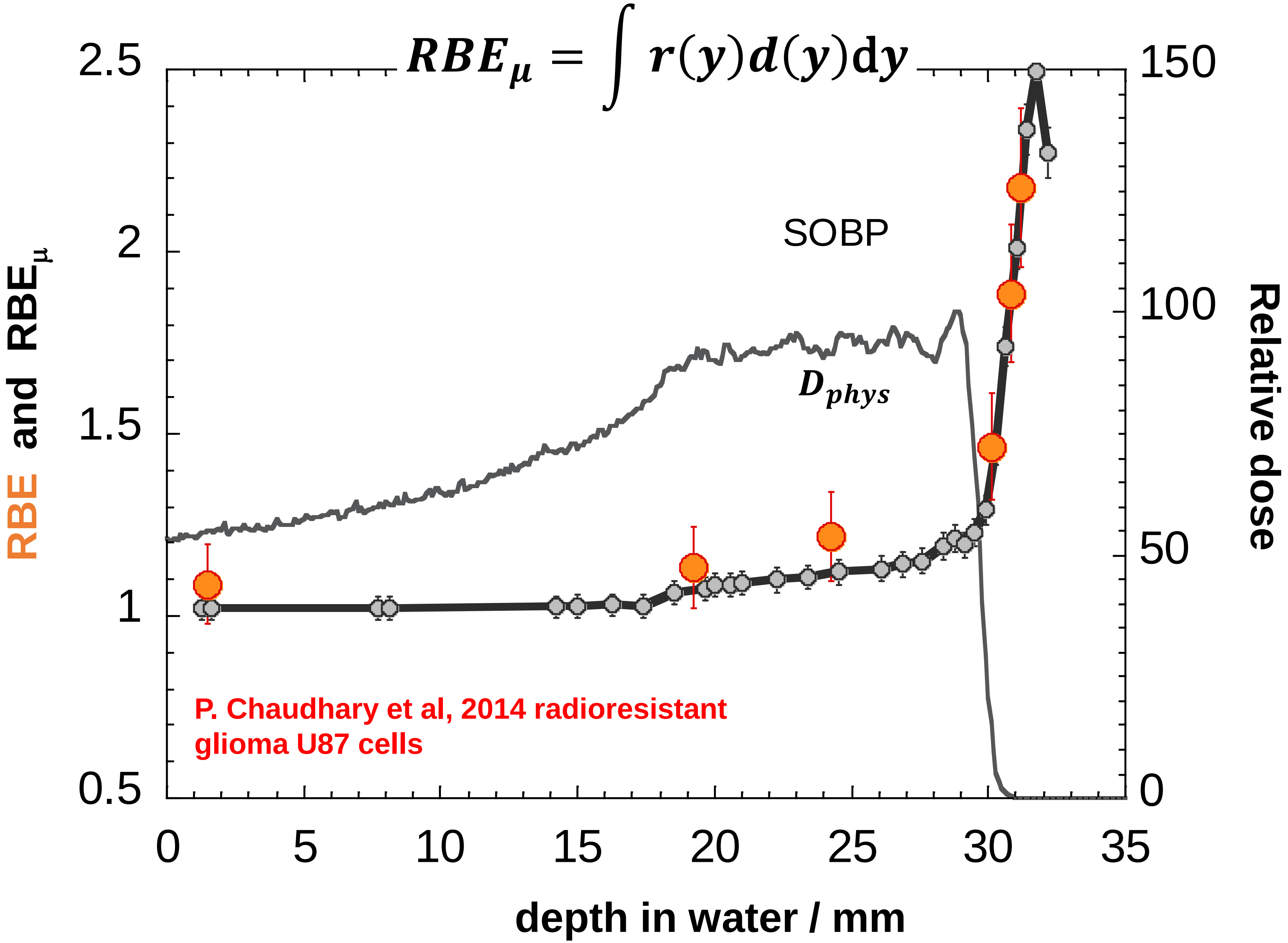
MICRODOSIMETRY at the 62 MeV Therapeutic Proton Beam of CATANA

$$RBE_{\mu} = \int r(y)d(y)\mathrm{d}y$$



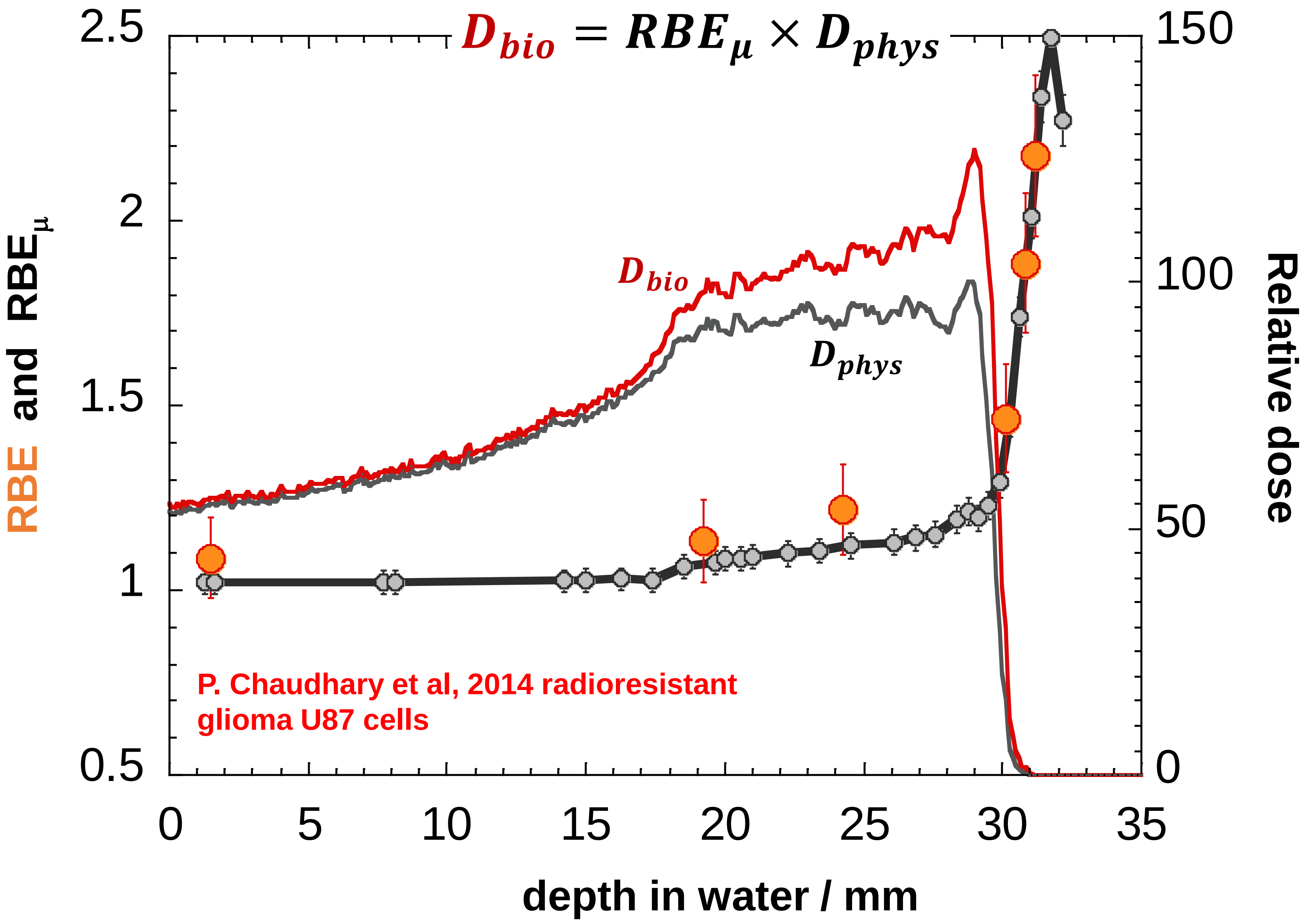
Loncoln T. et al., Radiat Prot Dosim 1994

MICRODOSIMETRY at the 62 MeV Therapeutic Proton Beam of CATANA



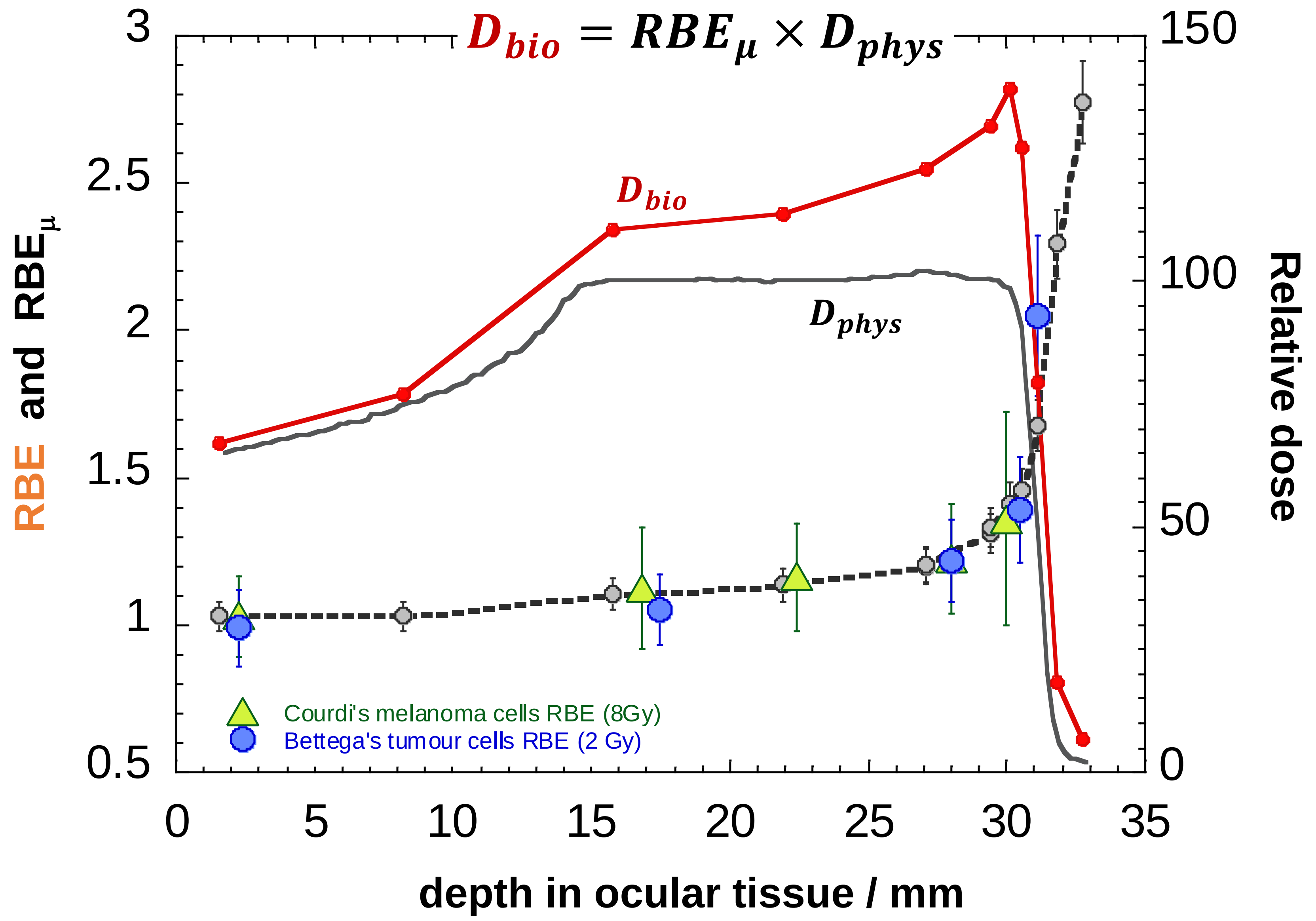
P. Chaudhary et al, 2014 radioresistant glioma U87 cells

MICRODOSIMETRY at the 62 MeV Therapeutic Proton Beam of CATANA



P. Chaudhary et al, 2014 radioresistant glioma U87 cells

MICRODOSIMETRY at the 65 MeV Therapeutic Proton Beam of NICE



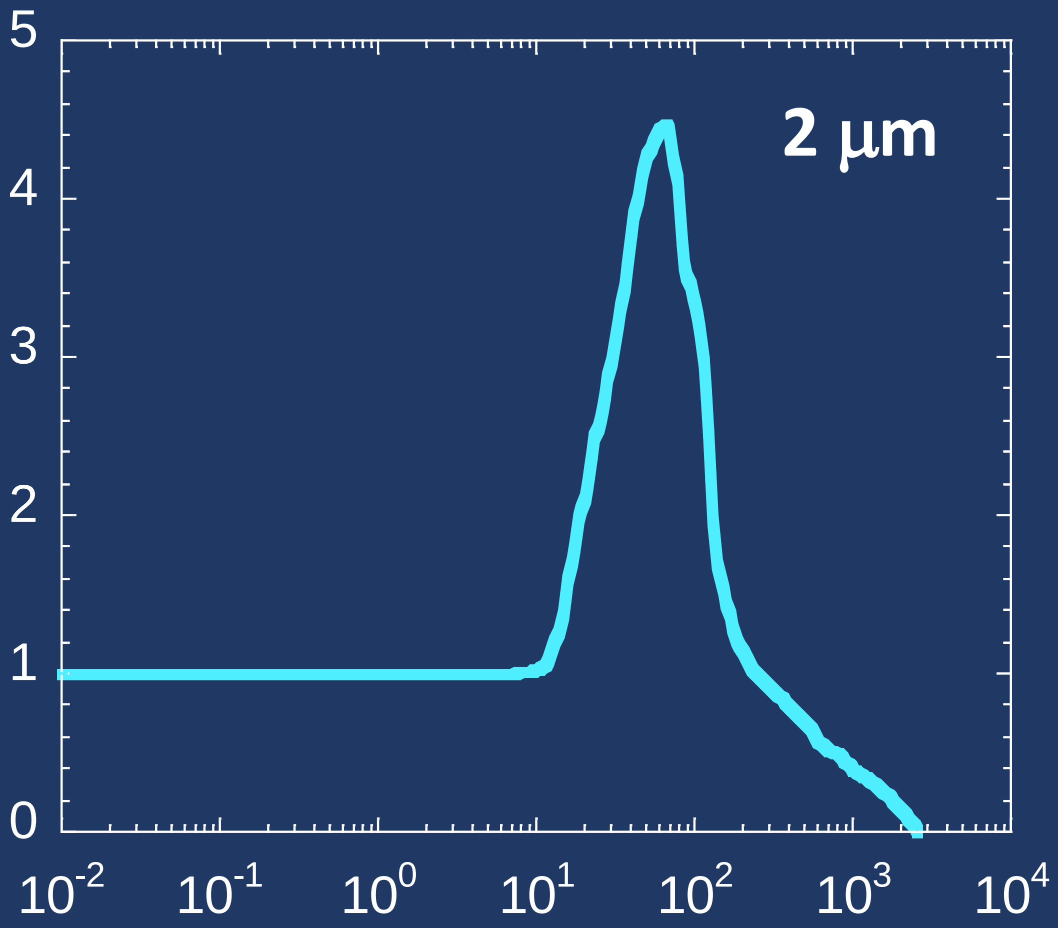
FROM RESEARCH TO CLINICS

TIFPA

INFN
LNS

INFN
LNL

The biological response function $r(y)$



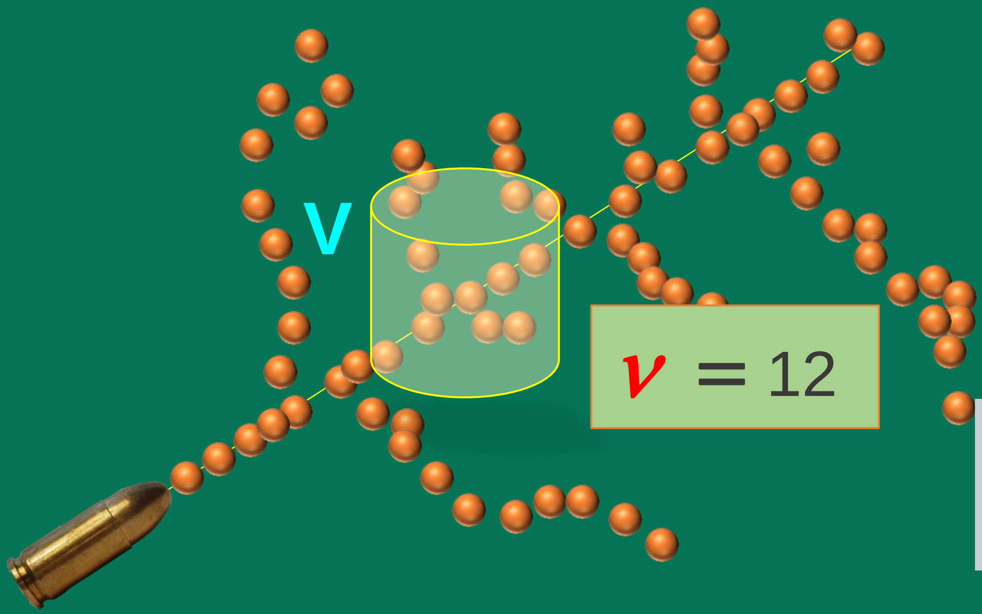
?

The biological response function is not universal

NANODOSIMETRY

A single ionizing particle crosses a target volume **V**

And the number ν of ionizations inside **V** is counted



$\boldsymbol{P}(\boldsymbol{\nu}|\boldsymbol{Q})$ represents the probability of measuring $\boldsymbol{\nu}$ ionizations

$\boldsymbol{M}_{\mathbf{1}}(\boldsymbol{Q})$ represents the mean ionization yield

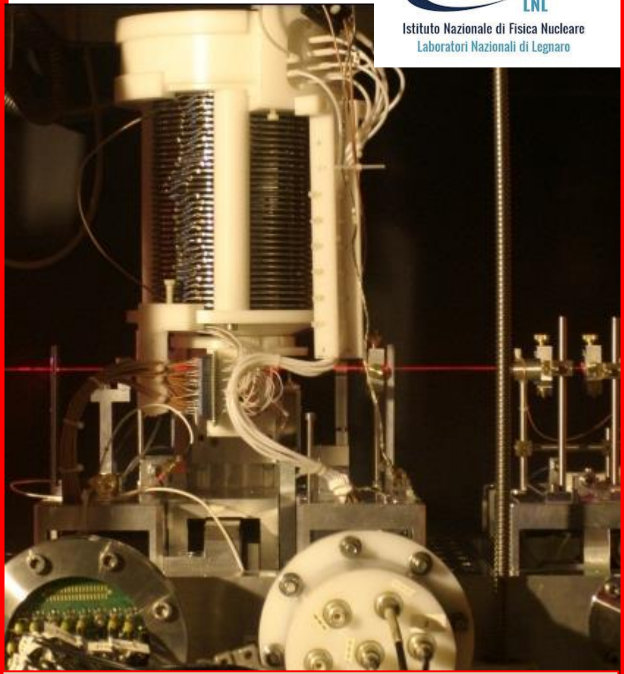
$\boldsymbol{F}_{\boldsymbol{n}}(\boldsymbol{Q})$ represents the probability of measuring at least $\boldsymbol{n}$ ionizations

THREE NANODOSIMETERS

nano-volumes of different size

Startrack

Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro



L. De Nardo et al., NIM A 484, 312 (2002)

Jet Counter

Narodowe Centrum Badań Jądrowych
National Centre for Nuclear Research
ŚWIERK

S. Pszona et al., NIM A 447, 601 (2000)

Ion Counter

Physikalisch-Technische Bundesanstalt
Braunschweig und Berlin

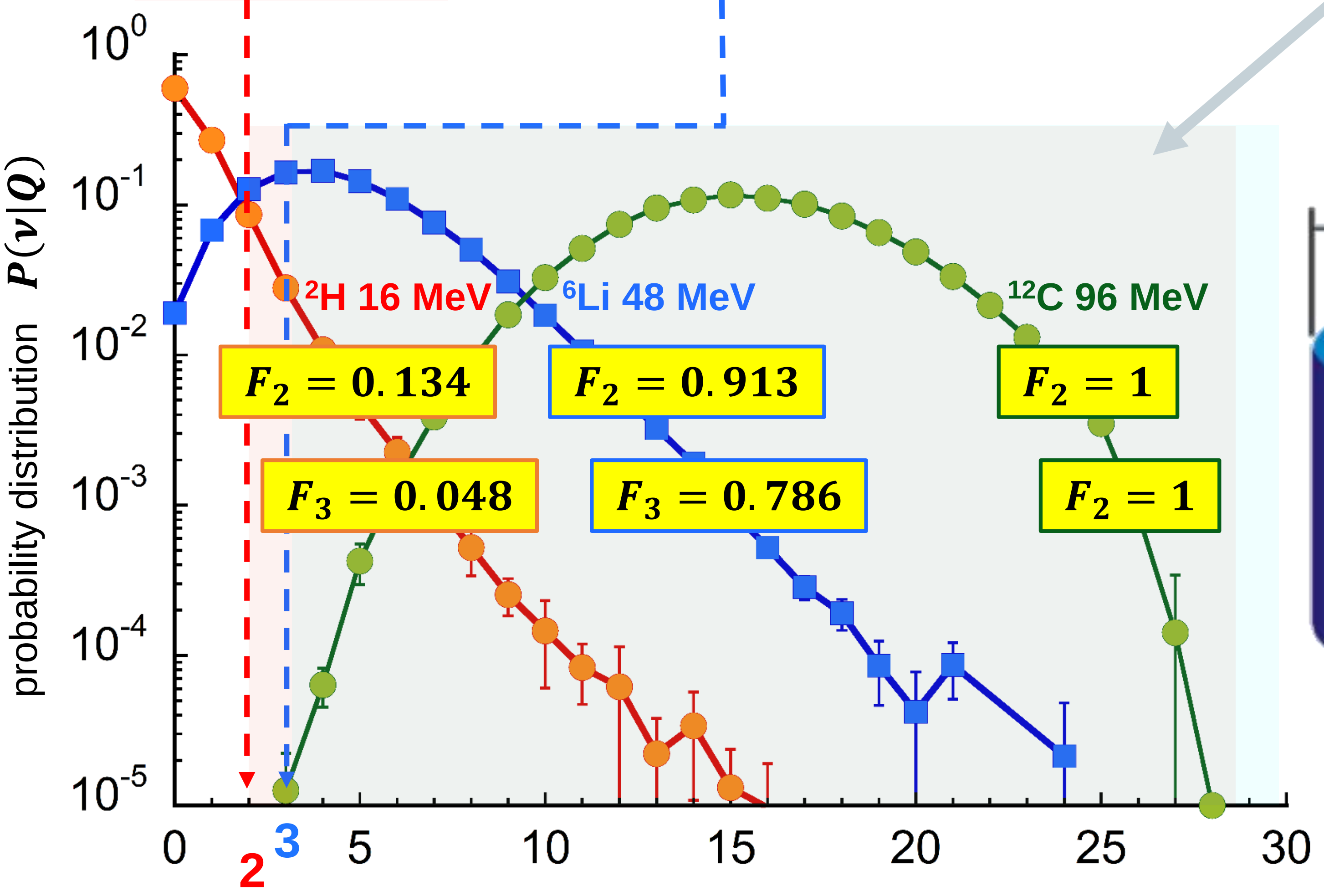
G. Garty et al., Rad.Prot.Dos. 99, 325 (2002)

NANODOSIMETRY of 8 AMeV particles with STARTRACK

$$F_2 = \sum_{\nu=2}^{\infty} P(\nu|Q)$$

$$F_3 = \sum_{\nu=3}^{\infty} P(\nu|Q)$$

Particles with the same velocity



$F_2 = 0.134$

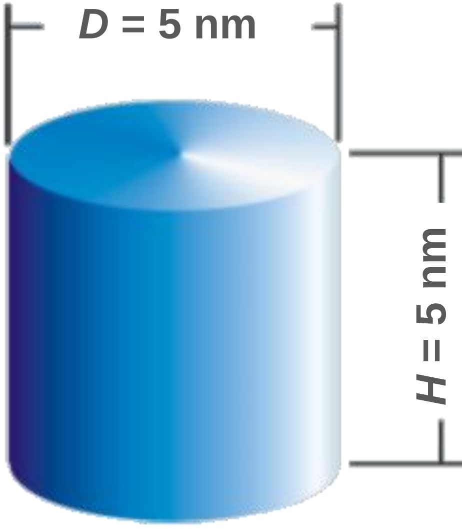
$F_3 = 0.048$

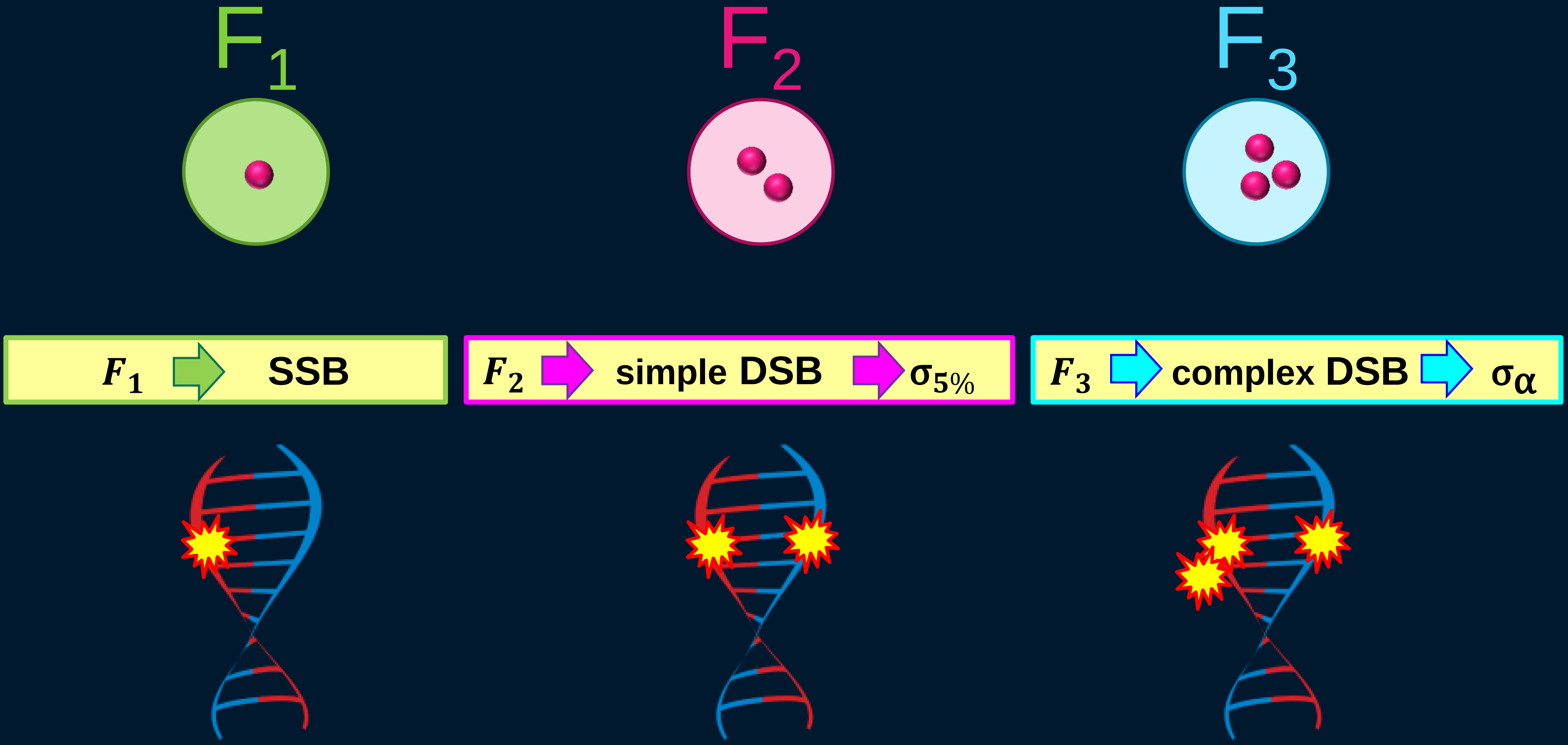
$F_2 = 0.913$

$F_3 = 0.786$

$F_2 = 1$

$F_2 = 1$





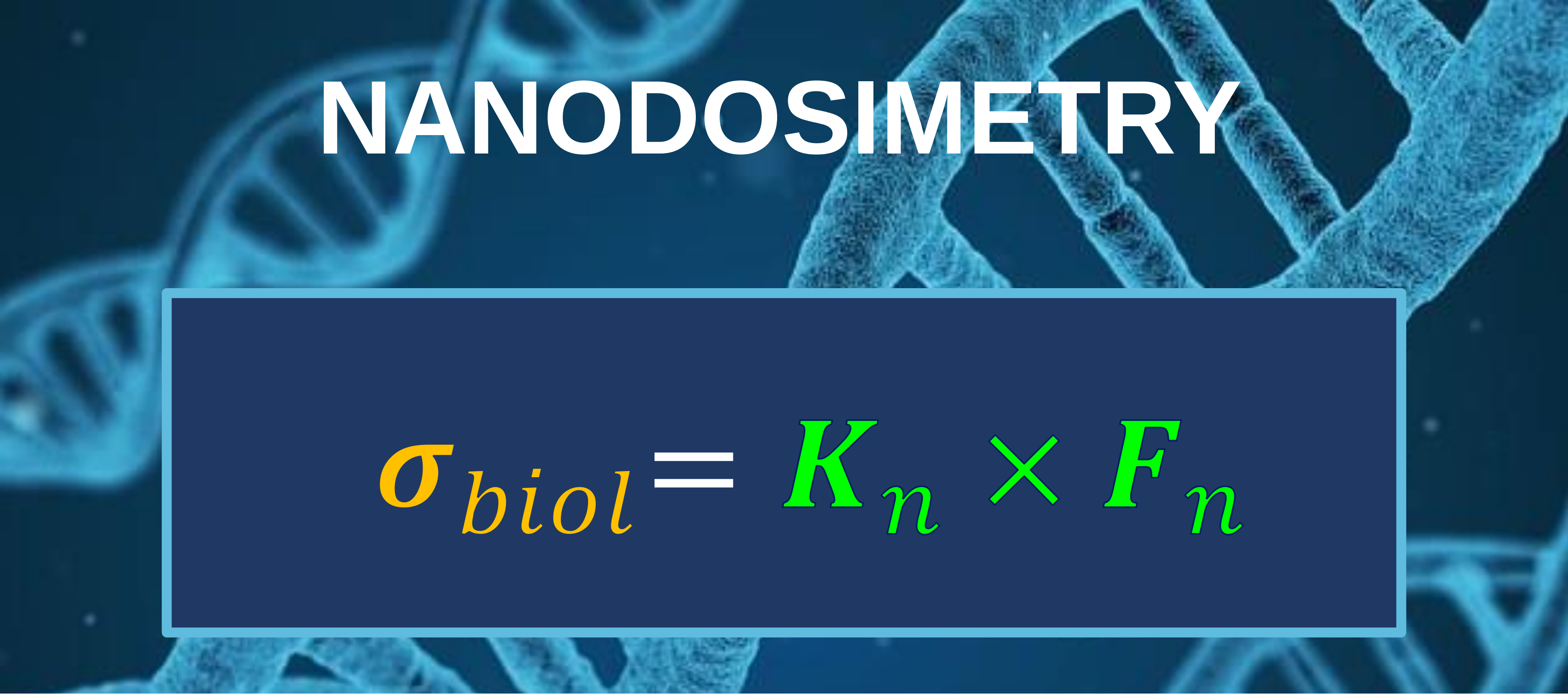
F_1 F_2 F_3

F_1 → SSB

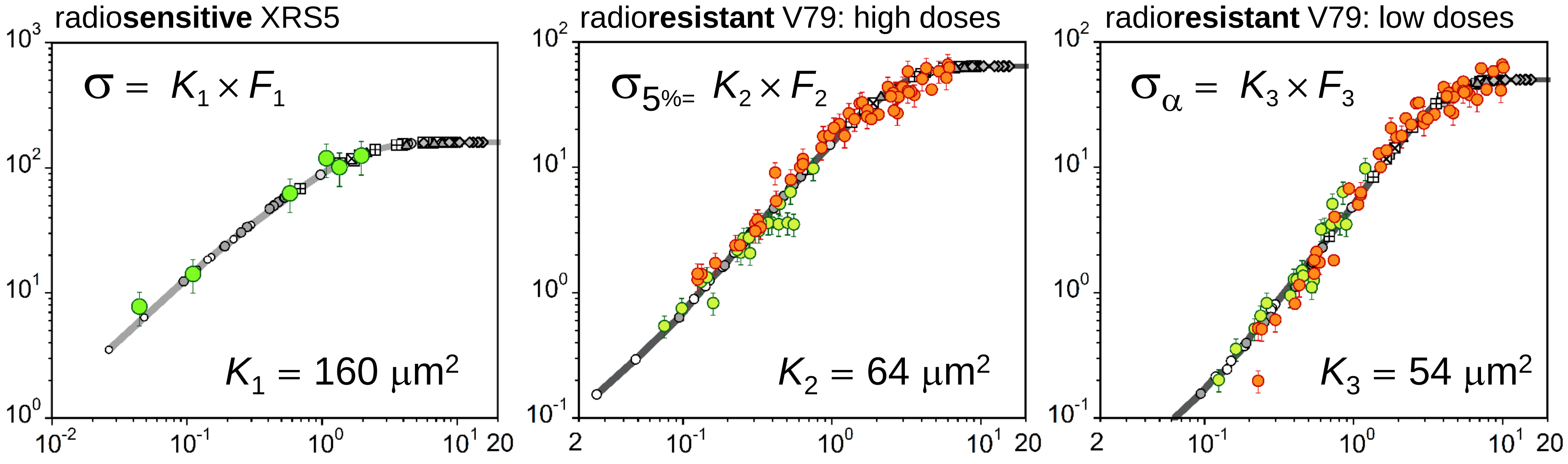
F_2 → simple DSB → $\sigma_{5\%}$

F_3 → complex DSB → σ_{α}

NANODOSIMETRY

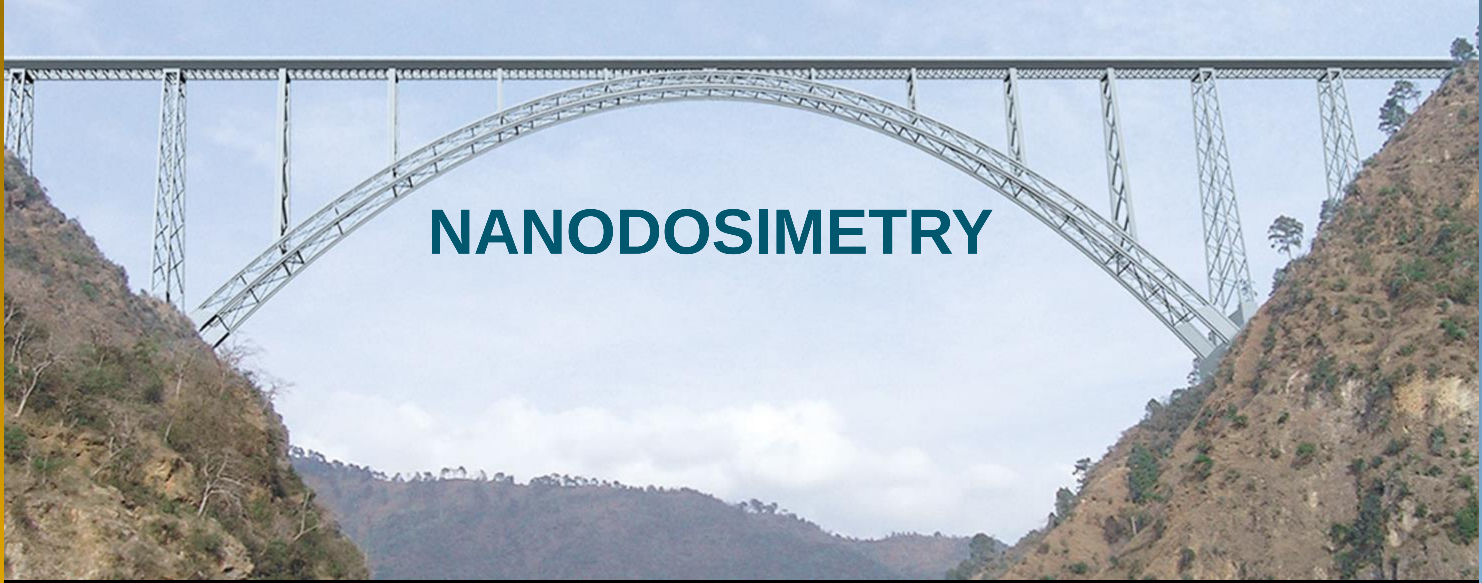


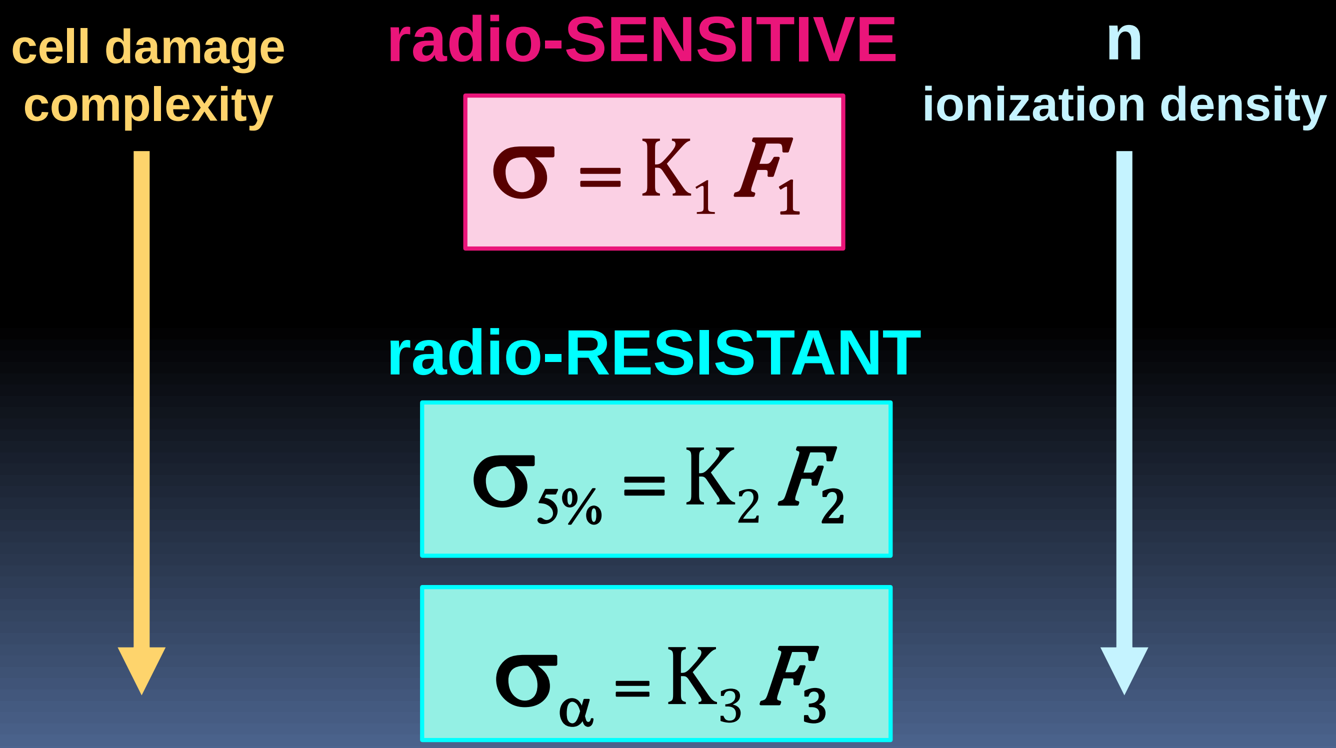
$$\sigma_{biol} = K_n \times F_n$$



RADIOBIOLOGY

NANODOSIMETRY





cell damage complexity

radio-SENSITIVE

$$\sigma = K_1 \boldsymbol{F}_1$$

radio-RESISTANT

$$\sigma_{5\%} = K_2 \boldsymbol{F}_2$$

$$\sigma_{\alpha} = K_3 \boldsymbol{F}_3$$

n
ionization density

RADIATION PHYS

MICRO & NANODOSIMETRY

Purpose: not the **unlimited** generation of data but their deliberate **reduction** to the most **essential parameters**

BIOLOGY

DNA damage complexity

radio-SENSITIVE

$$\boldsymbol{\sigma} = \mathrm{K}_1 \, \boldsymbol{F}_1$$

radio-RESISTANT

$$\boldsymbol{\sigma}_{5\%} = \mathrm{K}_2 \, \boldsymbol{F}_2$$

$$\boldsymbol{\sigma}_{\alpha} = \mathrm{K}_3 \, \boldsymbol{F}_3$$

$$\boldsymbol{\alpha} = \mathrm{K}_2 \times F_3 \times \left(\frac{F}{D}\right)$$

$$\boldsymbol{\beta} = \frac{\mathrm{K}_3^2 \times F_3^2 - \mathrm{K}_2^2 \times F_2^2}{4\ln(0.05)} \times \left(\frac{F}{D}\right)^2$$

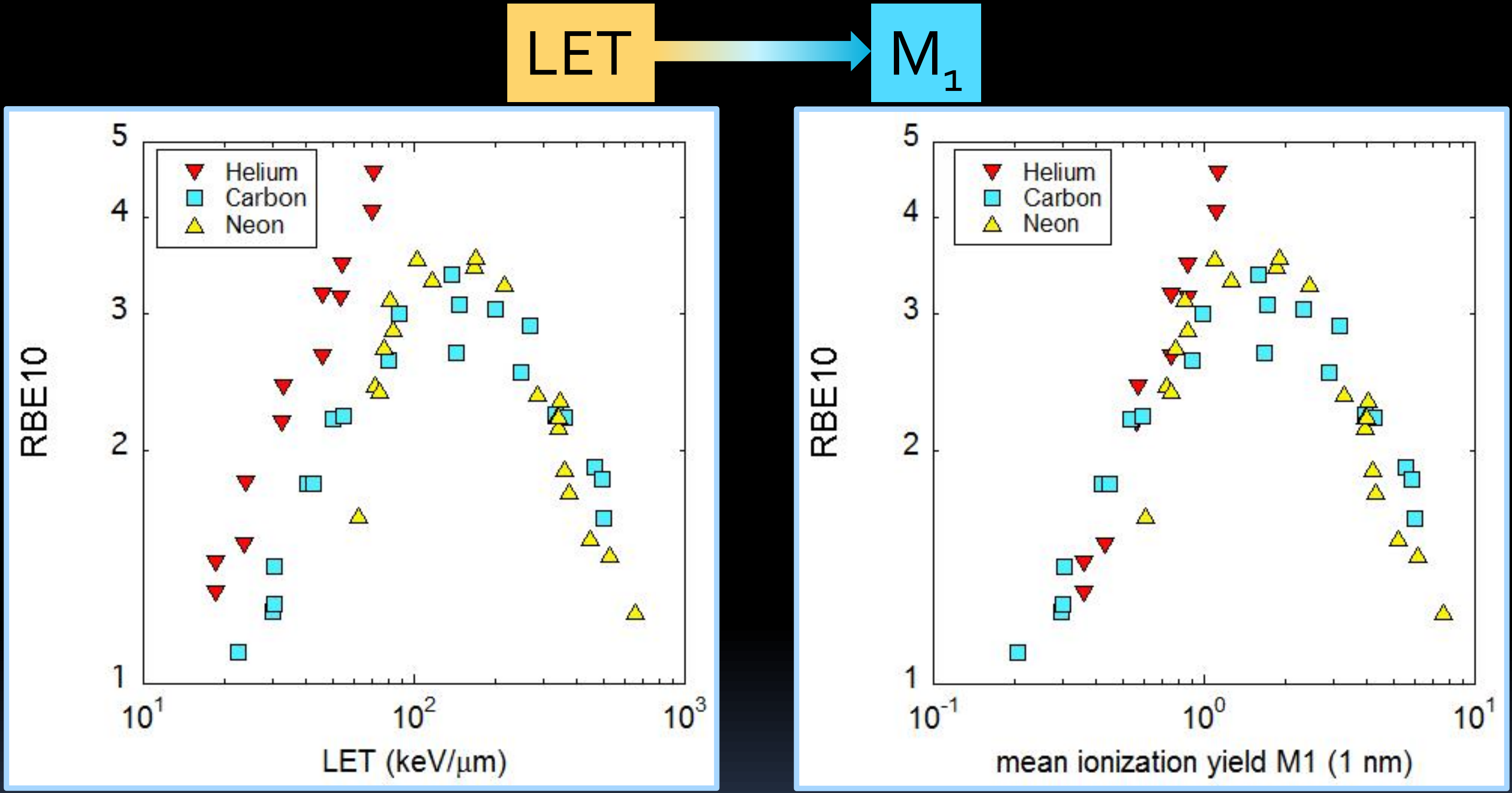
K

ionization density

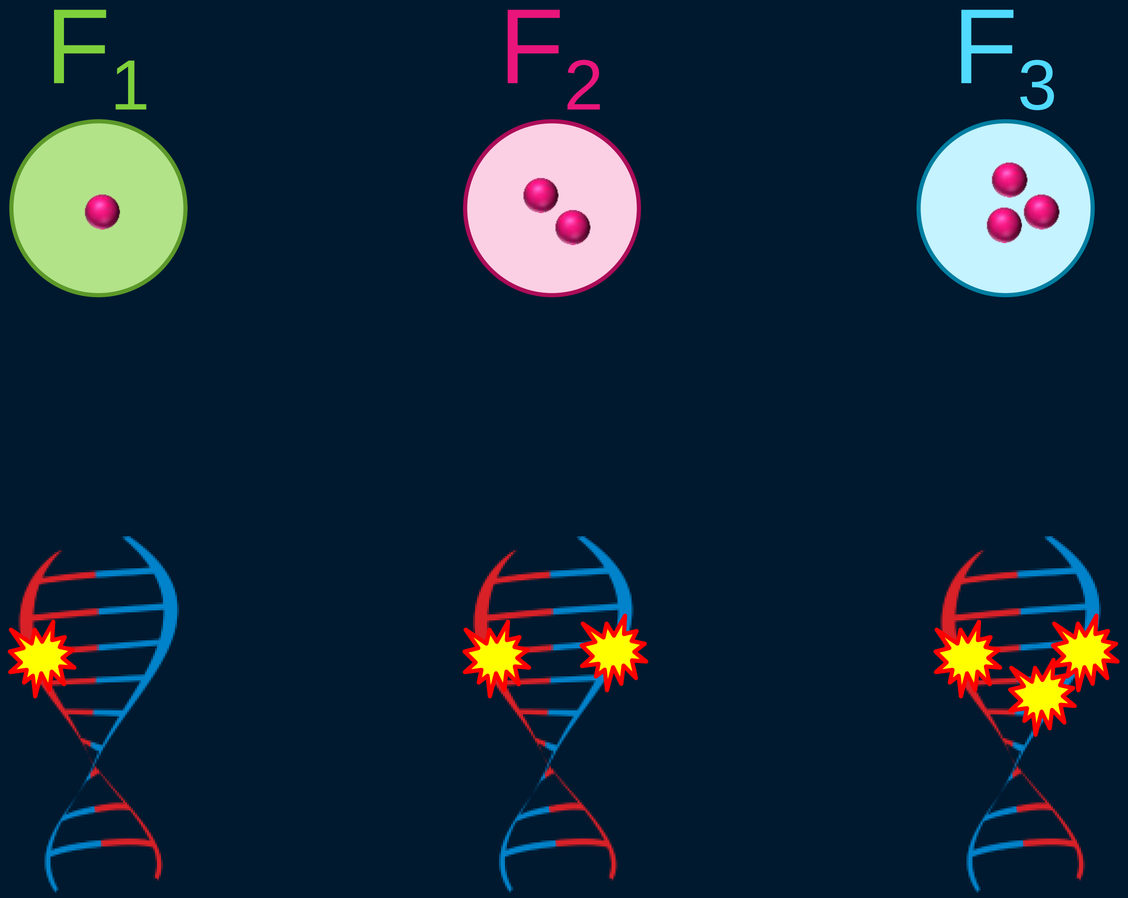
NANODOSIMETRY

"watching is not enough...you need to look with eyes that want to see, that believe in what they see" Galileo Galilei

INACTIVATION OF HSG CELLS



Inactivation of aerobic and hypoxic cells from three different cell lines by accelerated (3)He-, (12)C- and (20)Ne-ion beams.
Furusawa Y, Fukutsu K, Aoki M, Itsukaichi H, Eguchi-Kasai K, Ohara H, Yatagai F, Kanai T, Ando K.
Radiat Res. 2000 Nov;154(5):485-96.

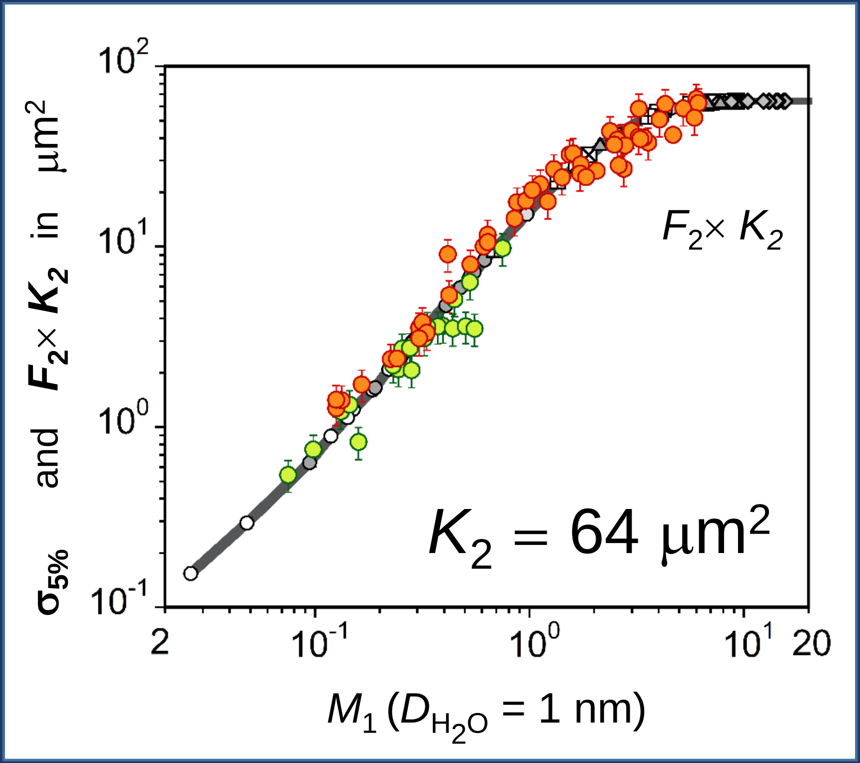

F_1
F_2
F_3

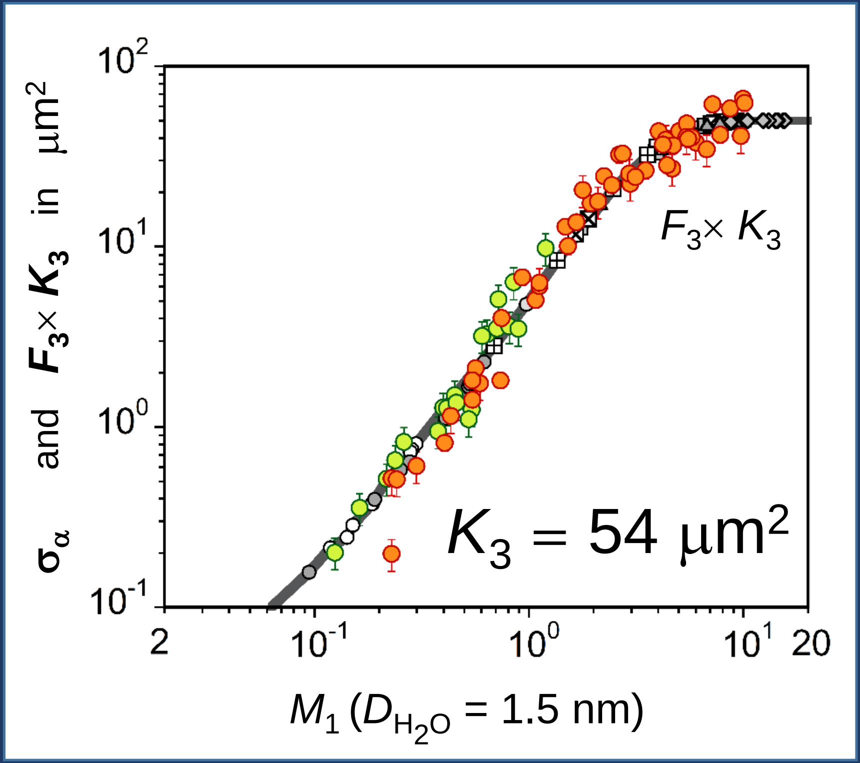
THE LINK TO RADIOBIOLOGY: RADIORESISTANT CELLS

V79: HIGH REPAIR CAPACITY

Inactivation cross sections at high doses
5% survival

Inactivation cross sections al low doses
1% survival



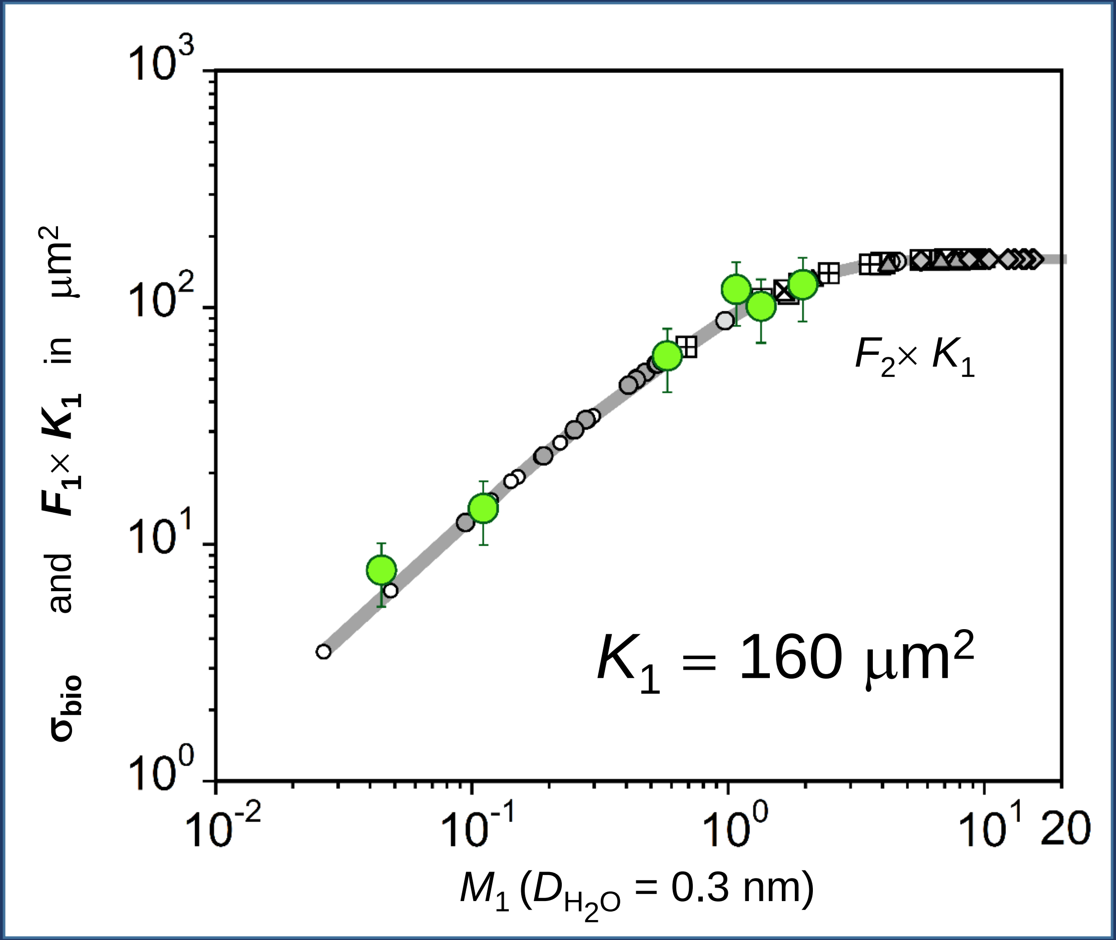


F_2 → simple DSB → $\sigma_{5\%}$

F_3 → complex DSB → σ_{α}

XRS5 CELLS irradiated by 12C ions

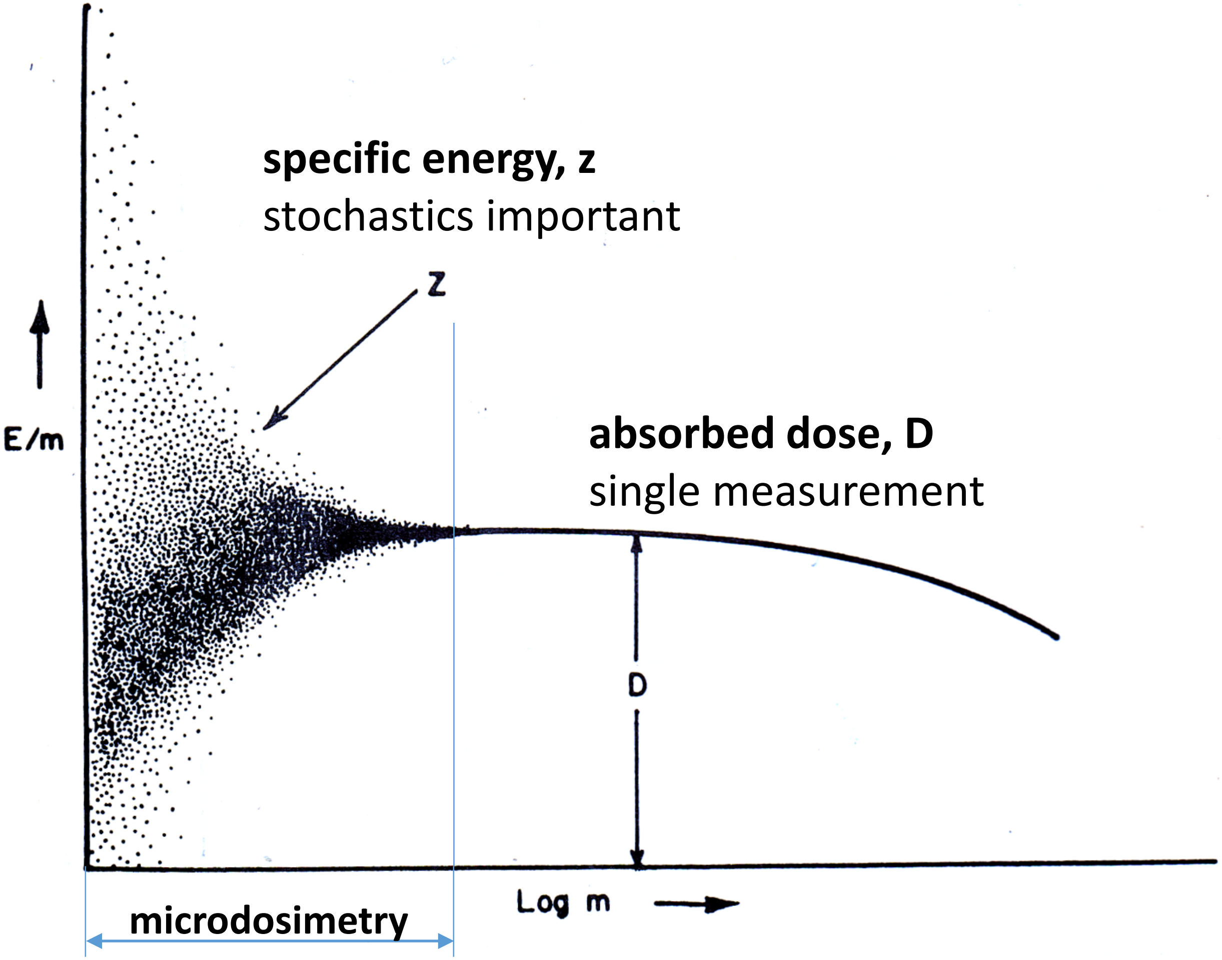
XRS5: LOW REPAIR CAPACITY



F_1 → SSB

MICRODOSIMETRY

Purpose: not the **unlimited** generation of data but their deliberate **reduction** to the most **essential parameters**



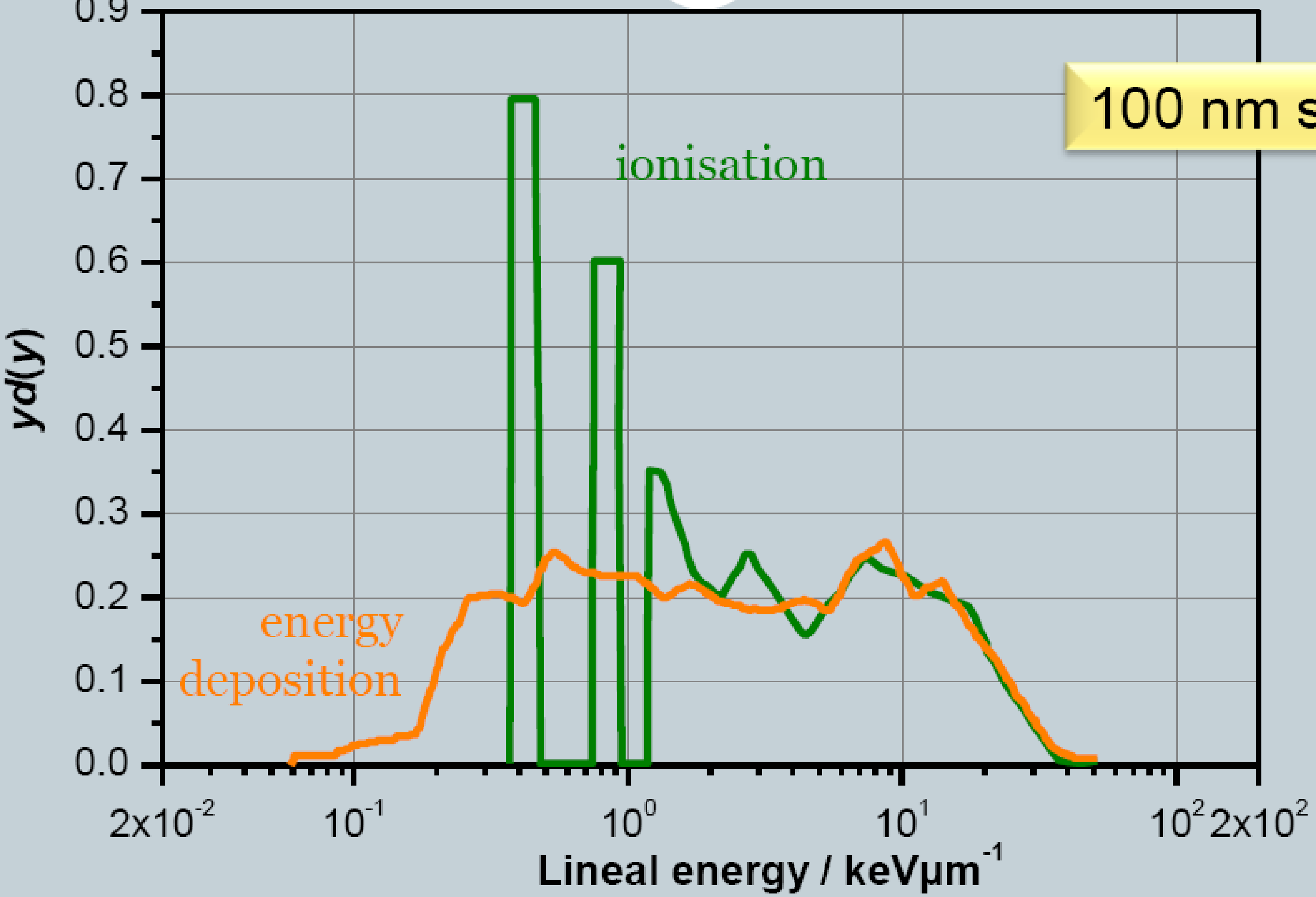
specific energy, z
stochastics important

absorbed dose, D
single measurement

microdosimetry

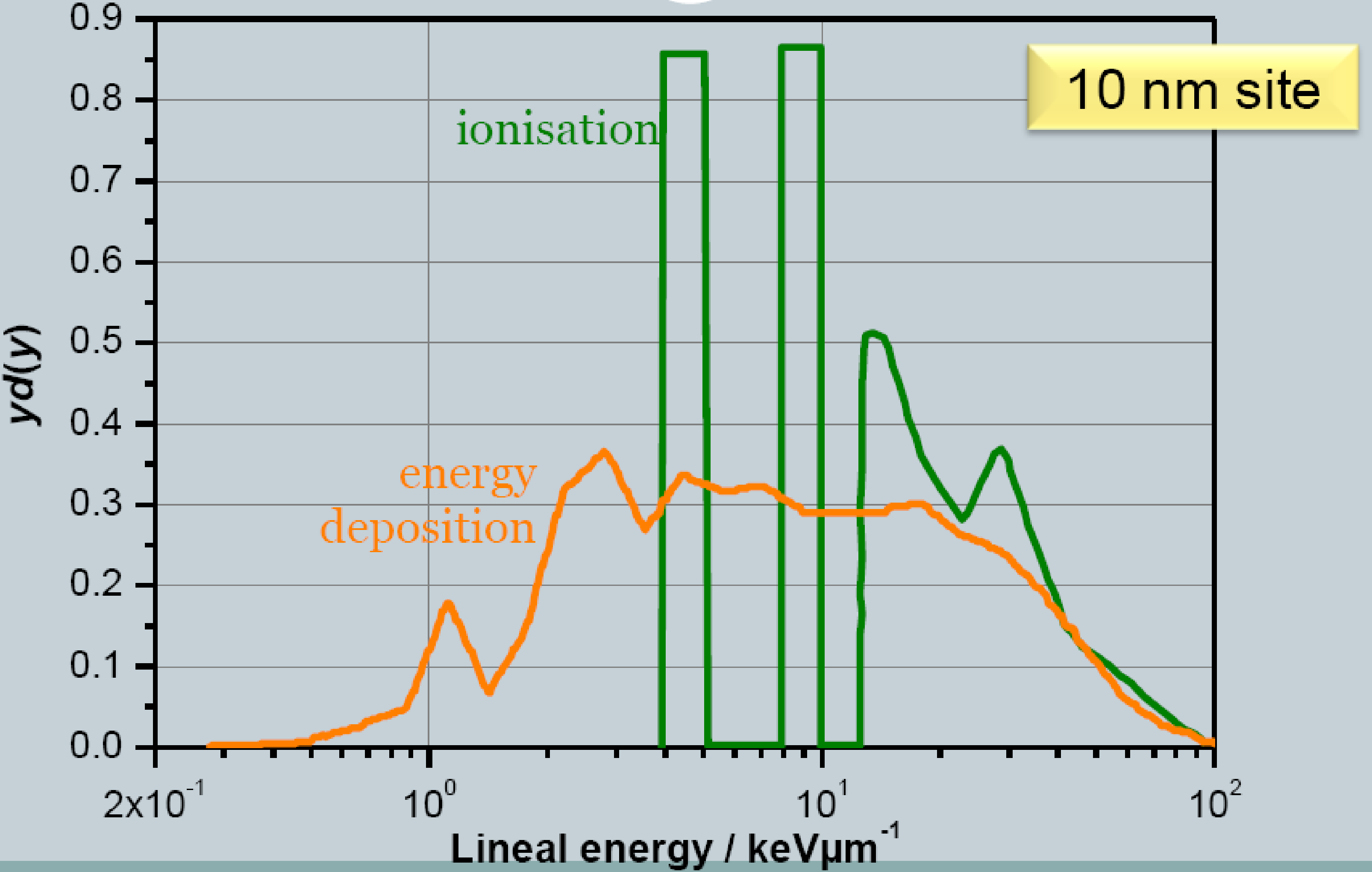
FIG. 1. Energy density as a function of the mass for which energy density is determined. The horizontal line covers the region in which the absorbed dose can be established in a single measurement. The shaded portion represents the range where statistical fluctuations are important.

Microdosimetry in sub-micrometer dimensions?



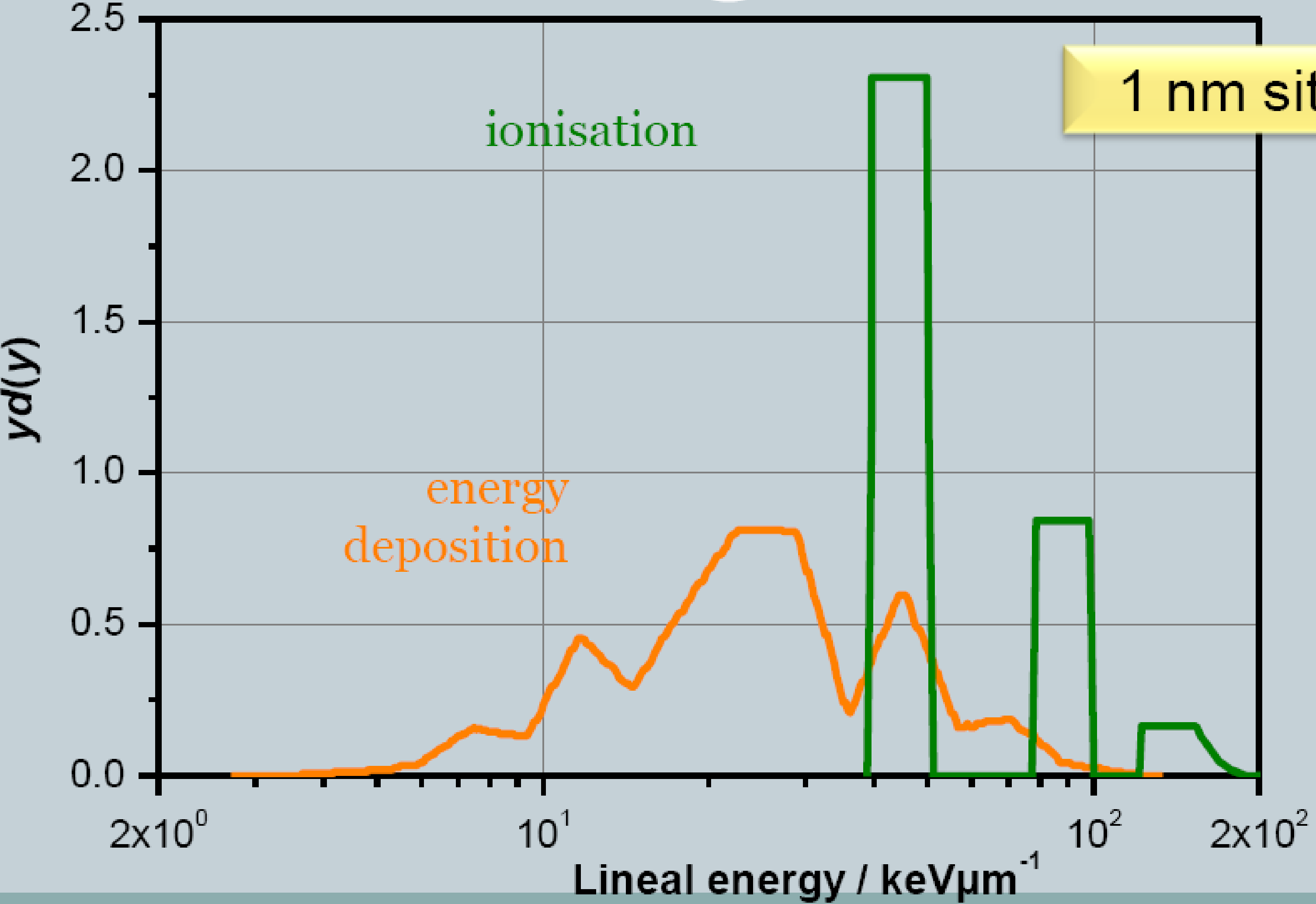
H.I. Amols et al., *RPD 31 (1990)*

Microdosimetry in sub-micrometer dimensions?



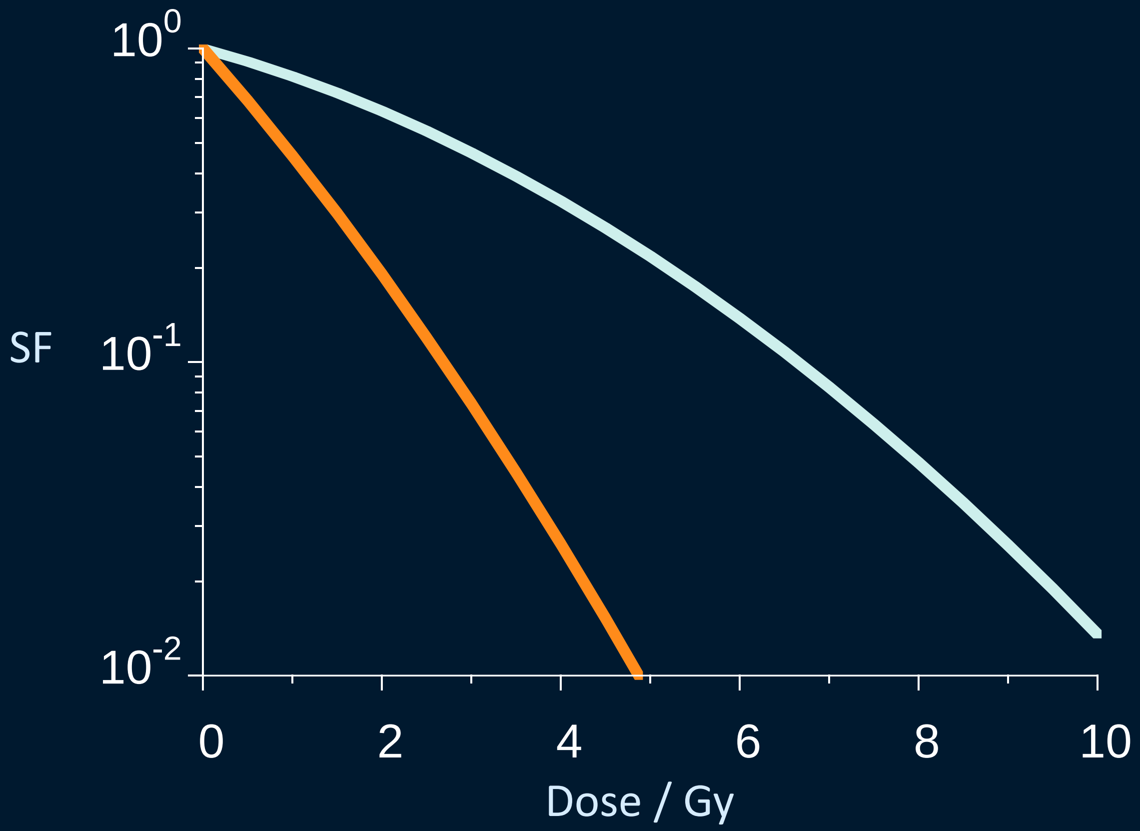
H.I. Amols et al., *RPD 31 (1990)*

Microdosimetry in sub-micrometer dimensions?



H.I. Amols et al., *RPD 31 (1990)*

FROM PHYSICS TO RADIOBIOLOGY

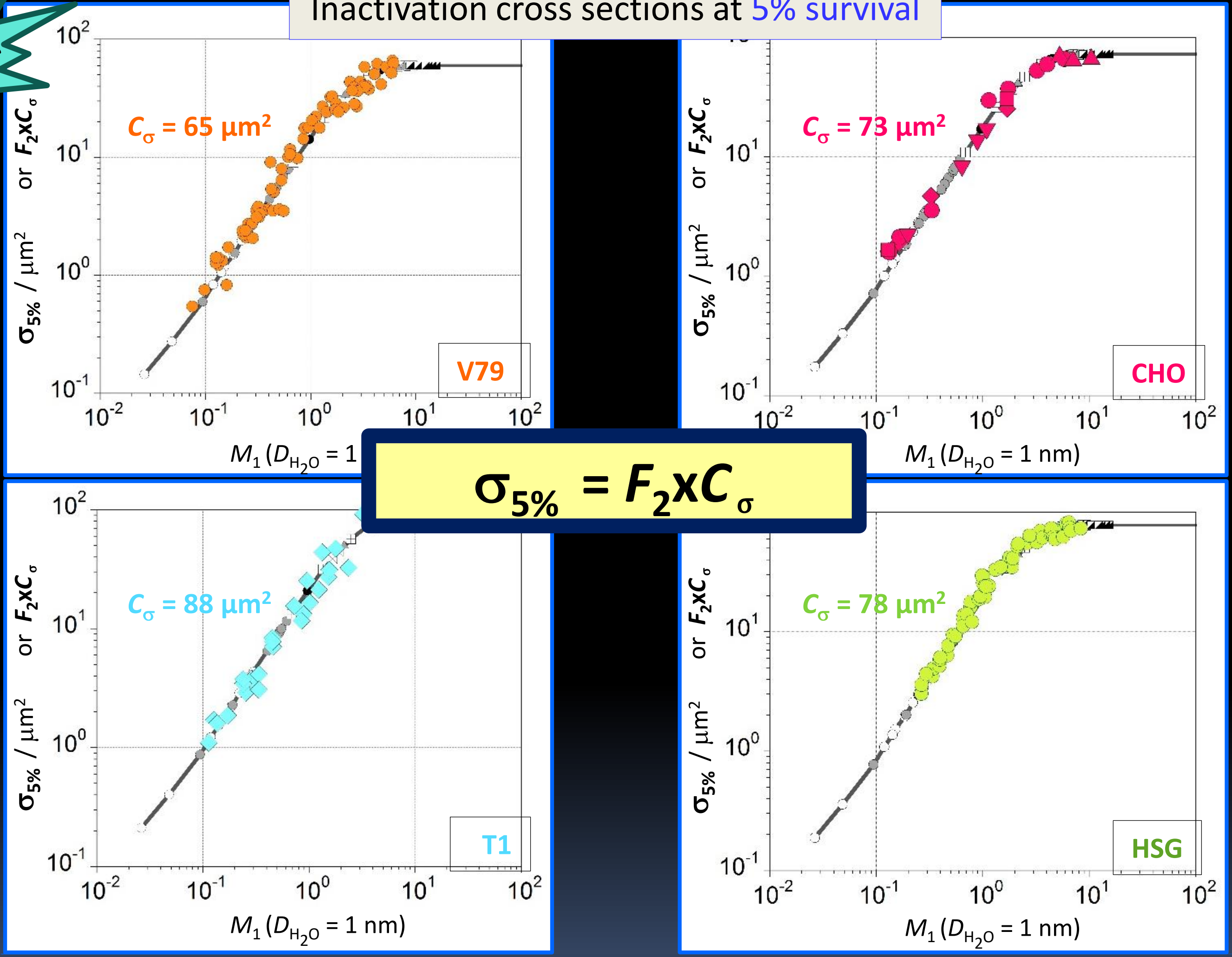


INACTIVATION CROSS SECTIONS

$$\sigma_X = \left(D_X / \Phi_X\right) \times \sqrt{\alpha^2 - 4\beta \ln(X)}$$

Inactivation cross sections at 5% survival

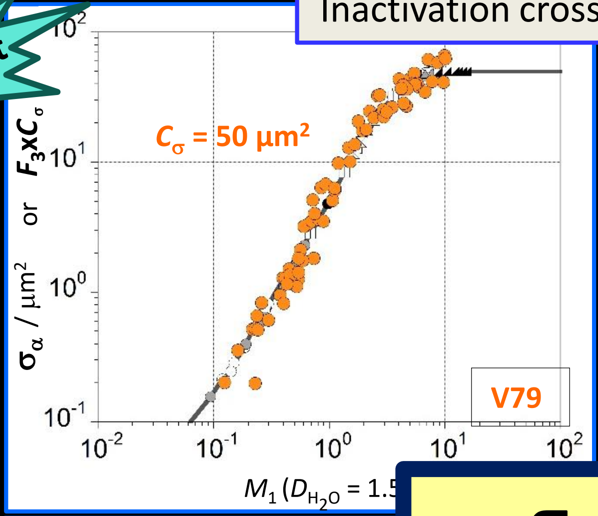
radioresistant

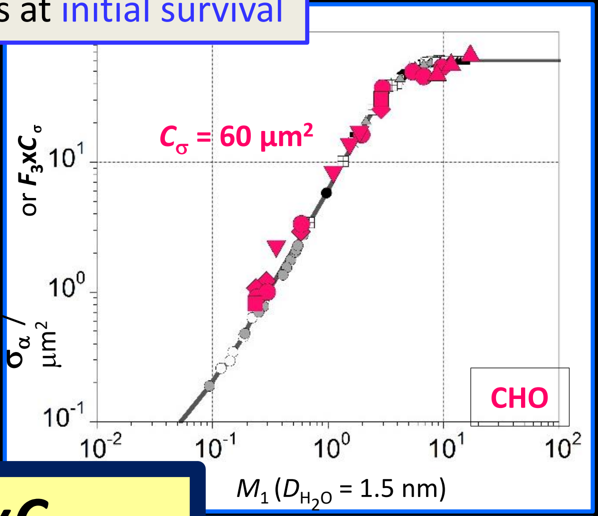


$$\sigma_{5\%} = F_2 x C_\sigma$$

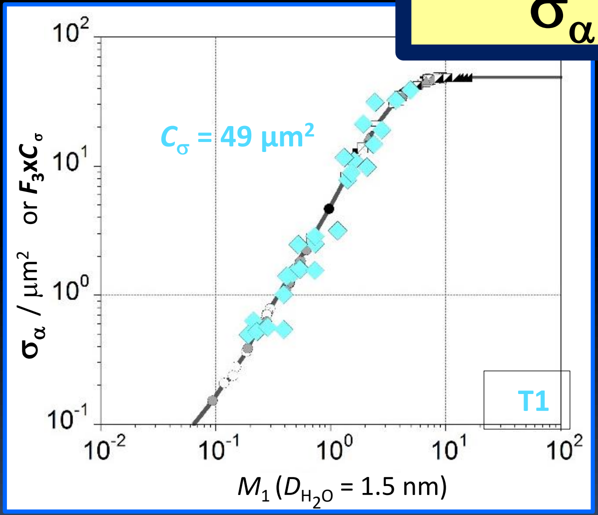
Inactivation cross sections at initial survival

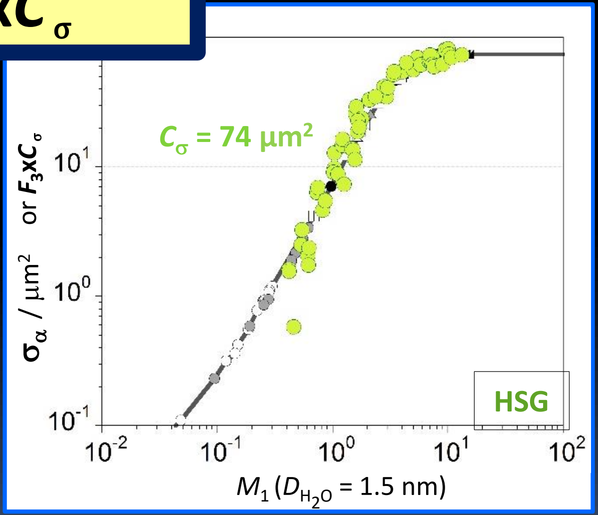
radioresistant





$$\sigma_\alpha = F_3 x C_\sigma$$





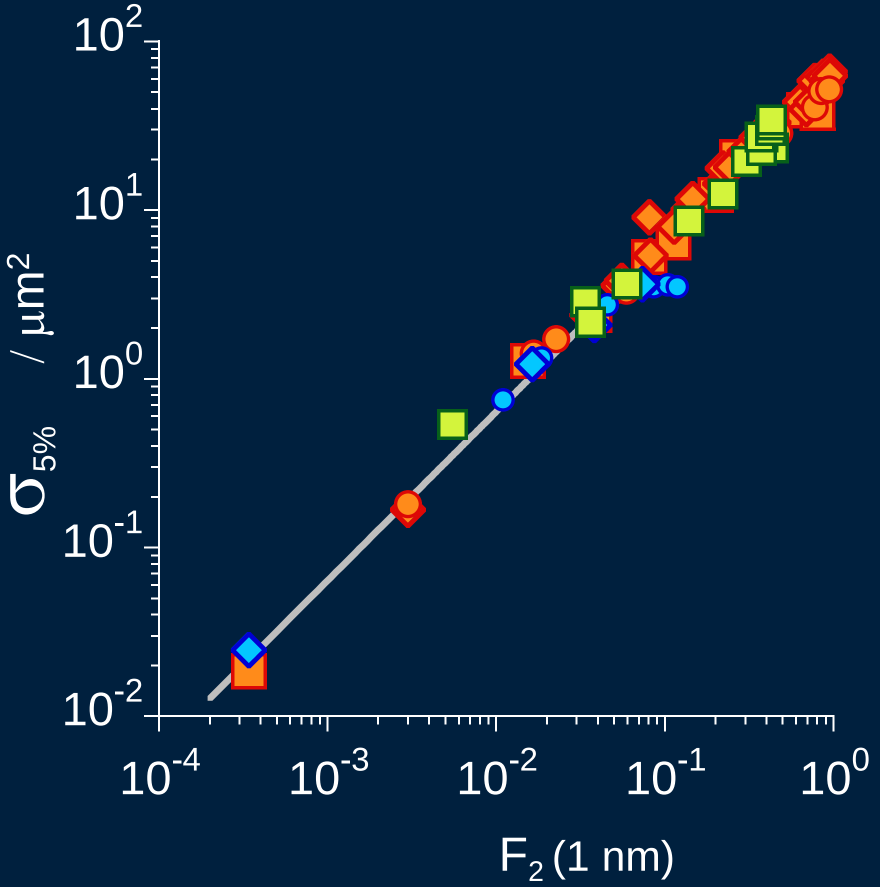
V79 CELLS

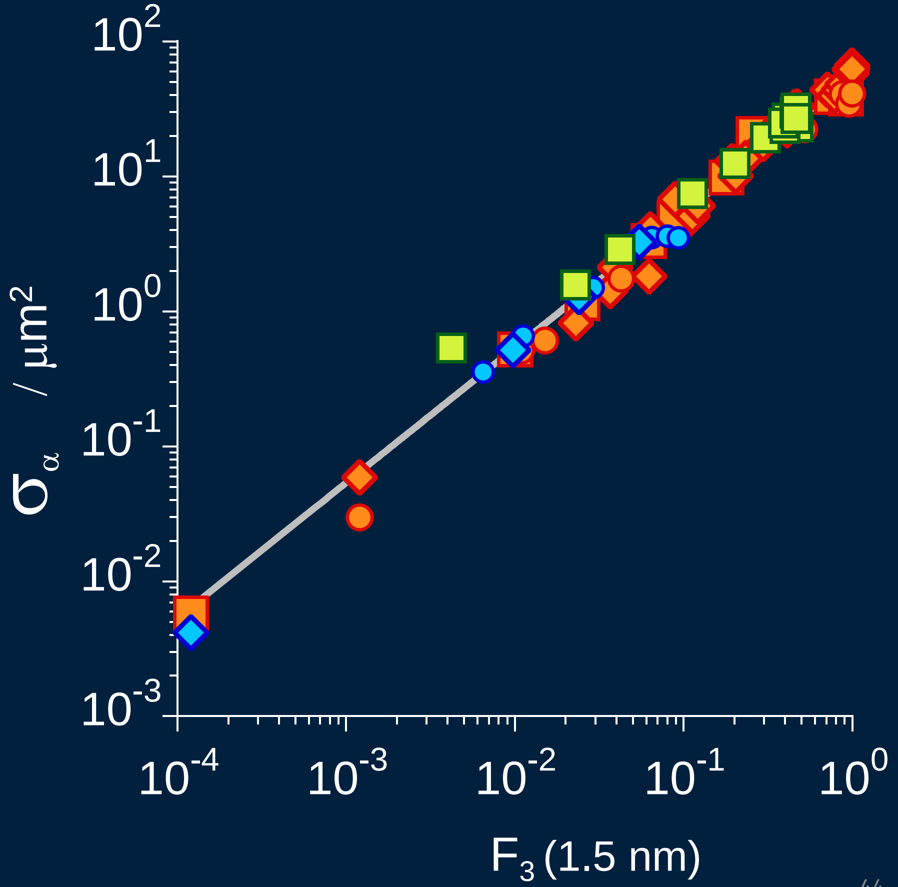
$$\sigma_{5\%} = K_2 \times F_2$$

$$K_2 = 64\ \mu m^2$$

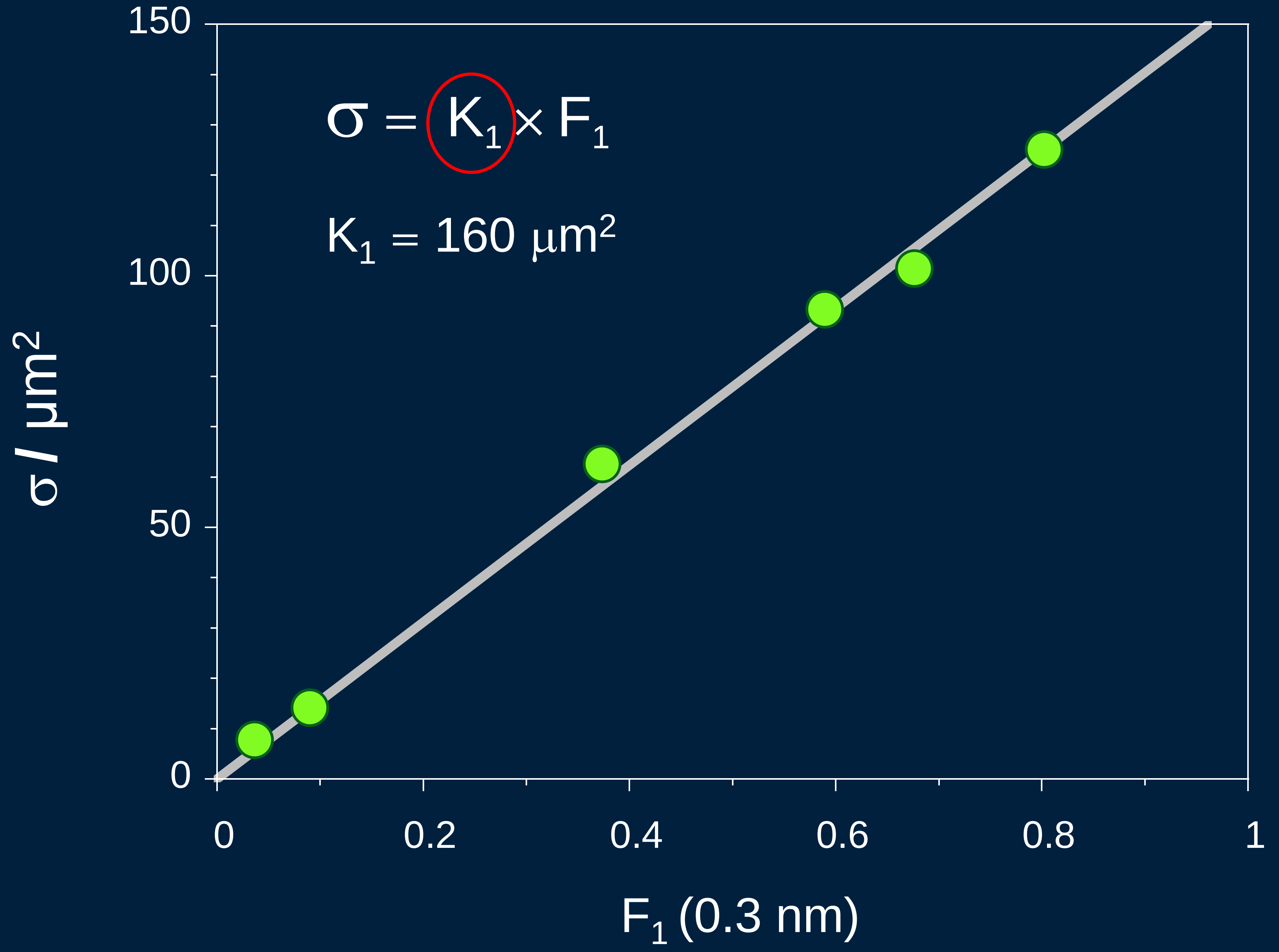
$$\sigma_{\alpha} = K_3 \times F_3$$

$$K_3 = 54\ \mu m^2$$





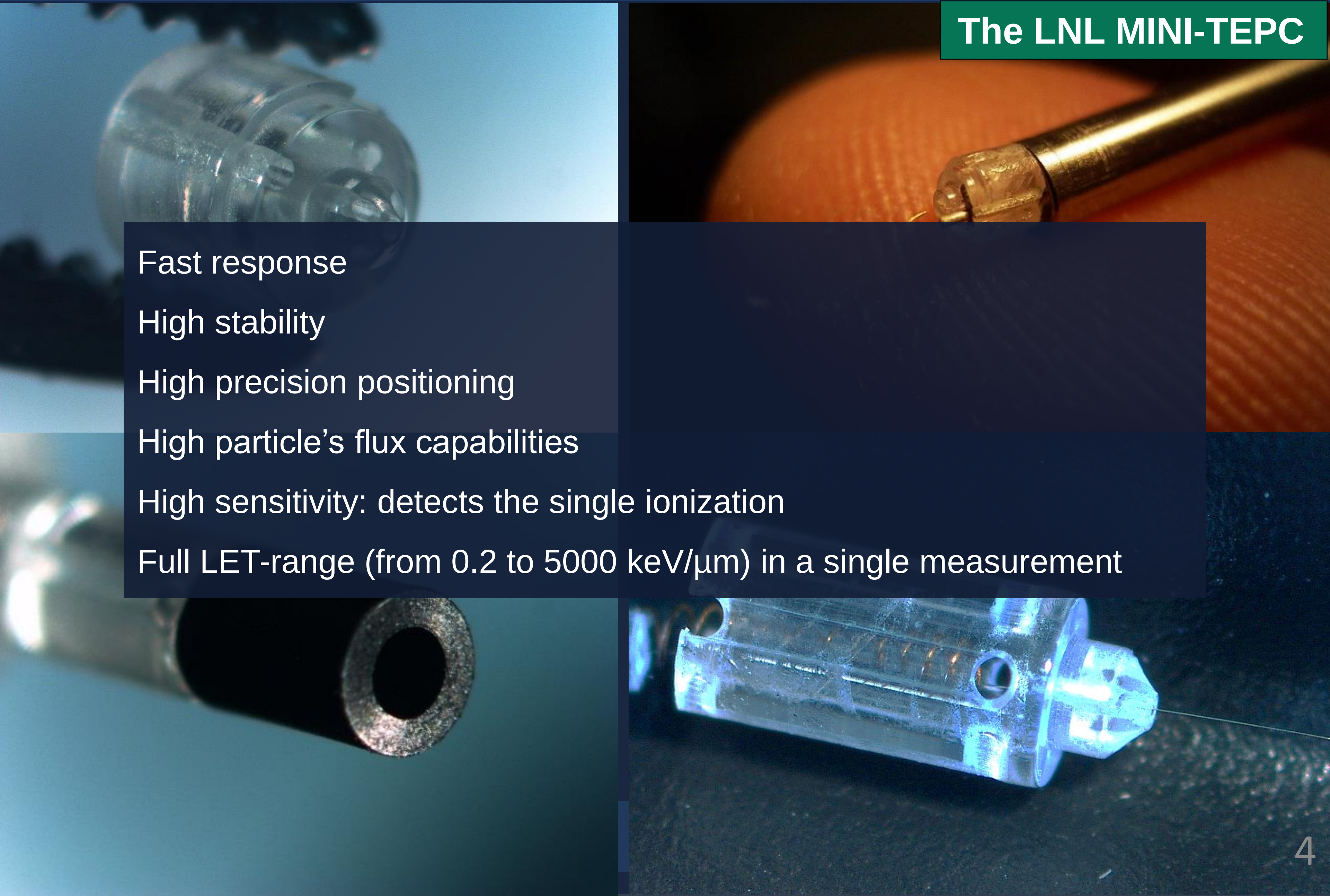
XRS5 CELLS



$$\sigma = K_1 \times F_1$$

$K_1 = 160\ \mu m^2$

MINI-TEPC FOR HIGH INTENSITY BEAMS



The LNL MINI-TEPC

Fast response

High stability

High precision positioning

High particle’s flux capabilities

High sensitivity: detects the single ionization

Full LET-range (from 0.2 to 5000 keV/µm) in a single measurement