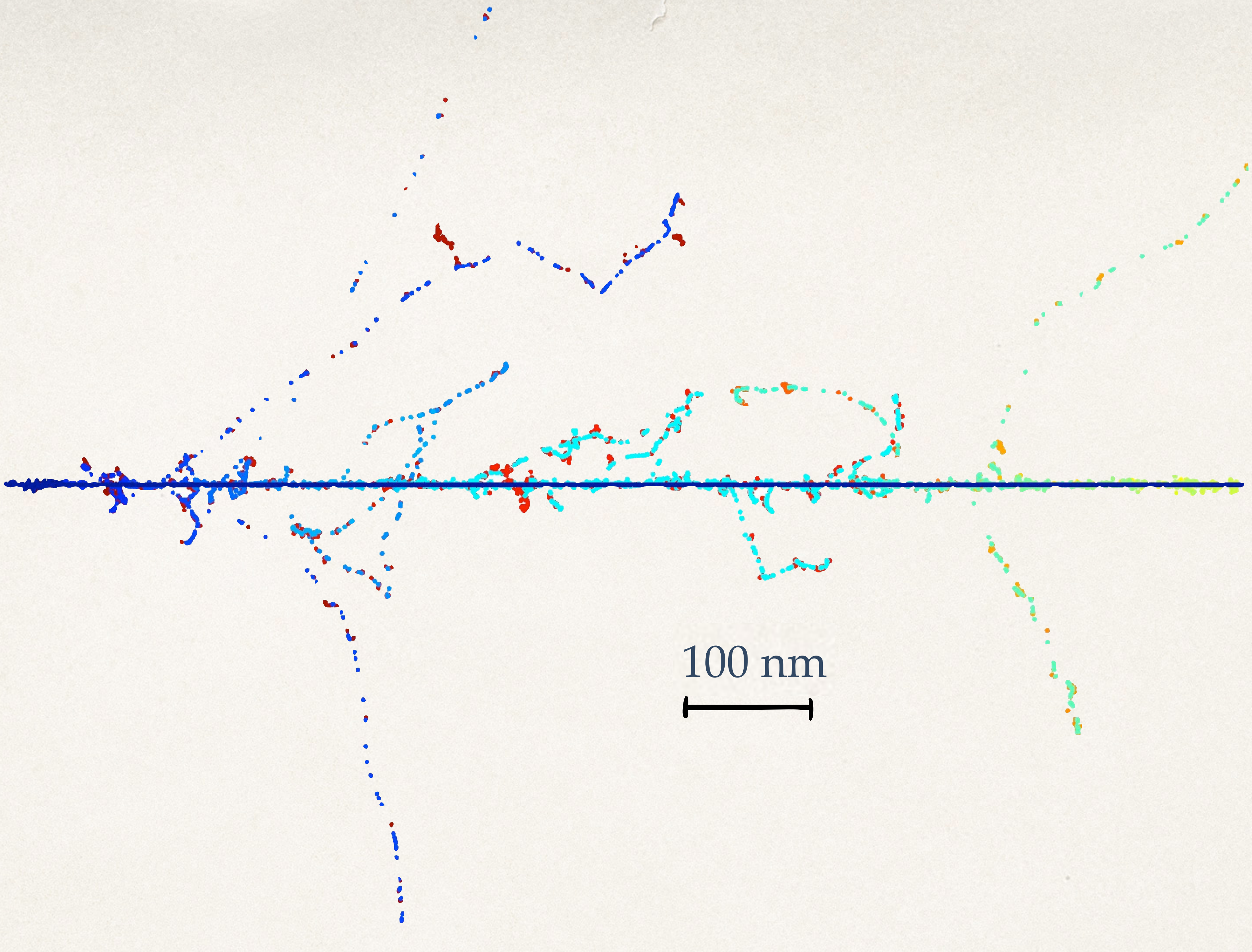


Micro-dosimetry of High-LET particles

Jorge Miguel Sampaio

First joint Workshop IGFAE / LIP , Universidade do Minho, Braga (4 de Maio, 2018)

Dosimetry

Dosimetry: is the theoretical and experimental investigation of the mean imparted-energy in a point of an arbitrarily small macroscopic volume.

- **Linear energy transfer (LET):** is the mean energy loss by charged particles owing to collisions with electrons that is the electronic stopping power

$$L = -\left(\frac{dE}{dx}\right)_e$$

- **Absorbed dose**: is the mean value of the energy imparted by ionising radiation to a volume of interest divided by the mass of that volume

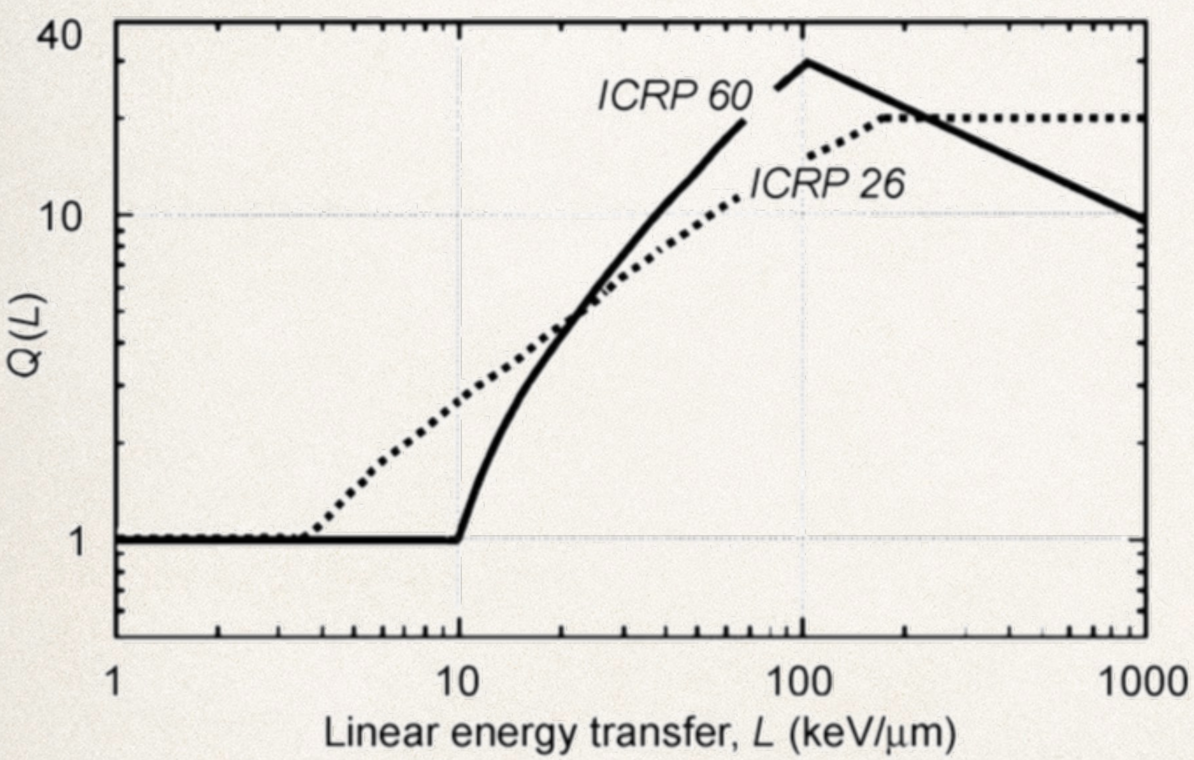
$$D = \frac{d\bar{\epsilon}}{dm}$$

S.I. unit "gray" (Gy)

Assessing radiation risks

At low doses and low dose rates, the stochastic effects are proportional to the absorbed dose (linear-non-threshold (LNT) model).

- **Dose equivalent:** $$H = \int Q(L) \frac{dD}{dL} dL$$ S.I. unit "sievert" (Sv)



ICRP Report 26, 1977
ICRP Report 60, 1991

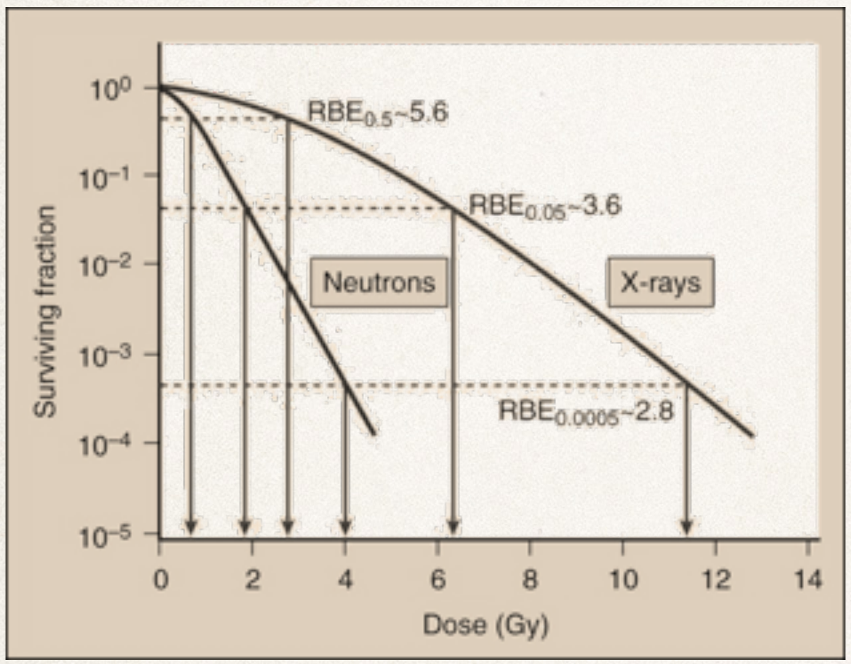
The quality factor Q accounts for the stochastic biological effects, it depends on the particle species and energy through the LET

$$L \sim Z^2/\beta^2$$

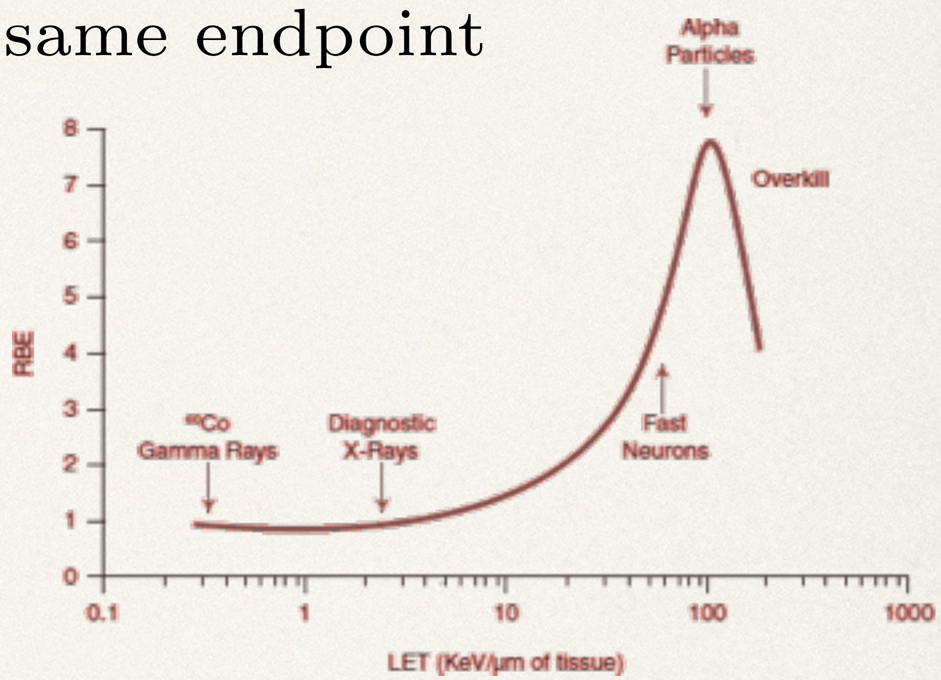
However it does not take into account the different track structures of HZE and LZE particles with the same LET.

Relative biological effectiveness (RBE)

- **RBE:** ratio of a dose of a low-LET reference radiation to a dose of radiation considered that gives an identical biological effect



$$RBE = \frac{D_X}{D_p}\Big|_{\text{same endpoint}}$$



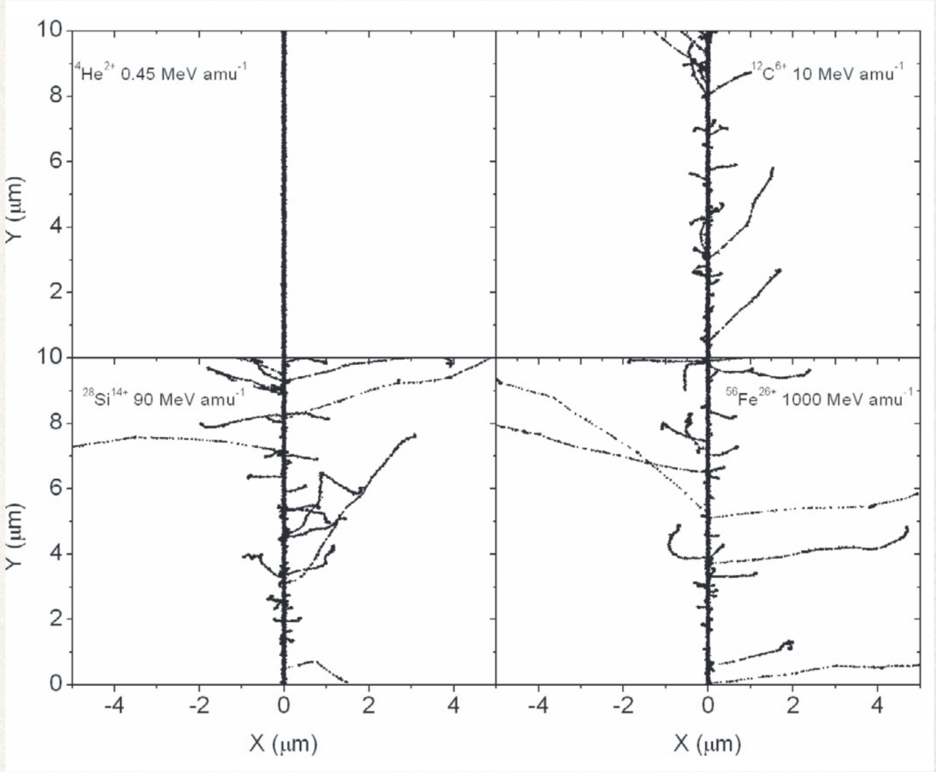
$$\left.\begin{array}{lr} RBE_M = RBE(D) & D \to 0 \\ RBE_M = RBE(D) * DDREF & D \gg 0 \end{array}\right\} \longrightarrow Q$$

ICRP Report 92, 2003

Factors affecting the RBE and Q

- **Source location:** the characteristics of the incident radiation are changed as it passes through deep tissues in the body or materials (ex: neutrons).

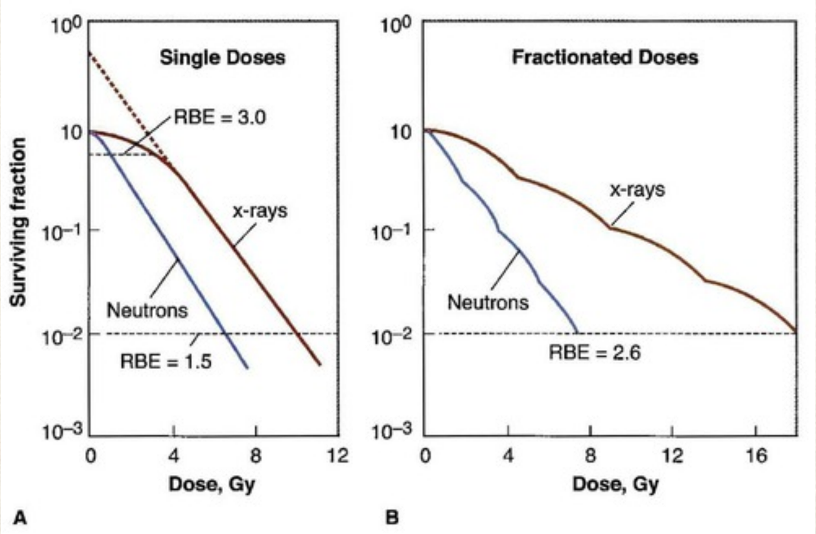
L=150 keV/μm



Plante and Cucinotta, J. Phys. 10, 2008

- **Track structures:** HZE particles produce more energetic δ rays than LZE particles for the same LET.

- **Dose fractioning:** several irradiations with small doses renders a larger RBE than a single irradiation with high dose.



- **Cell type and biological endpoint:** how is the cell death defined?

Q-factor for space missions

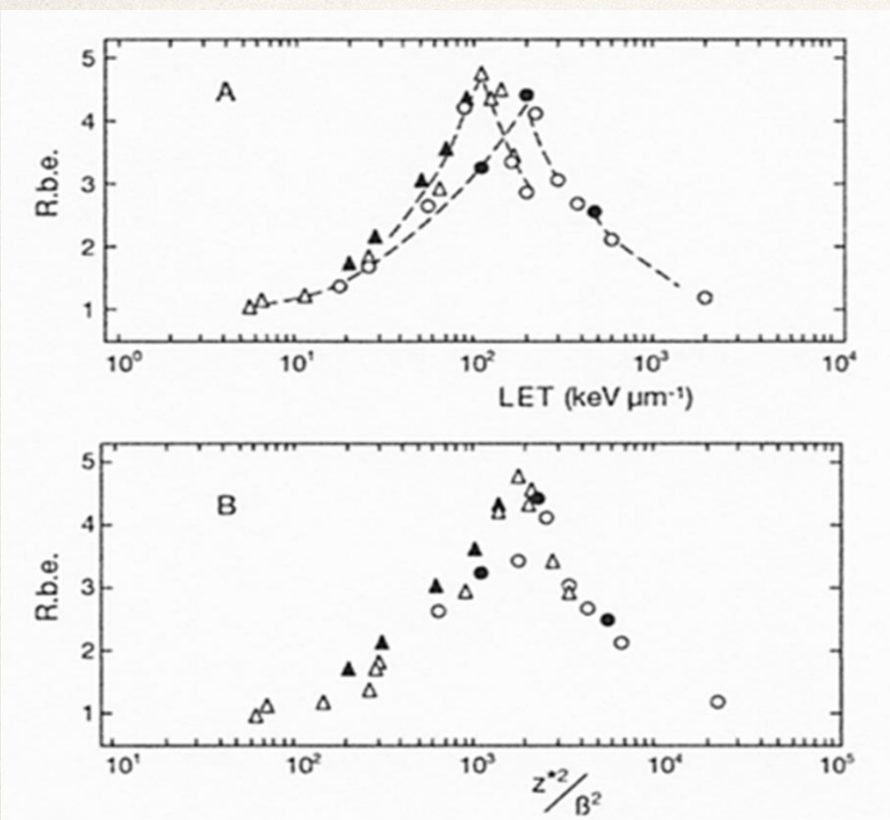
NASA approach (Cucinnotta et al. NASA/TP-2011-216155, 2011)**:**

- Different parameters for solid cancers and leukemia.
- $Q_{NASA} \sim Z^{\star}/\beta$

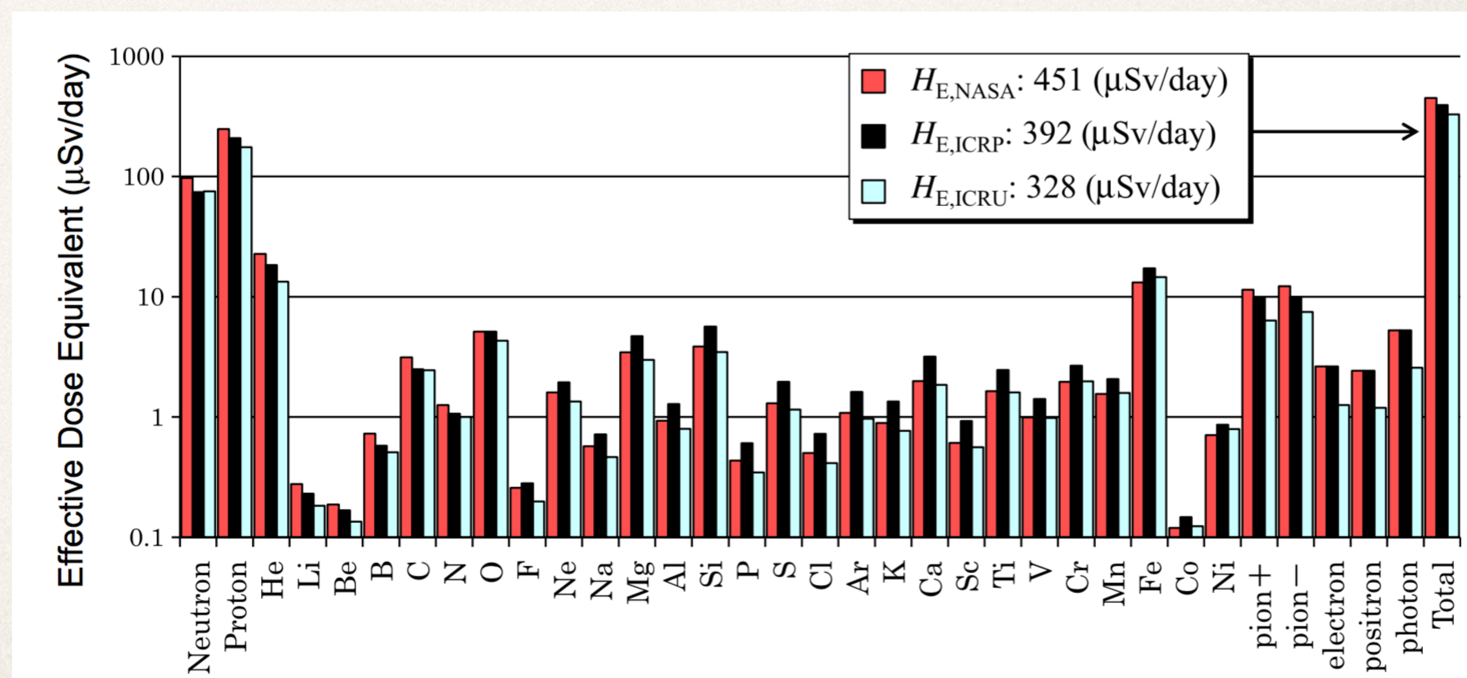
Ion effective charge

$$Z^{\star} = Z\left[1 - \exp(-125 Z^{-2/3}\beta)\right]$$

Cell survival RBEs for V79 cells and human T1 cells



Male astronauts inside de ISS



Sato et al. Adv. Space. Rad. 52, 2013

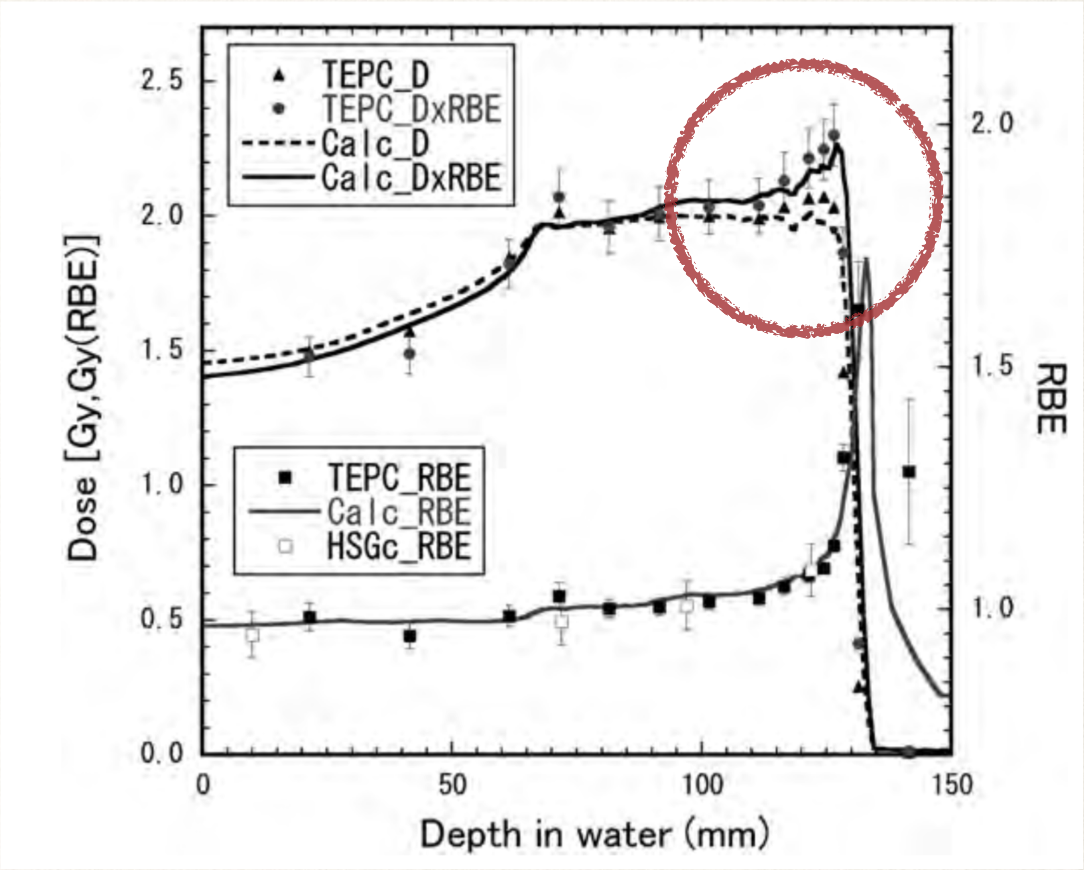
RBE for proton therapy QA

In vivo data and clinical experience support the use of an average RBE=1.1 at the SOBP.

Factors affecting the proton RBE:

- **LET:** distal RBE and range increase
- **Tissue type:** RBE seems to be higher to late responding (healthy) tissue
- **Dose:** RBE increases with decreasing dose but the effect seems to be small for in vivo.

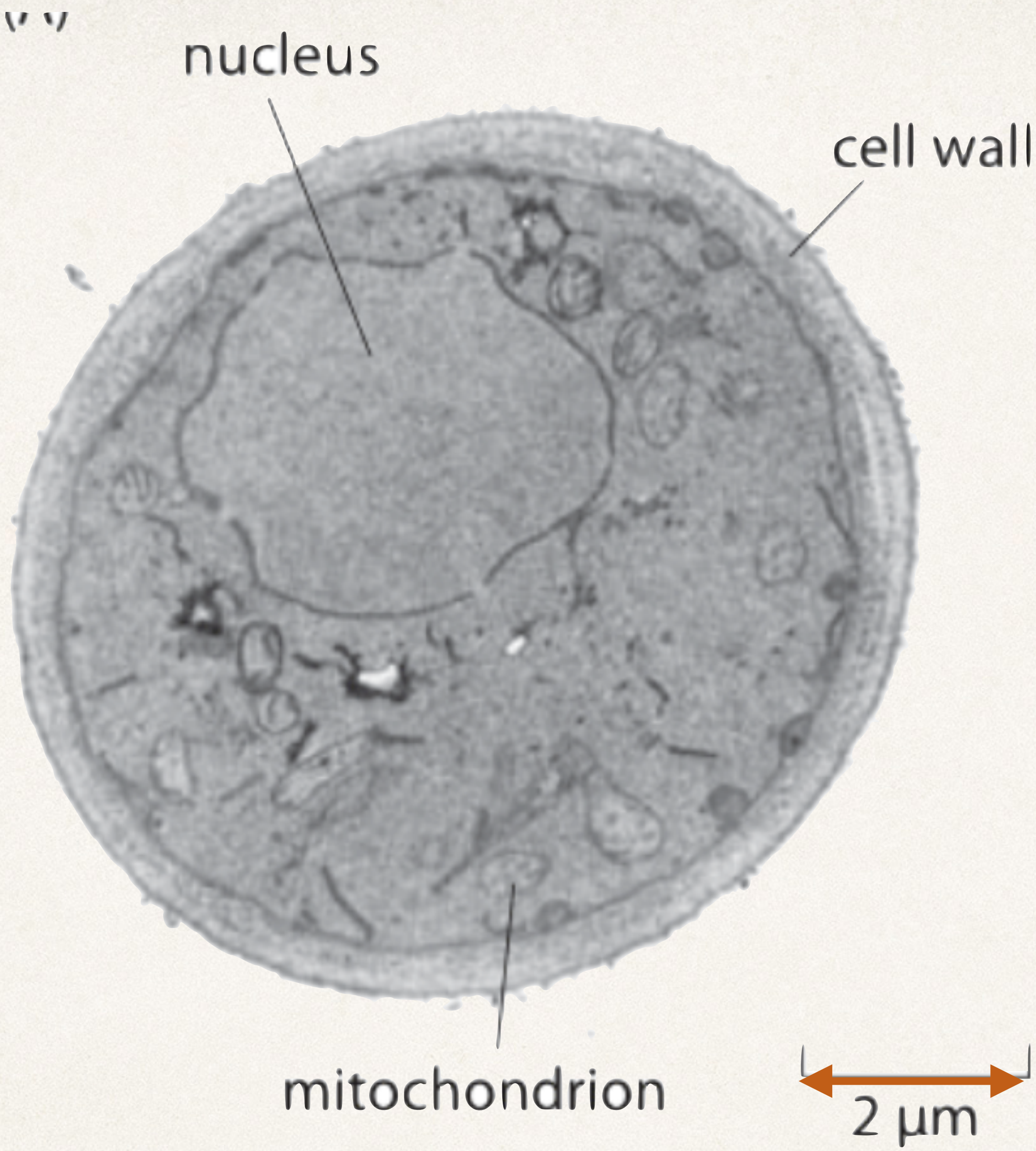
155-MeV proton beam with the 6-cm nominal SOBP width



Kato et al., J. Radiat. Res. 54, 2013

$$RBE[L, D, (\alpha/\beta)_x] = \frac{1}{D}\left[\sqrt{\frac{1}{4}(\alpha/\beta)_x^2 + (\alpha/\beta)_x \frac{\alpha(L)}{\alpha_x} D + \frac{\beta(L)}{\beta_x} D^2)} - \frac{1}{2}(\alpha/\beta)_x\right]$$

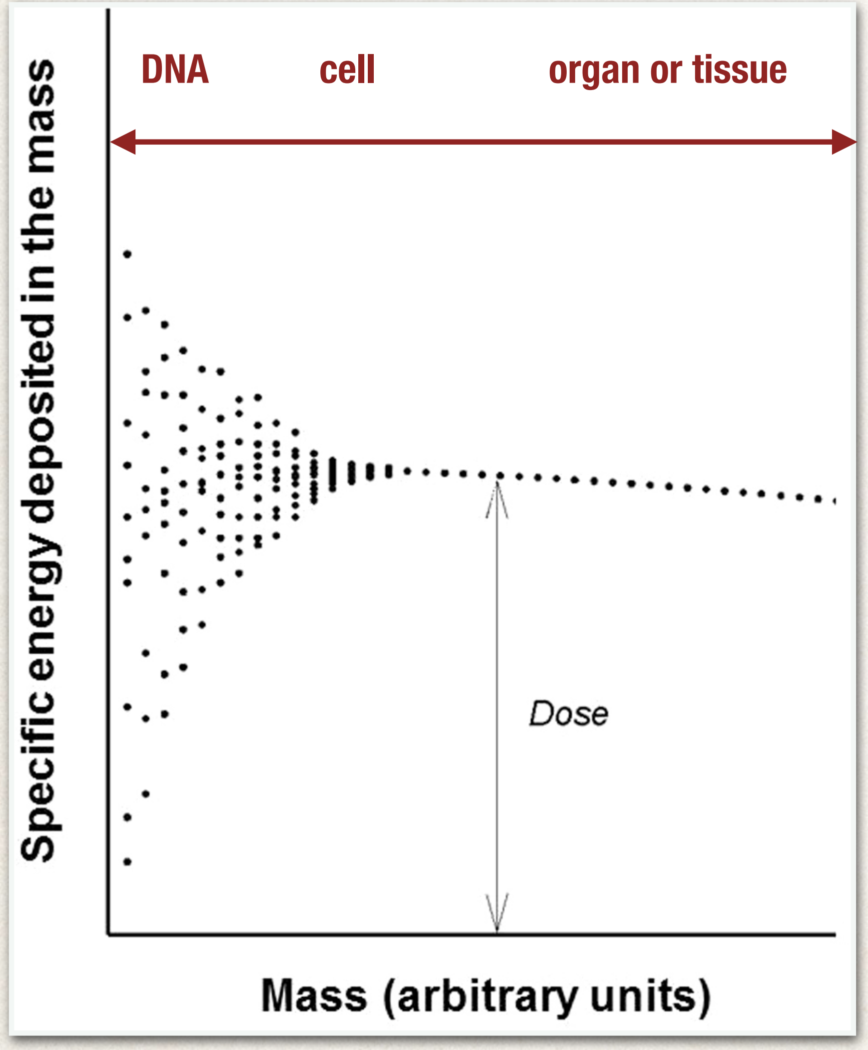
Paganetti, Phys. Med. Biol. 59, 2014


nucleus
cell wall
mitochondrion
2 μm


2 nm
3.4 nm

Micro-dosimetry

Microdosimetry: is the theoretical and experimental investigation of imparted-energy probability distributions in a volume of matter that is crossed by a single ionising particle.



Stochastic	Average	Macroscopic
Lineal energy $y = \dfrac{\varepsilon}{l}$	Frequency-mean lineal energy $\bar{y} = \int_0^\infty y f(y) dy$	LET $L = -\left(\dfrac{dE}{dx}\right)_e$
Specific energy $z = \dfrac{\varepsilon}{m}$	Frequency-mean specific energy $\bar{z} = \int_0^\infty z f(z) dz$	Absorbed dose $D = \dfrac{\bar{\epsilon}}{m} = \bar{\nu}\bar{z}_1$

$l = 4V/S$ is the mean chord length of a convex volume V

$f(y), f(z)$ multi-event distributions

number of “hits” single-event!

The ideal micro-dosimeter

Measuring doses at the (sub)cell scale requires detectors that ideally have:

- **Excellent spatial resolution:** order of the micrometer
- **Well defined sensitive volume:** to know the mean-chord length
- **Minimal wall effects:** similar scattering properties in the wall and SV
- **Tissue-equivalence:** walls and SV with compositions similar to tissues
- **Should have a low threshold:** < 1 keV/ μm (low noise)
- **Radiation resistant**, operate at low potentials, compact and low cost.

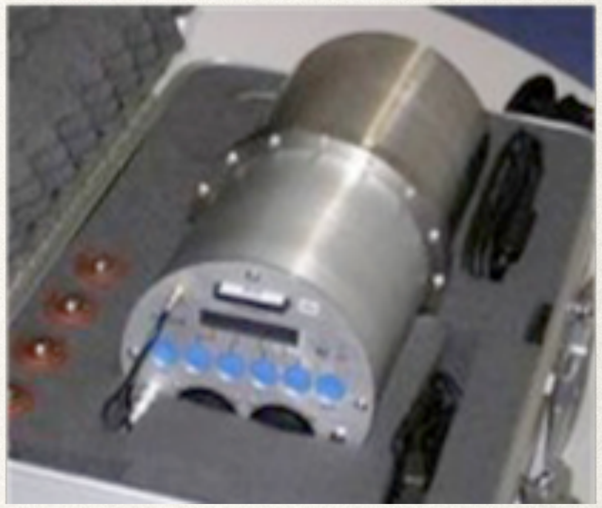
Tissue-equivalent proportional counters (TEPC)

The TEPC is based on the idea that the energy deposited in a gas filled cavity equals the energy imparted in a cell.

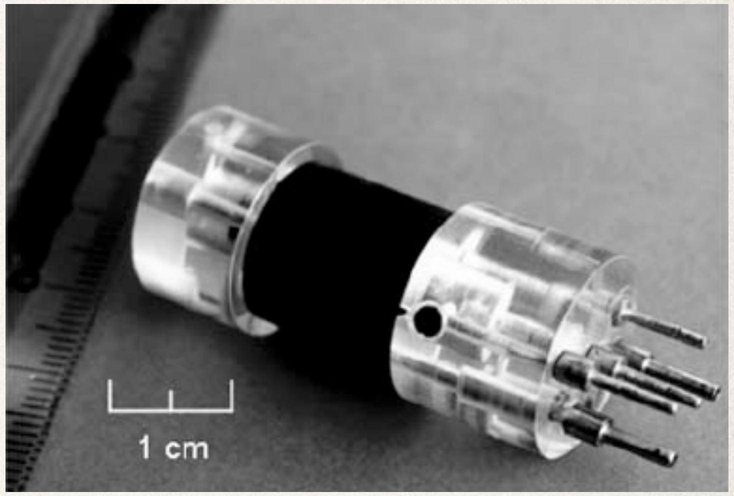
$$\bar{\epsilon} = -\Delta x_g \frac{1}{\rho_g} \left(\frac{dE}{dx} \right)_g \rho_g = -\Delta x_T \frac{1}{\rho_T} \left(\frac{dE}{dx} \right)_T \rho_T$$

- Tissue equivalent gas (methane/propane based)
- Tissue-equivalent plastic walls
- Pressure adjusted to equal the energy loss at the cell scale
- Well-known technology
- Too large to model arrays of cells
- Needs high operating voltages

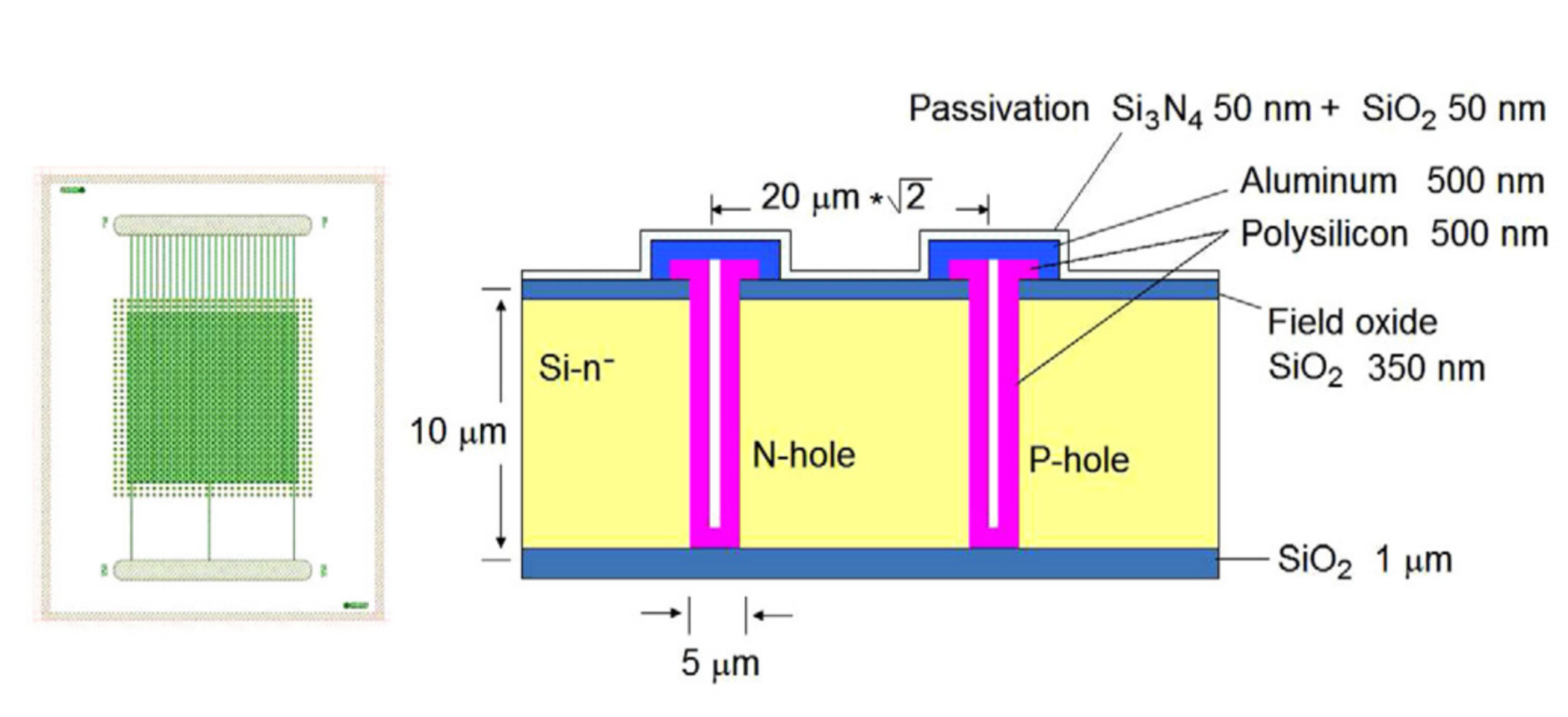
"HAWK" TEPC (NASA)



Sei TEPC (Seisbersdorf lab.)



Si-based micro-dosimeters



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Summary

- Detailed description of the energy deposition at the (sub)cell scale is needed to characterise the biological response of high-LET particles $\Rightarrow$ **Micro-dosimetry**

- This is the case of ion therapy and radiation risk assessment for air-flight crews and human space missions

- More measurements and simulations of micro-dosimetric distributions of high-LET radiation in vivo and different cell types are needed

Outlook

- LIP has a sound experience in simulations using Geant4 and wants to explore the capabilities of the Geant4-DNA extension for health and space applications.

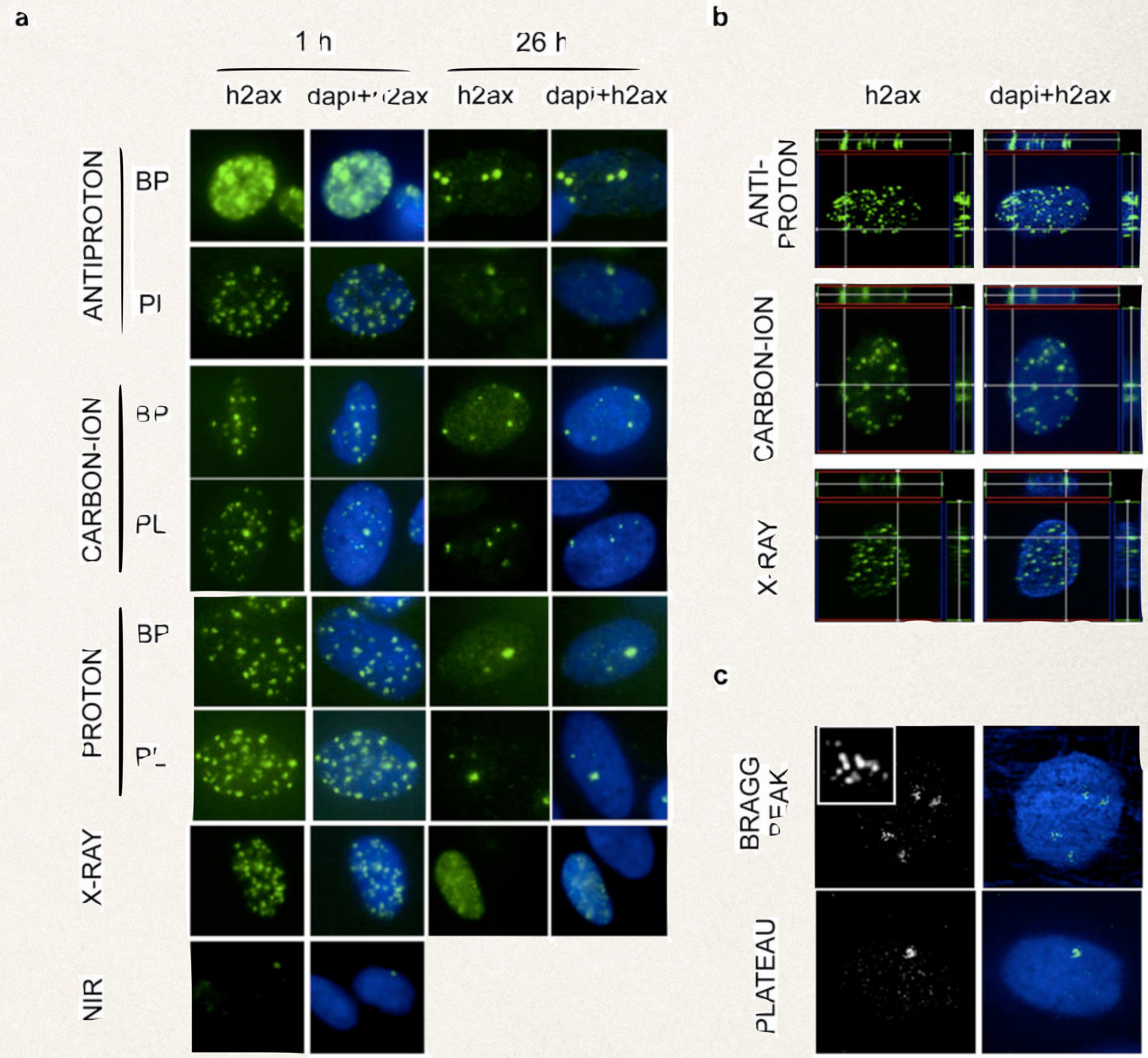
- LIP has a sound experience in the design and development of particle detectors. The development of instruments for micro-dosimetry is an area that intends to pursue (Si-based and using plastic scintillators).

- Collaborations with the biophysics group at GSI/FAIR are planned. A joint project is foreseen to be submitted in 2019/2020 to the GSI-PAC to study shielding designs and materials that minimise the effects of secondary radiation in human space missions.

- The installation of a proton therapy unit in Lisbon in the next years enhances the opportunities for research in the areas of radiobiology and micro-dosimetry. In this context a project is being developed with the radiobiology group at C^2TN.

Thank you!

Initial and residual γ-H2AX foci were observed in charged particle irradiated fibroblasts.



Kavanagh et al, Scientific Reports 3, 2013